UNIVERSITÉ DE STRASBOURG

UNIVERSITÉ DE STRASBOURG

AUGUSTIN COURNOT DOCTORAL SCHOOL

ÉCOLE DOCTORALE AUGUSTIN COURNOT

Bureau d'Économie Théorique et Appliquée, UMR7522

THÈSE présentée par :

Imad ISMAIL

soutenue le : **2 Décembre 2015**

pour obtenir le grade de : **Docteur de l'université de Strasbourg**

Discipline/ Spécialité : **Sciences Économiques**

Evaluation of the socio-economic impact of innovative hybrid surgical techniques:

Methodological developments and application to the IHU Strasbourg

THÈSE dirigée par :

Madame WOLFF Sandrine	Maître de Conférences, BETA, Université de Strasbourg
Monsieur SWANSTRÖM Lee L.	Professor of Surgery, Oregon Health and Sciences University Chief Innovations Officer, IHU- Strasbourg

RAPPORTEURS :

Madame MATT Mireille	Directrice de Recherche, Inra Grenoble, Université Pierre Mendès France
Madame GORDON Toby	Associate Professor, The Johns Hopkins Carey Business School

AUTRES MEMBRES DU JURY :

Monsieur LLERENA Patrick	Professeur, BETA, Université de Strasbourg

Dedicated to my family, especially my parents, without whom I would never have gotten to be where I am today.

Acknowledgements

The writing of a PhD thesis is a personal experience filled not only with scientific discoveries and knowledge creation but also with emotion. The work done in these last three years would not have been possible without the help of many individuals whom I wish to thank for their contributions and moral support.

I would first like to thank Professor Jacques Marescaux, IRCAD's president and IHU's chief executive officer, and Doctor Jean Luc Dimarcq, IHU's executive director, for offering me the opportunity to conduct this research project in their institute and for financing my work.

Second, I thank Strasbourg's University and the Augustin Cournot doctoral school for allowing me to join their doctoral program. I am particularly grateful to Professor Patrick Llerena for presenting me this PhD, providing me counsel during the first, admittedly difficult, steps and being part of the jury.

Throughout this work, my thesis supervisors have shown remarkable patience and interest, for which I am thankful, in helping me achieve the objectives we have set. More particularly, I thank:
Professor Sandrine Wolff for her incredible investment in my phd and for communicating her knowledge to me. She knew how to always motivate me to go farther, investigate further, and adopt different perspectives. My work appeared to have limitless extension possibilities with the feedback she continuously provided.
Professor Lee L. Swanström for his unconditional trust. He always made time for my numerous questions and also knew how to guide me especially when I either felt lost or in doubt. His intelligence and exceptional leadership had me truly believe in the utility of this project and the necessity of fully investing myself in it.

On several occasions, I had the opportunity of asking for feedback for my work from a number of professors. I would namely like to thank Bertrand Koebel, Véronique Schaeffer, Christophe Lerch, Laurent Bach, Pierre Levy and Agnès Gramain for accepting to share their experience and opinion. I am also very appreciative of Toby Gordon and Mireille Matt's acceptance to read and comment my thesis by being part of the jury.

I also thank Sylvine Kempf, management adviser at Strasbourg's hospital, for her enthusiasm and friendship. She was, and remain, my go to person when I needed any information on the healthcare system or the hospital's organization. She always fully invested herself in providing me with the answers, thus, showing her remarkable generosity and interest in helping me with my work.

I was very glad to have met the whole IHU team, too many to thank individually, with whom I shared unique moments leaving me with numerous nostalgic memories of my time spent at the institute. Similarly, the time I spent with the hospital's management advisers was very uplifting and informative. Every launch I had with them was full with reinvigorating humor.

Naturally, I thank my family to whom I dedicate this thesis. My father, Ghassan, for conveying his passion for knowledge and always insisting, rightly so, that I go the farthest possible in my education. My mother, Samia, for transmitting her values to me and teaching me honesty and respect. My big brothers, Firass and Hassan, for always watching over me and being there whenever I needed. And my sister-in-law, Ola, for encouraging me and proofreading my thesis.

Finally, I thank my Sophie for sharing all these lovely years with me and being there for me in both good and bad times. I am lucky to have found such a compassionate, understanding and intelligent woman.

Imad ISMAIL

Évaluation de l'impact socio-économique des innovations chirurgicales hybrides:

Développements méthodologiques et application à l'IHU Strasbourg

Résumé

Dans un contexte d'augmentation constante des dépenses de santé, la création et l'utilisation des technologies innovantes en chirurgie mini-invasive est de plus en plus tributaire de notre capacité à démontrer leur efficacité et évaluer leurs impacts. À ce jour, comme nous le montrons tout au long de cette thèse, la littérature en sciences économiques ne fournit pas aux décideurs et aux évaluateurs les outils adéquats pour réaliser de telles évaluations.

Notre travail combine les meilleurs aspects de l'économie de la santé et de l'économie de l'innovation afin d'établir un cadre méthodologique commun pour l'évaluation des innovations chirurgicales hybrides. En utilisant l'institut de chirurgie guidée par l'image (IHU Strasbourg) comme fondation pour nos analyses, nous créons les bases pour une évaluation coût-bénéfice globale couvrant aussi bien ses activités de soin que de R&D.

L'utilisation des outils développés dans cette thèse permettra à l'IHU, ou tout autre institut chirurgical, de justifier l'intérêt de ces types d'activités en démontrant que les impacts socio-économiques d'une innovation chirurgicale peuvent, éventuellement, compenser le coût supplémentaire qu'elle génère pour le système de santé.

Mots clés : analyse coût-bénéfice, développements méthodologiques, innovations chirurgicales, impact socio-économique, évaluation, économie de la santé, économie de l'innovation, IHU Strasbourg.

Abstract

With constant rises in healthcare expenditures, the creation and use of innovative technologies in Minimally Invasive Surgery (MIS) is increasingly dependent on our ability to demonstrate their efficiency and evaluate their impacts. To date, as we show throughout this thesis, the economic literature has not provided decision makers and analysts with the adequate tools to perform such evaluations.

Our work combines the best aspects of health economics and economics of innovation to establish a common methodological framework for the evaluation of hybrid innovations in MIS. Using the Institute of Image Guided Surgery (IHU Strasbourg) as a base for our investigations, we create the groundwork for a comprehensive cost-benefit evaluation covering the institute's patient care and R&D activities.

The use of the tools developed in this thesis will allow the IHU, or any other surgical institute, to provide advocacy for these types of activities by demonstrating that the socio-economic impacts of a surgical innovation can possibly outweigh the additional cost it incurs to the healthcare system.

Keywords : cost-benefit analysis, methodological developments, surgical innovations, socio-economic impact, evaluation, health economics, innovation economics, IHU Strasbourg.

Contents

Acknowledgements ii

Contents vi

List of Tables xii

List of Figures xiii

Abbreviations xiv

1 Thesis's general introduction 1

1 Introduction . . . 1
2 Surgical innovations and healthcare: a historical perspective . . . 5
2.1 Surgical innovations: the past . . . 5
2.2 Surgical innovations: the present . . . 6
2.3 French healthcare and the future of innovation . . . 7
3 Creation of the "Institut Hospital-Universitaire" . . . 10
3.1 IHU Strasbourg's background . . . 10
3.1.1 From its IRCAD origins . . . 10
3.1.2 Emergence with the "Investissement d'Avenir" program . . . 11
3.2 Description of the IHU Strasnourg . . . 12
3.3 The hybrid initiative for abdominal diseases . . . 14
4 IHU activities: sources of socio-economic impacts . . . 16
4.1 Innovation and treatment in partnership with the industry . . . 16
4.2 Research & Development of hybrid technologies . . . 17
4.3 Knowledge creation and teaching hybrid surgery . . . 19
5 Evaluating surgical innovations: the needed literature and our approach . . . 21
5.1 Health economics for evaluating treatments . . . 21
5.1.1 Economic evaluation as part of health technology assessment . . . 22
5.1.2 Types of health economic evaluations . . . 24
5.2 Economics of innovation and surgical Research & Development . . . 26
5.3 Methodological framework . . . 28
6 Conclusion and thesis plan . . . 31

2 Cost evaluation of minimally invasive surgical technologies: the existing methods and our contribution 33
1 Introduction . . . 33
2 Overview of the French healthcare mechanisms . . . 36
2.1 History of the French Social Security . . . 36
2.2 Introducing the T2A and PMSI principles . . . 38
2.2.1 T2A reimbursement mechanism: GHM vs GHS . . . 39
2.2.2 ICR as a tool for cost management . . . 41
2.3 Limits of the PMSI methodology . . . 45
3 Cost approaches in health economics: definitions and recommendations . 48
3.1 Economic definitions . . . 48
3.2 Health economic definitions . . . 50
3.3 Methods for cost analysis: recommendations . . . 51
3.3.1 Choice of perspective . . . 51
3.3.2 Costing approach . . . 53
4 Costing in the surgical literature . . . 56
4.1 Bariatric surgery and techniques . . . 56
4.2 Surgical literature cost comparison . . . 59
5 Costing method proposal for surgical technologies . . . 62
5.1 Cost methodology . . . 62
5.1.1 Fixed Cost - Medical Equipment . . . 62
5.1.2 Fixed Cost - Personnel . . . 63
5.1.3 Variable Cost - Re-usable Instruments . . . 64
5.1.4 Variable Cost - Disposables . . . 65
5.2 Benchmark for Validation . . . 65
6 Application 2012 . . . 68
6.1 Data collection . . . 68
6.1.1 Fixed Cost - Medical Equipment . . . 68
6.1.2 Fixed Cost - Personnel . . . 69
6.1.3 Variable Cost - Re-usable Instruments . . . 71
6.1.4 Variable Cost - Disposables . . . 72
6.2 Results . . . 73
7 Application 2013 . . . 75
7.1 Data collection . . . 75
7.1.1 Fixed Cost - Medical Equipment . . . 76
7.1.2 Fixed Cost - Personnel . . . 78
7.1.3 Variable Cost - Instruments . . . 80
7.2 Results . . . 81
7.2.1 Fixed Cost - Medical Equipment . . . 82
7.2.2 Fixed Cost - Personnel . . . 83
7.2.3 Variable Cost - Instruments . . . 84
7.2.4 Cost per Operation . . . 85
7.3 Sensitivity analysis . . . 86
8 Discussion . . . 89
9 Conclusion . . . 93

3 Extended health economic evaluation for medical devices 95

1 Introduction . . . 95
2 Economic evaluation approaches for medical devices: a literature review . 98
2.1 The particularities of medical devices . . . 98
2.2 Evaluation guidelines: a focus on outcomes . . . 100
3 Review of economic evaluation measures . . . 102
3.1 Direct and indirect costs . . . 103
3.1.1 Length of Stay and Complications . . . 103
3.1.2 Absenteeism . . . 105
3.1.3 Presenteeism . . . 107
3.2 Outcome measures . . . 109
3.2.1 Unvalued outcomes . . . 109
3.2.2 Preference based QoL measures . . . 110
3.2.3 QALY Willingness To Pay . . . 115
3.3 Medical tourism . . . 117
3.3.1 Market view . . . 118
3.3.2 Drivers of medical tourism . . . 119
3.3.3 Impact measurement . . . 120
3.4 Intangible factors and innovation opportunity . . . 121
4 Application: evaluation method . . . 124
4.1 Length of stay and complications . . . 124
4.2 Absenteeism and Presenteeism . . . 126
4.3 Quality of life . . . 127
4.3.1 Data collection . . . 127
4.3.2 Data analysis: T.test vs 2X2 ANOVA vs HLM . . . 128
4.3.3 Focus on hierarchical linear modelling . . . 130
4.4 Medical tourism . . . 132
4.4.1 Impact calculation . . . 133
4.4.2 Case Study: POEM . . . 134
4.5 Intangible benefits . . . 137
5 Results . . . 139
5.1 Length of stay . . . 139
5.1.1 Cost per day of hospital ward . . . 139
5.1.2 Application to 2013 protocol . . . 141
5.2 Absenteeism . . . 142
5.3 Quality of life . . . 143
5.3.1 BAROS . . . 144
5.3.2 GIQLI . . . 147
5.4 Medical tourism . . . 150
5.5 Survey results . . . 153
6 Discussion . . . 155
6.1 Limits . . . 163
7 Conclusion . . . 164

4 Impact of Research and Development in Healthcare 167
1 Introduction . . . 167
2 Overview of innovation definitions and process . . . 170
2.1 Nature of innovation . . . 170

2.1.1 The four "P" of innovation: Product, Process, Position and Paradigm . . . 171
2.1.2 Traditional Incremental vs Radical . . . 172
2.1.3 Incremental, Radical and Disruptive? . . . 173
2.2 Innovation creation and diffusion . . . 175
2.2.1 The innovator . . . 175
2.2.2 The user . . . 177
2.2.3 Cooperation, Communication and Interaction . . . 179
3 Research impact evaluation methods: the literature . . . 181
3.1 Overview of evaluation methods and general structure . . . 181
3.1.1 Perspective . . . 183
3.1.2 Objective . . . 184
3.1.3 Temporal dimension . . . 185
3.2 R&D evaluation elements . . . 186
3.2.1 Type of measures . . . 186
3.2.2 Measurement methods . . . 187
3.3 Health research evaluation example: Payback Framework . . . 191
3.3.1 Logic model . . . 192
3.3.2 Payback categories . . . 194
4 EvaRIO Method . . . 196
4.1 RI definition . . . 197
4.2 Evaluation approach . . . 198
4.3 Evaluation Metrics . . . 201
5 Application: IHU case study . . . 205
5.1 IHU partners and relationship . . . 205
5.1.1 IRCAD . . . 205
5.1.2 SIEMENS . . . 206
5.1.3 STORZ . . . 207
5.1.4 INRIA . . . 207
5.1.5 Surgical Perspective . . . 208
5.1.6 ICUBE - AVR Team . . . 209
5.2 Evario's evaluation guidelines . . . 210
6 Results . . . 213
6.1 Evario results . . . 213
6.1.1 Industry partners . . . 214
6.1.2 University and other research laboratories . . . 218
6.1.3 Fellows and IHU/IRCAD researchers . . . 223
6.2 EvaRIO reworked: focus on projects . . . 226
7 Discussion . . . 230
7.1 Limits . . . 235
8 Conclusion . . . 237

5 Thesis' general conclusion **238**
1 Introduction . . . 238
2 Cost evaluation of minimally invasive surgical technologies: the existing methods and our contribution . . . 240
2.1 Literature review . . . 240

2.2 Method . . . 240
2.3 Results . . . 241
2.4 Our main contributions and limitations . . . 242
3 Extended health economic evaluation for medical devices . . . 244
3.1 Literature review . . . 244
3.2 Method . . . 245
3.3 Results . . . 245
3.4 Our main contributions and limitations . . . 246
4 Impact of Research and Development in Healthcare . . . 248
4.1 Literature review . . . 248
4.2 Method . . . 249
4.3 Results . . . 249
4.4 Our main contributions and limitations . . . 250
5 Perspectives . . . 251

Bibliography **254**

A PMSI Description **271**

B Demonstration: Medical Equipment **273**

C Demonstration: Personnel **275**

D GIQLI Questionnaire **277**

E BAROS Questionnaire **281**

F Survey **284**

G EvaRIO Measures **287**

Résumé en Français **290**
1 Introduction générale . . . 290
2 Connaissances exploitées . . . 294
3 Évaluation du coût des technologies chirurgicales mini-invasives : les méthodes existantes et notre contribution . . . 296
3.1 Revue de la littérature . . . 296
3.2 Méthode . . . 296
3.3 Résultats . . . 297
3.4 Apports et limites . . . 297
4 Évaluation médico-économique des technologies médicales . . . 299
4.1 Revue de la littérature . . . 299
4.2 Méthode . . . 299
4.3 Résultats . . . 300
4.4 Apports et limites . . . 301
5 Impact de la recherche et du développement dans le domaine de la santé . 302

5.1 Revue de la littérature 302
5.2 Méthode 303
5.3 Résultats 303
5.4 Apports et limites 304
6 Conclusion générale 305

List of Tables

2.1 Extract from the Public Hospital GHS List - 2014 . . . 40
2.2 Cost per ICR point 2013 - Digestive Service . . . 44
2.3 DACEHTA - Cost perspective in economic evaluations . . . 52
2.4 ENC base OR Cost for GHM 10C131 . . . 67
2.5 Medical equipment data 2012 . . . 69
2.6 Personnel data 2012 . . . 71
2.7 Re-usable Instruments 2012 . . . 72
2.8 Robot specific disposables 2012 . . . 72
2.9 Most expensive common disposables 2012 . . . 73
2.10 Total cost per Gastric Bypass operation 2012 . . . 73
2.11 Medical equipment data 2013 . . . 78
2.12 Personnel data . . . 80
2.13 Re-usable and Disposable Instruments . . . 81
2.14 Personnel average presence as percent of operation duration . . . 83
2.15 Average cost per Gastric Bypass operation (Euro) . . . 86

3.1 Daily hours lost and economic impact per impairment . . . 108
3.2 EuroVAQ - Value of a QALY trimmed time variant chained approach (US Dollars) . . . 116
3.3 Number of medical tourists 2012 - in thousands . . . 118
3.4 Hourly employee cost . . . 126
3.5 Medical equipment data PEOM . . . 135
3.6 Personnel data POEM . . . 136
3.7 Most expensive disposables POEM . . . 136
3.8 Expenses allocated to "Pole Hepato-Digestif"'s hospital ward . . . 140
3.9 LGB charges convention based . . . 151
3.10 POEM charges convention based . . . 151
3.11 LGB charges cost calculation based . . . 152
3.12 POEM charges cost calculation based . . . 152

4.1 Measurement Methods . . . 189
4.2 Direct effect metrics . . . 201
4.3 Capacity effect metrics . . . 203
4.4 Indirect effect metrics . . . 204
4.5 Capacity effects' results . . . 226

List of Figures

1.1 Life expectancy at birth . . . 2
1.2 Health expenditure as % of GDP . . . 2
1.3 IHU Building . . . 13
1.4 IHU hybrid surgery . . . 14
1.5 IHU R&D Strategy . . . 18
1.6 CEA decision making . . . 25
1.7 IHU Impacts . . . 28

2.1 French Social Security Mechanism . . . 38
2.2 Example of Strasbourg University Hospital's Organization . . . 43
2.3 Types of hospital costing methodologies . . . 54
2.4 Sleeve Gastrectomy . . . 56
2.5 GastricBypassRouxenY . . . 57
2.6 Laparoscopic surgery . . . 58
2.7 Robotic surgery . . . 58
2.8 Kernel Density of Medical Equipment Cost . . . 82
2.9 Kernel Density of Personnel Cost . . . 83
2.10 Kernel Density of Instrument Cost . . . 84
2.11 Kernel Density of Room Occupation Time . . . 85
2.12 Kernel Density of Average Cost per Operation . . . 86

3.1 Patient care pathway . . . 103
3.2 EQ-5D Visual Analogue Scale . . . 111
3.3 EQ-5D-5L Descriptive System . . . 113
3.4 POEM . . . 134
3.5 Kernel Density of Length of stay . . . 141
3.6 Kernel Density of Days off Work . . . 142
3.7 Q-Q plot BAROS . . . 147
3.8 Q-Q plot GIQLI . . . 150

4.1 Research Evaluation . . . 186
4.2 Payback Logic Model . . . 193
4.3 EvaRIO Measures . . . 199
4.4 Framing Interview guideline . . . 210
4.5 Partners' Interview guideline . . . 211
4.6 EvaRIO reworked . . . 228

Abbreviations

ATIH	**A**gence **T**echnique de l'**I**nformation sur l'**H**ospitalisation
ANR	**A**gence **N**ationale de la **R**echerche
BMI	**B**ody **M**ass **I**ndex
CADTH	**C**anadian **A**gency for **D**rugs and **T**echnologies in **H**ealth
CEA	**C**ost **E**ffectiveness **A**nalysis
CBA	**C**ost **B**enefit **A**nalysis
CCAM	**C**lassification **C**ommune des **A**ctes **M**édicaux
CUA	**C**ost **U**tility **A**nalysis
DALY	**D**isability **A**djusted **L**ife **Y**ear
DACEHTA	**D**anish **C**enter for **H**ealth **T**echnology **A**ssessment
DC	**D**isposables **C**ost
DIM	**D**épartement **I**nformations **M**édicales
DREES	**D**irection de la **R**echerche, des **E**tudes, de l'**E**valuation, et des **S**tatistiques
DSS	**D**irection de la **S**écurité **S**ociale
EITS	**E**uropean **I**nstitute of **T**ele**S**urgery
ENC	**E**tude **N**ationale des **C**oûts
FDA	**F**ood and **D**rug **A**dministration
GBP	**G**astric **Byp**ass
GDP	**G**ross **D**omestic **P**roduct
GHM	**G**roupe **H**omogène de **M**alades
GHS	**G**roupe **H**omogène de **S**éjour
HAS	**H**aute **A**uthorité de **S**anté
HRQoL	**H**ealth **R**elated **Q**uality **o**f **L**ife
HTA	**H**ealth **T**echnology **A**ssessement
HUS	**H**opitaux **U**niversitaires de **S**trasbourg

IC	**I**nstruments **C**ost
ICER	**I**ncremental **C**ost **E**ffectiveness **R**atio
ICR	**I**ndices de **C**oût **R**elatif
IHU	**I**nstitut **H**ospitalo **U**niversitaire : Image-Guided Minimally Invasive Surgical Institute
IQWiG	**I**nstitute for **Q**uality and **E**fficiency in **E**fficiency in **H**ealth **C**are
IRCAD	**I**nstitut de **R**echerche contre les **C**ancers de l'**A**ppareil **D**igestif
LGBP	**L**aparoscopic **G**astric **Byp**ass
LoS	**L**ength **o**f **S**tay
MCO	**M**édecine **C**hirurgie **O**bstétrique
MEC	**M**edical **E**quipment **C**ost
NHS	**N**ational **H**ealth **S**ervice
MIS	**M**inimally **I**nvasive **S**urgery
NICE	**N**ational **I**nstitute for **H**ealth and **C**are **E**xcellence
NOTES	**N**atural **O**rifice **T**ransluminal **E**ndoscopic **S**urgery
OR	**O**perating **R**oom
PC	**P**ersonnel **C**ost
PMSI	**P**rogramme de **M**édicalisation des **S**ystèmes d'**I**nformation
QALY	**Q**uality **A**djusted **L**ife **Y**ear
RSS	**R**ésumé de **S**ortie **S**tandardisé
RUM	**R**ésumé d'**U**nité **M**édicale
RYGBP	**R**oux-en-**Y** **G**astric **Byp**ass
SB	**S**euil **B**as
SD	**S**tandard **D**eviation
SH	**S**euil **H**aut
T2A	**T**arification **A** L'**A**ctivité
UF	**U**Unité **F**onctionnelle
WHO	**W**orld **H**ealth **O**rganization

Chapter 1

Thesis's general introduction

1 Introduction

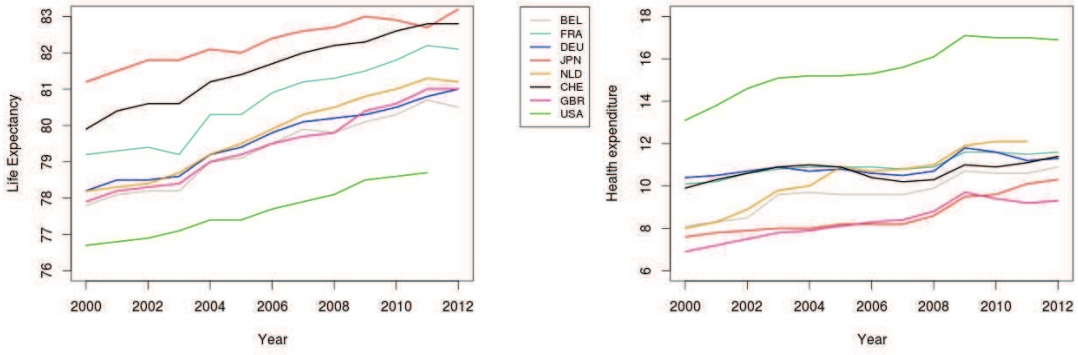
In a context of international competition, every government lusts for progress with innovation as its main driver of economic performance. In all sectors of the economy, neither institutes nor firms can survive without innovating as it is essential for their development and adaptation to changing market demands.

In the past, innovation in healthcare often constituted a series of great leaps forward in terms of improvements in both care quality and life expectancy, most noticeably marked by the change from open to minimally invasive surgical procedures. The pursuit of lower mortality and complication rates, considered as satisfactory and sufficient measures of effectiveness at that time, was only hindered by technological limitations. It was particularly the case for endoscopy for which *"innovation has been highly dependent on scientific and engineering advances that are generated outside of the medical sectors, such as fiber optics, color television, and charge couple devices"* [Rosenberg et al., 1995].

Today however, there is a widespread governmental and public recognition that a large component of health costs is due to inefficient care and unnecessary complications. But it is also perceived that the introduction of new technologies in medicine is leading to higher costs. This effect is admittedly observable through the study of laparoscopic surgery's history which lead to a considerable increase in healthcare expenditures. This increase, however, was proven to be compensated by the benefits that laparoscopic techniques offer patients, surgeons and the Research&Development (R&D) community.

FIGURE 1.1: Life expectancy at birth

FIGURE 1.2: Health expenditure as % of GDP



Source: based on OECD data - Life expectancy at birth and health expenditure as % of GDP per country

The situation is all the more dire as the steady increase in healthcare expenditure over the last decades has sparked much controversy over its legitimacy and the need for its control. The comparison of cross-country life expectancy (Figure 1.1) and healthcare expenditure levels (Figure 1.2), for example, emphasizes the need for such discussions as the disparities become more apparent especially between Japan and the USA.

Modern governments are unsure as to how to invest in technological innovations and improve the quality of care all the while limiting, or at least justifying, the increase in care cost. As resources become scarcer, the improvement of our healthcare system becomes increasingly dependent on the development of comprehensive methodologies for evaluating the impacts of innovations.

Today, the performance assessment of medical activities and innovations has begun shifting from its traditional mortality and morbidity measures to include changes in length of stay as well as in social and economic impacts. However, although the health economics discipline has developed increasingly sophisticated evaluation methods, they remain either general in nature or more oriented towards the pharmaceutical industry [Barkun et al., 2009].

Our thesis attempts to fill the gap in published methodological guidelines by creating a surgery oriented evaluation methodology to assess the impacts of minimally invasive surgical innovations. To do so, we focus on the evaluation of "hybrid" techniques currently considered as some of the most innovative surgical practices developed in France.

The creation and use of hybrid surgical technologies is spearheaded by Strasbourg's Institute of Image Guided Surgery (IHU Strasbourg), who is also this thesis' initiator. Their objective, at this thesis' origin, consist in understanding how they may and should conduct medico-economic evaluations of their innovative surgical technologies. Additionally, due its multiple, complementary and innovative activities in surgery, the institute represents an ideal application terrain for more comprehensive evaluation and methodological developments which we also sought to undertake.

Our work hence builds around one central question: **how do we evaluate the efficiency and the socio-economic impacts of minimally invasive surgical innovations?** First, however, in this introductory chapter, we justify why we seek to answer this question; where we will apply such evaluations; what we will evaluate; and how we will conduct our study.

In the following section, we start out by presenting a historical overview of the developments in minimally invasive surgery to highlight the reasons that stimulated their emergence as well as the obstacles that hindered their adoption. To provide advocacy for our work *(answer the why? question)*, we also go over the current state of French healthcare and the impacts that it has on the future of such innovations.

To define our analysis' perimeter *(answer the where? question)*, we present, in the third section, the events that led to the creation of Strasbourg's "Institut Hospitalo-Universitaire" (IHU), the initiator of this research project. To be more precise, we present the institute's history through a description of its parent organization and the investment plan that enabled its creation. Then, we provide a general presentation of the institute and the particularities that make it an ideal terrain for our work.

In the fourth section, we describe each of the IHU's activities and the role they play in generating socio-economic impacts that are at the heart of our analysis *(answer the what? question)*. Throughout this section, we also point out the link between the different activities and how it influences our economic evaluations.

The fifth section details the scientific knowledge we collect and exploit to conduct our evaluations and create our methodological tools. A presentation of the methodological framework we establish and follow is also provided as to better understand the idea behind our work *(answer the how? question)*.

Finally, in the last section, we present a synthesis of this thesis' objective, research question and analysis plan. The knowledge used in each chapter is also detailed as to better express the complexity of this work.

2 Surgical innovations and healthcare: a historical perspective

In this section, we try to understand the changes in surgical practice by looking back at the reasons that motivated the emergence and adoption of "Minimally Invasive Surgery" (MIS). This historical perspective also allows us to better grasp the importance of evaluating such technologies, especially as the current innovation trends seem to concentrate on this field.

The evaluation of MIS innovations is all the more important in a context of economic hardship and increased monitoring of healthcare expenditures such as in France. Therefore, we also present a description of the French healthcare's current state as to better understand the stakes at hand and how they influence the emergence of such innovations.

2.1 Surgical innovations: the past

The last decades have seen rapid technological and scientific advancements that sparked radical changes in our lifestyle and demonstrated our capability to move forward. With a GDP per capita in high income countries that has increased to more than 31 times that of 1960's (World bank - GDP per capita (current US$)), the standard of living improved to the point where all essential services have become affordable to almost everyone.

Healthcare is one of these services that has seen many breakthroughs demonstrated through the extension of average life expectancy by 11 years from 1960 to 2000 (World bank - Life expectancy at birth, total (years)). Vaccines, antibiotics, cancer treatment, imaging and modern surgical discoveries played crucial roles in improving healthcare quality and limiting the impacts of previously untreatable diseases.

The development of modern surgical practice takes root in the introduction of operative procedures for treating diseases that had previously either been treated medically or not treated at all [Gordon and Cameron, 2000; Rosenberg and Schlich, 2012]. During the early stages, however, innovations often resulted in an increase in the number and complexity of surgical procedures as they sought to decrease disease induced mortality and morbidity.

Over the years, surgeons and hospital managers became increasingly aware that surgery related morbidities were not a result of the surgical procedure itself, but rather due to the trauma caused by gaining access to the area being treated. Hospitalization following open Cholecystectomy, for example, was essentially required so that patients could recover from the trauma caused to the abdominal wall, and not from the removal of the gallbladder itself [Mack MJ, 2001].

A subsequent shift in the methods for evaluating the performance of surgical operations marked an increased interest in minimizing "invasiveness" [Gordon and Cameron, 2000; Mack MJ, 2001] and evaluating long-term outcomes [Barkun et al., 2009; Rosenberg and Schlich, 2012]. For many procedures, the reduction in invasiveness through minimally invasive surgery was expected to significantly improve survival, decrease complications, and result in a quicker return to work and a healthy life [Mack MJ, 2001].

At first, the adoption of MIS was subject to considerable controversy due to the lack of teaching and training, coupled with long learning curves and an increase in complication rates [Darzi and Munz, 2004]. It was rather unclear whether these types of procedures were ethical or even safe to use [Harrell and Heniford, 2005].

Nevertheless, technological breakthroughs in endoscopy and laparoscopy have allowed for smaller and fewer MIS operations that marked the foundations on which modern surgery is built. Many historical developments that were at the origin of endoscopy, also played an important role in improving laparoscopy [Harrell and Heniford, 2005] and even in preparing for the emergence of robot/computer assisted surgery.

2.2 Surgical innovations: the present

The twenty first century is now considered as an enabler of constantly more sophisticated and miniaturized devices be it in imaging, instrumentation, communication, information, medical or non medical [Rosenberg and Schlich, 2012]. Dramatic advances in healthcare are continuously driving the quality of care upwards but, at the same time, rendering traditional surgical treatments obsolete. This "creative destruction" as Joseph Schumpeter would call it [Schumpeter, 1934] is considered to be at the heart of economic growth.

The advent of robotic surgery, for example, is allowing surgeons to significantly enhance their dexterity enabling the application of microscopic tasks neither feasible with human hands nor using laparoscopic instruments. One example of such procedures include the use of needles to administer a local therapy for retinal vein thrombosis through retinal vein cannulation (involving cannulation of a 100-micron structure) [Mack MJ, 2001], otherwise impossible to achieve.

Recent technological advances are also introducing procedures that can be performed endoscopically, through natural orifices, using miniaturized flexible instrumentation. Treatments for esophageal reflux disease, for example, are now being performed transorally rather than laparoscopically, significantly reducing access-related trauma [Mack MJ, 2001].

In their pursuit of an ever less invasive and more effective surgical treatments, researchers and surgeons continue to create increasingly expensive technologies. Admittedly, the nature of technological advances in medicine and the changes in clinical practice that followed them have always tended to significantly raise spending [CBO, 2008].

Today, the available evidence suggests that the advances in medical technologies account for, on average, 50% of OECD countries' healthcare expenditures [Sorenson et al., 2013] with a large portion attributed to pharmaceuticals and 5% to medical devices [Skinner, 2013]. In Europe, the medical device and diagnostics industry was estimated to employ over 500 000 individual across 25 000 companies of which more than 80% are small businesses (2012 data). The total sales of medical devices in the European Union were estimated at 95 Billion Euro representing 33% of the world's market share (European Commission - Medical devices in EU (Infographic)) and, therefore, an important strategic investment.

2.3 French healthcare and the future of innovation

According to the World's Health Organization (WHO) 2000 report [WHO, 2000][1], French healthcare has been described as the most performant system in the world ranking at first place followed by Italy and San Morino. This classification is based on a "performance index" determined by each healthcare system's degree of reactivity, respect

[1]The World Health Organization has not updated the ranking since 2000.

of individuals, confidentiality/respect of privacy, respect of patients (time before being treated, social security access), capacity to improve health, respond to the population's needs, and ensure equity in distributing the system's expenses.

In 2013, 91% of the French population were registered in the National Health Insurance Fund which covered 86% of all health insurance expenses [DSS, 2014]. As one of the top healthcare investors, France's 2013's healthcare expenditure reached 247.7 Billion Euro, representing 11.7% of the country's GDP [DRESS, 2014], accompanied by a social security deficit of 12.5 Billion Euro and 130 Billion in debt [DSS, 2014]. Although the quality and innovative nature of the French healthcare system has been recognized worldwide, the French government has deemed the current state of healthcare expenditure unsustainable.

The government's application of the Social Security financing Act in 2013 constituted the first step to better manage healthcare spending. Indeed, historically, the efficiency of medical devices and pharmaceutical products was only assessed in the context of a more general medical treatment care pathway. Today, as stated by the "Haute Autorité de Santé" [HAS N37], the act ensures that all drugs and medical devices are subject to a medico-economic evaluation individually to determine their price and whether they should be registered on the list of reimbursable products.

In a second effort, the Prime Minister Manuel Valls announced on the 26th of April 2014 a plan to save 50 billion Euro by 2017. The project would affect all public sectors of the economy, especially health insurance whose expenditure are to be reduced by 10 billion Euro. The measure should also directly affect publicly financed hospitals who will see their budgets reduced and their activity reorganized.

Tightening the healthcare provider's budget may seem as one solution. However, this decision risks doing more harm than good in the long run as it sets back the adoption and diffusion of technology leveraged innovations. That is all the more true for institutes that specialize in the development and use of innovative technologies and procedures.

In this context, innovative surgical institutes will now have a dual responsibility when developing, using and diffusing their technologies. The first will consist in ensuring that innovations are cost-effective, compared to existing practice, as to maximize their chances of getting reimbursement and being adopted. The second relates to the need

of either creating affordable (for the healthcare system) technologies that drive down expenditures, or advancing innovations that have higher social and economic impacts than the additional cost they incur.

In the surgical field, these responsibilities are rarely filled from the start - that is at an innovations' adoption - due to the high learning curves and the importance of surgeons' experience. Institutes that advance innovative technologies will need to continuously update their evaluations as its results may drastically change with the increase in adoption.

3 Creation of the "Institut Hospital-Universitaire"

Although minimally invasive surgery is a technology driven specialty that tends to increase expenditures, the French government expressed its willingness to bet on this field's future through their investment in the Institut Hospitalo-Universitaire (IHU), also known as the Institute of Image Guided Surgery. However, this bet comes with one main condition: the ability to prove that the "return on investment" is worth it.

In this section, we go over the events that led to the institute's creation starting with an overview of its parent company, the "Institut de Recherche contre les Cancers de l'Appareil Digestif" (IRCAD) and the government's investment plan. We then provide a description of the IHU and its "hybrid surgery" focus as to better define our analysis' perimeter.

3.1 IHU Strasbourg's background

3.1.1 From its IRCAD origins

The "Institut de Recherche contre les Cancers de l'Appareil Digestif" (IRCAD) is a private medical research center, founded in 1994 by Professor Jeacques Marescaux, internationally known for its minimally invasive surgery centered activities. Since its creation, IRCAD has gained considerable renown as a leading research and education institute.

The institute's research's focus is directed towards the development of minimally invasive procedures and instruments. In 2007, for example, the first fully Natural Orifice Transluminal Endoscopic Surgery (NOTES) was carried out on a human by one of IRCAD's teams marking the possibility of "scarless" procedures.

The IRCAD also founded a training structure, named European Institute of TeleSurgery (EITS), that provides minimally invasive training to over 4 300 surgeons from all over the world every year. Courses are presided by a team of 800 international experts who continuously ensure a high level of skill and experience transfer.

Since 2000, the institute has also been developing an online training platform (WeBSurg) to complement its Strasbourg's training courses. The success of this free service is

marked by its developmental in 6 languages and its gain of over 300 000 registrations since its creation.

IRCAD's international success led to the emergence of two twin institutes in Taiwan (Asia IRCAD – AITS) under the guidance of M. H. Huang, president of Show Chwan Memorial Hospital, and Brazil (State Sao Paulo) reflecting the partnership with Henrique Prata and the "Hospital de Cancer de Barretos". In Strasbourg, this success has led professor Marescaux to become the instigator of "Institut hospitalo-universitaire" (IHU) Strasbourg's creation in the context of the "Investissement d'Avenir", or "investment of the future" in English.

3.1.2 Emergence with the "Investissement d'Avenir" program

Starting 2010, the French National Research Agency "ANR" published an investment project of up to 47 Billion Euro in an effort to stimulate innovation and progress in industry, sustainable development, research and education. At its origin, the Juppé-Rocard report was established by two previous Prime Ministers to define the six strategic priorities at the heart of the "Investissement d'Avenir" program:

- Higher education and formation: *stimulate the emergence of university poles of excellence able to withstand and face world competition*;
- Fundamental research and its economic value creation: *accelerate technology transfer and provide laboratories with the means of reaching excellence*;
- Industrial sectors: *support the development of small and medium-sized enterprises, and innovating middle-market companies as well as consolidate the strategic sectors of the future*;
- Sustainable development: *strongly contribute to energy and ecology based transitions, sources of a new more sustainable growth model*;
- Digital economy: *deploy high bandwidth infrastructures over the entire French territory and stimulate the development of new uses for companies and households alike*;

- Health and biotechnologies: *stimulate progress in knowledge, develop new solutions, and allow anticipating, improving, developing and validating new medical and agronomy approaches.*

Of the 21.9 Billion Euro invested in the research and education sector, 850 Million were dedicated to the creation of 5 medical centers of excellence known as IHU. An international jury evaluated 19 project submissions with respect to four essential roles that each IHU must fulfill:

- Develop innovative therapies;
- Train students in the use of innovative therapies;
- Evaluate the economic impacts of scientific innovations;
- Create a network of partnerships with the industry.

In Mars 2011, the French government announced the validation of 6 IHU projects instead of the 5 initially anticipated. Great attention, and recognition, was given to the fact that the Institute of Image-Guided Surgery, IHU Strasbourg, was the only one that included a mandate to track the socio-economic impacts of its activity. A decision that led it to be placed equal first with two other projects and granted 67.3 Million Euro in total public investment.

3.2 Description of the IHU Strasnourg

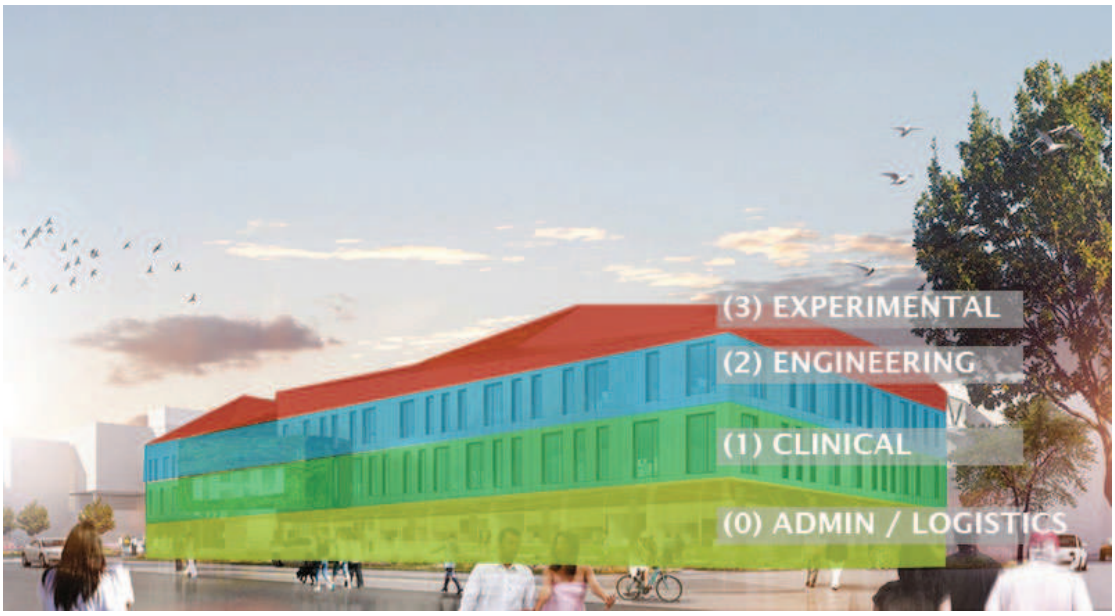
Strasbourg's institute of image guided surgery was hereby created late 2012 following the government's "Investissement d'Avenir" plan for stimulating innovation and progress in industry, sustainable development, research and education. At its conception, the institute's visionaries combined their expertise to attempt merging specialties, that have historically been considered to be distinct, through what they call "MIX-Surg" or "hybrid surgery".

Their project, as described in the call for proposals' submission, is centered around the creation of a multifunction center to create and enhance hybrid approaches, develop innovative medical devices and train the physicians of the future. The ultimate goal

being the emergence of hybrid physicians who can see inside the body as clearly as possible and combine surgical tools, flexible endoscopy and radiology to deliver targeted therapy.

The IHU is therefore considered as the cornerstone of Strasbourg's medical technology campus in which medical, research and education facilities interact with industry R&D centers and technology incubators. In partnership with industry leaders, the IHU heavily invests in building and maintaining hybrid operating rooms used to instigate collaborations and development.

FIGURE 1.3: IHU Building



All activities will be centered in a new 13 000 m^2 building[2], see Figure (1.3) that connects the IHU, hospital and IRCAD through dedicated corridors. The administrative staff's offices and meeting rooms will be located on one side of the ground floor, while the other side will be exclusive to patient consultations.

The first floor will consist of nine operating rooms (OR) three of which are reserved to endoscopy, three to laparoscopy and another three to hybrid procedures. A section of the floor will have dedicated beds for outpatient recovery, while the rest will be used for sterilizing medical instruments. A corridor connecting this floor to the hospital's will permit easy transfer of patients from the IHU ORs to the hospital's wards in the case of inpatient procedures.

[2]The new building is expected for 2016.

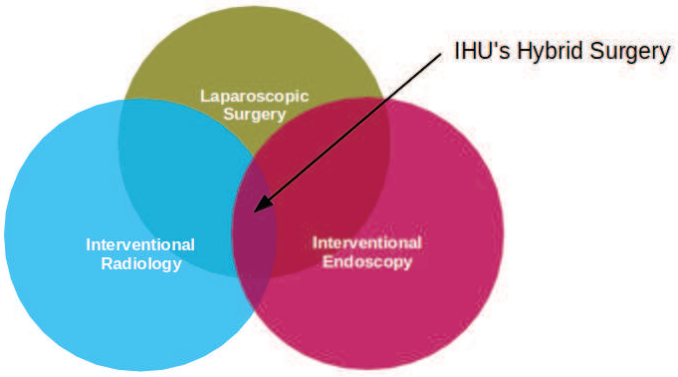
All engineering, research and development will take place in the second floor which is split into offices as well as laboratory, education and workshop spaces. Products conceived at the IHU can then be tested in the third floor's ORs dedicated to large animal experimentation. A corridor connecting this floor to the IRCAD's will allow for an easy transfer of animals, namely pigs, between the two institutes; thus providing France, and even Europe, with one of the very few experimental plateforms able to receive large animals.

3.3 The hybrid initiative for abdominal diseases

The IHU's activity mainly focuses on the treatment of abdominal diseases and pathologies of the digestive tract (liver, pancreas, esophagus, stomach, small intestine, colon, rectum and peritoneal cavity) which are a significant issue for public health systems due to their high incidence and major economic impacts. In France, for example, 262 713 patients were admitted in 2013 for digestive cancers alone, consequently considered as the most frequent type of cancer [INCA, 2015].

The complexity and variety of abdominal diseases demands the attention of multiple medical specialists – usually digestive surgeons, gastroenterologists and interventional radiologists. Each specialist focuses on a specific approach to abdominal diseases: surgeons focus on organ resection and repair, gastroenterologists on medical and endoscopic therapy and interventional radiologists on image-guided procedures. Unfortunately, minimally invasive techniques were developed by these separate and distinct specialties and are inevitably limited by the expertise of individual specialists such as surgeons, radiologists and gastroenterologists.

FIGURE 1.4: IHU hybrid surgery



The IHU Strasbourg's objective is to combine the best aspects of minimally invasive techniques from laparoscopic surgery, interventional radiology and interventional endoscopy in what they qualify as hybrid surgery (Figure 1.4).

Treatment of common bile ducts is a prime illustration for hybrid surgery which, until recently, required two procedures to treat the disease. First, a gastroenterologist used an image-guided endoscope to reach the common bile duct via the intestines to clear out the stones. At a later time, a minimally invasive surgeon removed the gallbladder through laparoscopy.

In 2006, a single intervention combining both image-guided endoscopy and minimally invasive surgery was demonstrated to be feasible by Morino *et al.* [2006] in Italy. The so-called "rendezvous procedure" has reportedly lead to better stone clearance, decrease in operating time, reduction in hospital stay, decrease in morbidity, and significant reduction in the overall cost of treatment.

The development of this hybrid surgery is spearheaded by the IHU's I-SIP school of innovation under the direction of Professor Lee L. Swanström, IHU's Chief Innovation Officer. Every year, 3 medical students join the school to conduct one or several projects of surgical innovation under the supervision of senior surgeons all the while benefiting from the IHU staff's expertise in terms of study design, prototyping, testing and preclinical validation.

As a scientific non-profit organization specialized in developing innovative surgical technologies through its fellowship program, the IHU Strasbourg is constantly faced with the challenges of resource allocation decision making. Furthermore, considering that the introduction of MIX-Surg comes at a cost, there is also a constant need for evidence of the benefit of such sophisticated approaches through economic evaluations.

The assessment of economic measures is clearly needed to guide the medical devices' industry in technology design paths and marketing campaigns. Similarly, economic evaluations' cost/benefit ratios are also required to both guide treatment approaches and provide information to the funding sources of the IHU on the value of their investments.

4 IHU activities: sources of socio-economic impacts

As a young institute, IHU Strasbourg currently focuses on developing and using hybrid medical devices for the treatment of abdominal diseases as well as training physicians in the use of said innovations. After defining hybrid surgery, as viewed by the institute, we describe the three main activities that are expected to play a significant role in generating socio-economic impacts.

4.1 Innovation and treatment in partnership with the industry

Historically, medical specialties have been separated into distinct departments which have lead to competition among practitioners and inefficiencies in care coordination. The goal of the IHU is to create a combined procedural unit for surgery, gastroenterology and radiology thus becoming a world leading and attractive healthcare center for image guided and minimally invasive hybrid surgery.

In partnership with Siemens and Karl Storz, the IHU is creating nine patient dedicated unique "MIX Surg" operating rooms equipped with advanced high speed telecommunications for surgery transmissions and computer/robotic assistance. The medical facility will also be housing two additional experimental operating rooms designated for the testing and the validation of innovative imaging solutions for interventional procedures.

Three intelligent operating rooms are thus being set up for laparoscopy based on Storz's "OR-1" model which connects all equipment and instruments to a central hub, allowing users to control the entire OR from one point. For computer-assisted surgery, surgeons will also be benefiting from a DaVinci robotic system developed by Intuitive Surgical.

Using Siemens' expertise in imaging, the new technological platform is being equipped with three operating rooms fitted out for interventional MRI, interventional PET-scanner and the new generation of robotized-arm scanners (Artis Zeego system). The platform is being designed as to allow the movement of the operating table between rooms to access different imaging tools. Rooms are also being designed in a modular fashion as to allow rapid upgrades and additions of new technologies as they are developed.

Finally, three hybrid operating rooms adapted for flexible endoscopy in a surgical environment are being set up with endoscopic ultrasound (Olympus) and confocal endomicroscopy (CellVizio - MaunaKea Technology) devices as well as endoscopy (by Karl Storz), angiography (C-arm, Siemens Healthcare) and high intensity focused ultrasound (EdapTMS, Imasonic) systems. The chief medical officer will ensure that all hybrid procedures performed in these operating rooms are part of a clinical protocol guaranteeing that all procedural data is recorded and available for research protocols.

To ensure that future patients will be receiving the most **cost-effective care**, the impacts of "MIX Surg" will be continuously estimated and monitored through prospective and longitudinal gathering of data, as well as the **creation of new metrics and measuring tools**. A health outcomes registry is therefore needed to track all patient treatments to determine the impacts of "MIX Surg" on patients' quality of life, disease cure rates, and its effect on the health of the region's population.

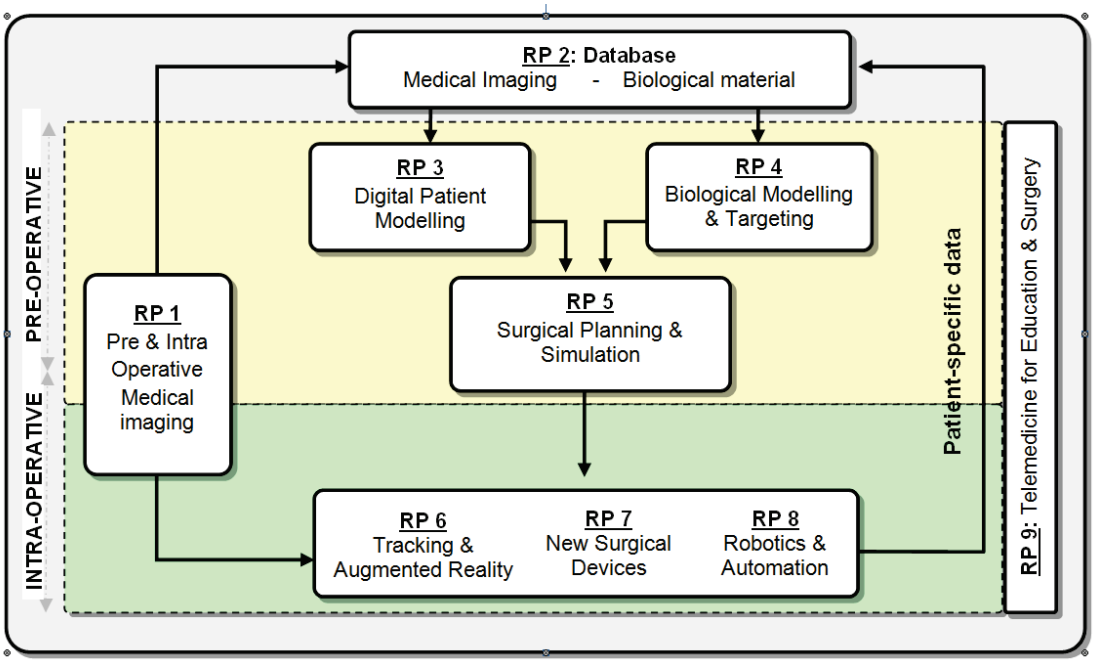
A first part of this thesis will therefore be dedicated to establishing the methodological tools to exploit this future registry. Mainly, we focus on creating methods for precise and fast cost calculations, and for identifying the "benefit" of introducing surgical innovations in the operating room.

4.2 Research & Development of hybrid technologies

To treat patients with innovative hybrid technologies, the IHU must first either acquire them or invest in its Research and Development (R&D) process to create them. A hybrid treatment can therefore be viewed as a continuation of the R&D activity, which is of particular importance when the used technology is developed by the institute itself.

To be more precise, when a hybrid surgical technology is bought and then used, the relevant impacts to evaluate are generated by the "usage" activity. However, when the technology is also developed by the IHU, the impacts can extend to those of the development process itself (more on this in section 5.2).

FIGURE 1.5: IHU R&D Strategy



Source: IHU call for proposals' submission

The IHU's R&D activity supports the adoption of hybrid surgery by following a dual objective: conception and validation. In that respect, nine research programs (RP) have been designed to outline the pathway from identified needs, to the laboratory and finally to clinical application, with long term follow-up to determine their benefits (Figure 1.5).

RP1 focuses on improving preoperative and intraoperative imaging systems to optimize their use for "MIX Surg" procedures. Collected images are used to plan hybrid procedures and guide physicians through superposition of preoperative data over real-time images.

To get a step further in patient specific data acquisition, medical imaging is combined with biological data to provide an overview of both the anatomy and metabolism, and build patient-specific models for preoperative simulation and intraoperative image guidance (RP3). In the same way, biological information from samples is used to build advanced biological models for improving therapeutic targeting and specificity (RP4). The resulting RP3 and RP4 models are combined to develop preoperative MIX-Surg planning and simulation (RP5), necessary to define and practice the optimal procedures before the intervention.

For accurate positioning, precise tasks, and possibly automation (RP8), hybrid procedures require innovative research programs on real-time tracking and augmented reality (RP6) for the development of Robotic systems. The development of new hybrid devices (RP7), adapted to the new surgical operating rooms, is also central to this objective.

Finally, the IHU develops a specific research program dedicated to telemedicine for education and surgery (RP9). The program focuses on the development of online services for distant sharing of patients' data as well as distant mentoring and assistance.

The complexity of the IHU's research program highlights an intrinsic **dynamic** between its components. Each project, in any program, is expected to generate effects on other projects leading to improvements in the research process altogether.

A second part of this thesis will therefore be dedicated to establishing the methodological tools to **measure this dynamic and the R&D activity's impacts**. We first attempt an application of an existing method, developed by the University of Strasbourg, which we then adapt to better suit the IHU (and more specifically the surgical field) case.

4.3 Knowledge creation and teaching hybrid surgery

Developing and using hybrid surgical innovations may be sufficient on their own for the advancement of minimally invasive technologies. However, the adoption process can be further accelerated through educational and training activities provided by the IHU.

The IHU begins MIX-Surg specialty training with two fellowship programs:

- Clinical fellowships are offered for physicians who have completed their standard medical training. These fellowships are generally one to two year programs that present an opportunity for physicians to develop advanced skills in medical practice and research as well as learn hybrid techniques in Strasbourg's operating rooms;
- Research fellowships focus on training physicians to perform scientific investigations and development of new "MIX Surg" techniques under the guidance of seniors. These research fellows are considered to be at the core of the IHU's ability to study and advance new hybrid techniques.

A 3 year specialization training program is also developed to combine the expertise of all image guided minimal access interventions: laparoscopic surgery, flexible endoscopy and interventional radiology. Enrolled physicians have the opportunity to become specialists in "MIX Surg" after an initial 2-year surgical internship to earn basic imaging and procedural skills as well as the ability to care for complex patients.

Based on Standford university's BioDesign program, the IHU also offers a 1 year curriculum to teach physicians the basics behind technology transfer and medical device commercialization from ideas to reality. By collaborating with the "Ecole Nationale Supérieure de Physique de Strasbourg" (ENSPS), a new focus on technologies needed for MIX-Surg disciplines is also being included within the bioengineering curriculum.

Taking example off IRCAD's training activity, the IHU will also train physicians, nurses and other healthcare professionals in its hybrid operating rooms. These medical education courses benefit from the support of industrial partners as well as medical experts from around the world.

From our point of view, as with R&D, the institute's educational activity can also be considered as generating its own impacts. However, considering that this activity was the least developed by the institute at the time of this thesis, we mostly focus our work on the treatment and R&D activities.

5 Evaluating surgical innovations: the needed literature and our approach

The IHU's activities are expected to generate unique impacts, the evaluation of which should provide advocacy for further investing in hybrid surgery. To conduct such an evaluation, however, analysts need to collect and exploit knowledge from two distinct disciplines: health economics and economics of innovation.

Aside from these two main branches of economics, we also utilize our knowledge in cost management and econometrics for performing our evaluations. The former has proven to be particularly useful in determining the impacts of innovations on the cost of surgical care while the latter is used for conducting comparative analysis in case studies by exploiting the IHU's clinical trials' database.

In this section, we try to describe the literature necessary for conducting socio-economic impacts evaluation of the IHU's activities; namely health economics and economics of innovation. Each discipline is put in context by describing how it will be used: health economics for evaluating treatments and economics of innovation for evaluating R&D.

5.1 Health economics for evaluating treatments

Health economics is a relatively new branch of economics that can be traced back to 1963 with the early works of Professor Kenneth Arrow considered as one of the pioneers in the field [Arrow, 1963]. At its appearance, the concept of economics in the healthcare sector revolved around the study of manpower issues and care quality.

Over the years, greater acknowledgement of the usefulness of economic evaluation in healthcare decision making has paved the way for a number of methodological developments. Today however, as skilled labor becomes abundant and care quality reaches its highest levels, the existing methods are no longer sufficient to fully capture the added value of innovation.

The IHU understands the underlying difficulties in published methodologies, and the need for health economic evaluations as an integral part of using hybrid surgical technologies. For this reason, throughout this thesis, we utilize our amassed knowledge in

health economics to attempt and create adapted methodologies for evaluating surgical procedures.

5.1.1 Economic evaluation as part of health technology assessment

The World Health Organisation (WHO) defines health technology assessment (HTA) as *"a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology"*. The goal of HTA, as described by Taylor *et al.* [2009], is to assess the clinical evidence and cost effectiveness of medical devices and pharmaceutical products in order to inform the policy decisions of healthcare decision makers on therapy access. Through this process, it is possible to improve the adoption of cost-effective new technologies and prevent the use of technologies that are of doubtful value for the healthcare system.

Economic evaluation is one of the four pillars of HTA that mainly addresses the question of allocative efficiency for scarce resources where decision makers face two or more choices with different levels of inputs and outputs. To better understand the role of economic evaluation in the healthcare environment, we outline the principles by which the healthcare market is driven as presented by Arrow [1963] and outlined by Morris *et al.* [2007]:

Demand

- There is no possibility of learning through trial and error. Recovery from a disease is as unpredictable as is its incidence, patients are therefore uncertain of the quality of the product (treatments);
- The physician naturally have better knowledge of treatment effects than the patient who cannot test the product before consuming it. Both parties are aware of the information asymmetry;
- The existence of medical insurance removes the incentive on the part of patients to search for the best value for money.

Supply

- Entry to the profession is restricted by licensing which tends to increase costs;

- Physicians' behavior is, theoretically, governed by a concern for the patient's welfare and is, in principle, completely divorced from self-interest;
- Providers (hospitals) with goals other than profit maximization dominate the provision. Social and ethical factors play an important role in their behavior.

With modern tools of information gathering and access, patients have the possibility to be better informed about their illness/procedure but they still lack the medical experience and knowledge to have any significant (and rational) impacts on the choice of treatment. When we add up the existence of uncertainty in outcomes, patients are automatically forced into a trust relationship with their physician who becomes the decision maker.

In a publicly financed activity-based payment healthcare system, the moral hazard tends to reduce the importance of cost for both consumers and providers. Patients will seek the best care at all cost and hospitals will tend to increase their profit margins by inducing additional activity. The latter is theoretically possible considering that the trust relationship discussed in the previous paragraph shifts all the decision making power to the physician.

As a regulating agent and main source of funding, the government's response consists in formulating best practice recommendations and making sure they are followed through an increase in activity monitoring. However, these measures have proven inefficient as shown by the current French healthcare's financial deficit.

In a context of financial deficit and information asymmetry where the healthcare providers are the decision makers, economic evaluations serve as a guarantee for hospitals, physicians, patients and the government. Hospitals and physicians back up their choice of care by demonstrating the effectiveness of their procedures/technologies; patients are guaranteed the highest utility from their treatment and; finally, governments can expect the highest cost-benefit ratio from the practice they reimburse.

5.1.2 Types of health economic evaluations

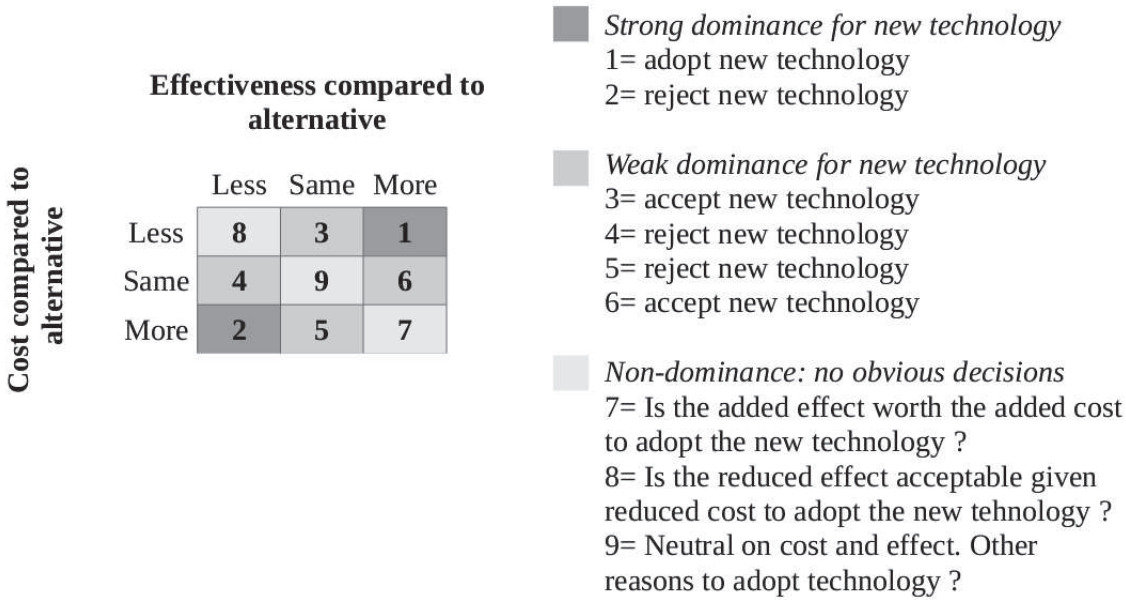
One of the most cited books in health economics by Drummond *et al.* [2005] describes four methods for the economic evaluation of healthcare programs: cost-analysis (or cost-minimization), cost-effectiveness, cost-utility and cost-benefit.

Cost-minimization only addresses the question of resource use and whether a new technology or program reduces cost compared to its alternative. In healthcare, this approach is only pertinent when the programs being compared yield the same outcome in which case the choice is restricted the the least costly. Note, however, that the results from this approach are likely to vary depending on the costing method used and viewpoint adopted by the analyst for an item may be a cost from one point of view but not from another.

Cost-effectiveness (CEA) is a full economic evaluation that examines both costs and consequences of healthcare programs. It is most pertinent in situations where the decision maker with a limited budget is considering a limited number of options.

The particularity of CEA lies in the fact that only one outcome measure is taken into account and is expressed in natural units. A comparative cost-effectiveness is therefore restricted to programs that influence the same outcome measure, examples include "cases detected", "cases prevented" or even "life years saved".

FIGURE 1.6: CEA decision making



Source: Drummond *et al.* - "Methods for the Economic Evaluation of Health Care Programmes"

When the comparison between two technologies show either weak or strong dominance, the conclusion as to whether reject or adopt the new technology is quite straightforward. When non-dominance is shown, the decision making process would then consist in determining an incremental cost-effectiveness ratio (ICER) expressed as the ratio of the variation in cost over benefit.

The ICER is then compared to a threshold value λ with the new technology being worth the investment if ICER $< \lambda$. In 2005, the World Health Organisation published the threshold values for its 14 regions from which they derived three categories of cost-effectiveness: highly cost-effective (less than GDP per capita); cost-effective (between one and three times the GDP per capita); and not cost-effective (more than three times GDP per capita).

Cost-utility (CUA) is a type of analysis commonly used in pharmacoeconomics, where the outcome measure takes into consideration the notion of preference. The most common example being Quality Adjusted Life Years (QALYs), or some variant such as Disability Adjusted Life Years (DALYs), which combines life expectancy and Health-Related Quality of Life (HRQoL). The latter is typically measured through surveys,

such as the EQ-5D or SF-6D, that assess the patient's physical, psychological and social wellbeing.

This method is most pertinent when the technology being assessed is expected to have an impact not only on mortality but also on morbidity/QoL and when health-related quality of life is considered an important outcome. In these cases, the analyst's role is to determine a cost per QALY that is then compared to a threshold determined by the willingness to pay for a healthy life year.

Cost-Benefit is much broader in scope for, while CEA and CUA only focus on one outcome measure, **it does not force any limit on the inclusion of consequences**. It is therefore possible to include the impacts of a new practice on patients, hospitals, employers and the government. However, the most notable difficulty in this type of analysis is the need to **translate all outcome measures into monetary terms** and avoid double-counting. The decision rule boils down to a comparison of the total cost and total benefit.

While all four health economic evaluation methodologies focus on the impacts of using an innovative technology, they do little to analyze the impacts of the R&D process that precedes usage. To be fair, combining the evaluation of both activities into one study appears to be rather uncommon.

From our point of view, the IHU's impact assessment in terms of "innovation" should be central in any health economic evaluation. Indeed, while the latter focus on studying a technology at a given, static, moment in time, the "innovation" approach takes interest in measuring the evolution of a technology, or process, and the changes in its impacts. The question should not revolve around calculating one cost-benefit ratio, but around integrating an iterative evaluation process into the institute's activity to continually update its evaluations.

5.2 Economics of innovation and surgical Research & Development

Economics of innovation is a branch of economics that dates back to Joseph Schumpeter's 1942 most influential work on the factors of economic growth [Schumpeter, 1934]. In his theory, Schumpeter argues that main economic changes are induced by innovation, entrepreneurship and market power. Technological innovations, as he highlights, create

profitable temporary monopolies which provide firms with an incentive to develop new products and processes [Wikipedia, b].

In surgery, the relationship between innovation and practice is complicated by the many different means through which innovation could occur. In one of a series of three articles on surgical innovation and evaluation, international healthcare professionals have taken care in pointing out this relationship as well as the possible means of evaluating it [Barkun et al., 2009; Ergina et al., 2009; McCulloch et al., 2009].

According to their observations, many reasons exist to innovate including reputation, personal reward, or even personality traits such as curiosity, ambition or search for knowledge. In surgery, however, the need often stems from having previously encountered a clinical problem during a surgical operation. The solution to such a problem can either be a result of meticulous planing, improvisation or flat-out serendipity [Barkun et al., 2009].

Technological and procedure focused developments are innovations, generally viewed as following a gradual or planned course. In surgery, the innovation process heavily relies on iterative approaches through which surgeons experiment, modify, enhance and then re-experiment their product. As Barkun *et al.* [2009] point out, the high variability in this process makes it difficult for analysts to decide whether the operation is simply an evolutionary variation or the first step in a new experiment.

It appears that a certain dynamic exists between projects and the surgical practice itself. The expected gains are not only financial but can also be expressed in various ways be it in terms of knowledge gain, reputation or network extension for example. In innovation economics, these factors form one of the core concepts by not simply being considered as outputs, but also as inputs for the R&D process and its associated socio-economic impacts.

With respect to the particularities of the surgical field, the IHU's process of creating hybrid surgical technologies should be viewed as an integral part of their hybrid treatments. Therefore, to analyze the impacts of the R&D activity, we contribute to **creating an adapted evaluation methodology** the results of which can be combined with those of the health economic analysis.

5.3 Methodological framework

According to its business model, the IHU conducts highly interdependent activities of care, development and education focused on hybrid surgical innovations. Each activity, according to the institute, is expected to generate impacts on different types of actors the measurement of which is currently hindered by a lack of methodological tools. In particular, we have not identified any methodology that would evaluate all three activities and combine their impacts in a unique cost-benefit ratio.

Through this thesis, we contribute to the development of a more unified framework that allows the IHU to evaluate the efficiency and socio-economic impacts of its innovations. To do so, we mainly focus on assessing the impacts of **the creation as well as the use** of innovative technologies considering that they were, at the time of conducting the analysis, the institute's most developed activities.

Indeed, this thesis started at exactly the same time as the IHU's creation date, late 2012. As such, the three years that make up the timeframe for our work were also essential to start developing the institute's different activities.

FIGURE 1.7: IHU Impacts

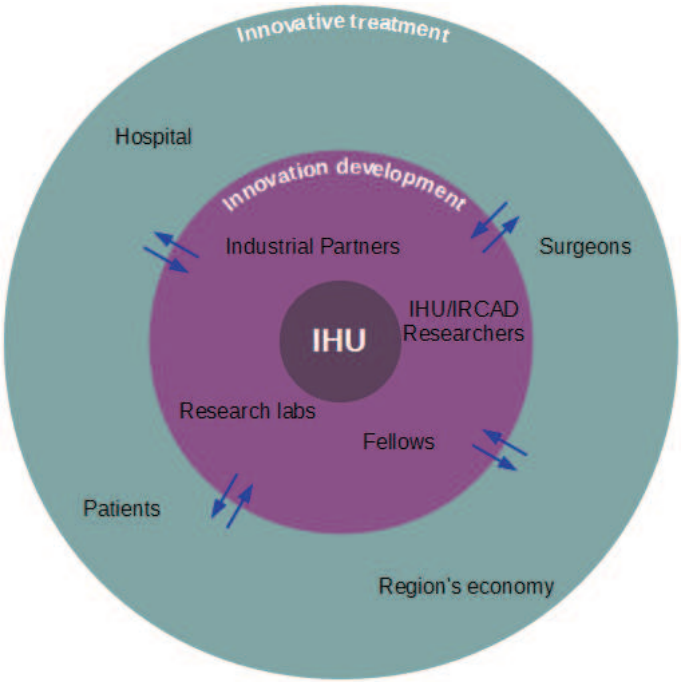


Figure 1.7 describes the general idea behind our work. At the center, we position the institute of image guided surgery (IHU) whose missions, at least those that we

evaluate, involve the creation (innovative development) and use (innovative treatment) of innovative surgical technologies.

The development of hybrid surgical technologies is expected to impact not only the IHU but also its different partners, namely the industry, research laboratories, fellows and IHU/IRCAD researchers. Such an impact can be translated in various ways such as an increase in each partner's reputation, network or general pool of knowledge.

The fruit of IHU-Partner collaborations is mainly meant to manifest itself in the form of innovative cost-effective treatments. New procedures and surgical technologies are expected to increase patients' quality of life, control hospitals' expenditures, improve surgeons' performance, and even boost the region's economy. The research and development process is therefore an integral part of the treatment activity.

One particularity of the surgical field, as argued in section 5.2, is the role of surgical practice in R&D. To be more precise, the IHU expects a translation of R&D into innovative treatments but also the participation of surgeons, along with clinical experimentation, in the emergence of new research projects or the improvement of existing innovations.

To evaluate the impacts of these activities and the dynamics that exists between them, we decompose our study into three points corresponding to the analysis of:

- The impact of introducing an innovative surgical technology on the surgical operation's cost, thus covering the first part of the innovation treatment circle;
- The benefit for the patients, the hospital and the economy generated by using the surgical innovation, thus covering the second part of the innovation treatment's impacts;
- The impacts of the research and development process at the origin of the used surgical innovation's creation, thus covering the innovation development side and the interactions that exist between the two circles.

We start with the cost analysis as healthcare expenditures are currently a "hot topic" in France. Furthermore, in health economics, analyzing the cost of an innovation is the first step for conducting any economic evaluation.

To complement the creation of our costing methodology, we turn our focus on the quantitative assessment in terms of "benefits" of introducing innovative minimally invasive surgical technologies in the operating room. This second step logically follows the cost analysis considering our objective to create a comprehensive cost-benefit evaluation methodology.

Despite the fact that, chronologically, the R&D process precedes the use of an innovation as a treatment, we analyze this activity in the last chapter. This decision is mainly due to the complexity of this qualitative analysis and the need for the IHU to implement its R&D activity before we are able to evaluate it.

6 Conclusion and thesis plan

History has shown a growing interest, on the part of governments and decision makers, in the use of economic evaluations to determine the cost and benefit of surgical innovations. In France, current political decisions appear to further emphasize this interest as the future will be increasingly dependent on technology assessments for justifying adoption and development.

As a French institute specialized in the creation and use of innovative surgical technologies, the IHU has a clear need for adapted socio-economic impacts evaluation methodologies. From our point of view, current health economic methodologies cannot fulfill this need on their own. They should be further developed, transformed and completed, potentially borrowing concepts from other economic disciplines.

Throughout this thesis, we will seek to answer the question we posed in the introduction: **how do we evaluate the efficiency and the socio-economic impacts of minimally invasive surgical innovations?** To do so, we decided to decompose our study into three main chapters.

Following this introductory chapter, Chapter 2 will be dedicated to the development of a methodology for calculating the cost of surgical operations that use hybrid innovations. After identifying common cost calculation practices in the literature and providing a description of current methods used in Strasbourg's hospital, we develop our own methodology using the highly innovative technology Da Vinci robotic surgical system as a case study. Our choice for this technology is based on its consideration by the hospital's surgeons as the typical example of a minimally invasive innovation, and on the possibility of directly accessing a detailed database created by the IHU.

Chapter 3 focuses on cost and effectiveness measures that the literature considers to be of relevance for the assessment of surgical care. Using this collected information, we expand our cost analysis started in Chapter 2 by covering the cost of the entire care pathway. We then provide some elements that we consider as possibly reflecting the impacts of minimally invasive surgical innovations on the hospital, the society and the economy.

Chapter 4 is mainly concerned with the impact assessment methodologies for evaluating the creation process of hybrid surgical technologies. After reviewing the literature on the

subject, we apply then adapt an established evaluation method, created by Strasbourg's University in 2013, to better reflect the particularities of the surgical field's R&D.

The last chapter concludes our work recalling the objective of the thesis as well as summarizing our contributions to achieve it. We present different directions for future research that will, from our point of view, help advance discussions over the assessment of the impacts of minimally invasive surgical innovations.

Chapter 2

Cost evaluation of minimally invasive surgical technologies: the existing methods and our contribution

1 Introduction

Until recently, the cost management of surgical care in developed countries, especially in publicly funded institutions, has been considered a secondary objective to all parties involved. Patients were (and still are) covered by state or private insurance, hospitals had access to a seemingly unlimited amount of funding and surgeons were focused on caring for their patients no matter the cost.

Today's economic context has marked a shift in the governments' interest to address the financial situation of all sectors, healthcare included. Multiple requests to control, and even reduce, expenditures have put a considerable strain on hospitals who appear to lack the necessary means to comply.

The main problem stems from the hospitals' lack of precise surgery cost evaluation methodologies, which is particularly threatening to the emergence of surgical innovations whether hybrid or otherwise. Without consistent metrics, it is practically impossible

to perform comparative health economic evaluations and provide guidance to decision makers or hospital managers as to which procedure is cost-effective.

Furthermore, in health economics, cost is the central piece of all forms of evaluations whether we choose to apply a cost-effectiveness, cost-utility or cost-benefit methodology. The first question to answer when deciding to adopt an innovative minimally invasive technology is therefore: "how much would it cost to use?".

At the start of the thesis project, we took interest in analyzing how the hospital would approach this question with a particular emphasis on a robotic system considered as its most innovative possession. As expected, they expressed their inability to provide a precise answer with the currently used data collection and analysis mechanisms.

In this chapter, we focus on understanding the reasons behind the hospital's lack of methodological guidelines for evaluating the cost of innovative surgical technologies. We also attempt to remedy this problem by creating a costing methodology based algorithm to be used by the IHU and, possibly, the hospital.

To start, following this introduction, the second section will go over the historical changes in French healthcare and the associated tools that are made available to hospitals for managing their costs. Both the strength and weakness of these tools will be pointed out, especially regarding the evaluation of innovative minimally invasive surgical technologies.

The third section will provide the reader with an overview of multi-national recommendations for cost approaches in economic evaluation studies. We will also emphasize the difference between economic and health economic terms as to avoid any confusion.

In a fourth section, we will describe the minimally invasive procedure used as a case study for establishing our surgical cost evaluation methodology. We will also present a survey of how cost calculation and reporting is done in the surgical literature with an emphasis on computer assisted surgery.

The fifth section will be dedicated to describing our proposition for a surgery focused costing method. We will also establish a benchmark value, using national average data and method, for validating our results and proposed methodology.

The sixth and seventh sections will demonstrate how our costing method can be applied following two different approaches. The choice of which version to apply will highly depend on the available data and the analyst's objective.

The discussion section will be dedicated to interpreting our results, discussing the proposed method's usefulness as well as presenting its limits. Finally, we conclude by summarizing our findings and discussing ideas for future work.

2 Overview of the French healthcare mechanisms

To understand the reasons behind the hospital's reluctance to communicate a cost per operation of an innovative surgical technology, we must first understand how they perform their cost calculations. To do so, however, we must also be aware of the historical events that led them to possess the management tools they use today.

This section begins by going over the French Social Security's history from its creation until today with an emphasis on the reimbursement mechanisms. We then attempt to describe Strasbourg hospital's cost calculation methodology, with as much detail as possible, along with a critical overview of its limits.

2.1 History of the French Social Security

With the declaration of human rights during the French revolution, a great shift was marked in the view citizens had of social assistance. Every unfortunate or poor citizen acquired a right for assistance that is considered as a divine obligation to be fulfilled by the society.

The nationalization of hospitals and the creation of an aid fund ensued as the state assumed control of assistance related activities. The revolution, however, was unable to secure the funds necessary for the government to fill such a role.

The 1830 to 1905 period saw the emergence of philanthropy during which the rich and business owners often covered the cost of medical care, pensions and training of their personnel. Fraternal benefit societies were formed based on voluntary collective prevention while being limited to either a few activities or businesses.

It is only in July 1893 that the first social assistance law for free medical help ("Aide Médicale Gratuite") [Sécurité Sociale] was voted, thus forcing every community to cover the basic rights of its needy. For the first time in history, the concept of reimbursement appeared along with the emergence of healthcare centers.

In the first half of the 20th century, the influence of Germany's chancellor Otto von Bismarck's reforms for the institutionalization of social protection became a desirable prospect for the French social assistance system. The principles by which the Birsmarckien model functions exclusively favor the working force who, by working, gain the

right to benefit from social insurance. The adherence to this system, however, was only compulsory for employees whose salary was under a certain quota.

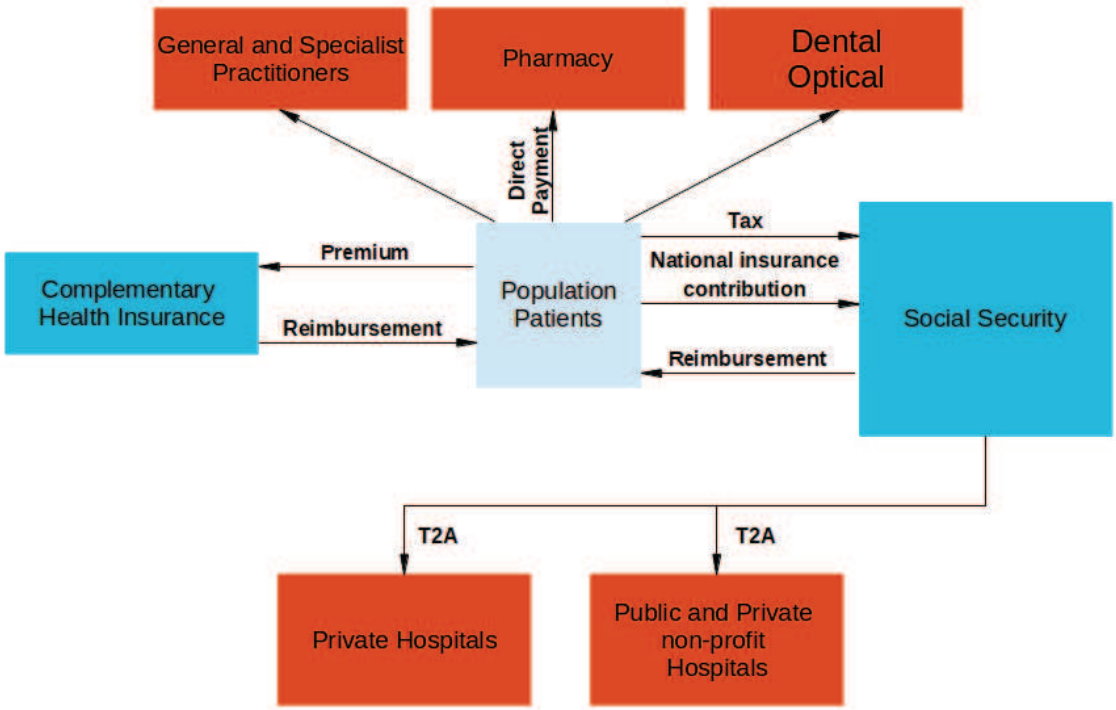
The term Social Security only appeared after the second World War with the influence of Lord William Beveridge's reforms for a universal, uniform and unique system. Universality of coverage for the whole population without distinction, uniformity of care providing the same quality for all the insured and uniqueness in that all risks are covered by the same system.

The French Social Security was historically considered as a Beveridge/Birsmark mixed model with a universal coverage system compulsory for both employees and those of similar grade. The funding of this system imposed a contribution from employees and employers on a relatively equal scale along with several other sources of revenue (fiscal tax, generalized social contribution, etc.).

On the one hand, up until 2003, public healthcare centers were endowed with annual and limited financial envelopes called "Dotation Globale" [DGOS]. The calculation of this financial envelope's value depended on the center's total activity and was revised every year; adjusted for a reference rate of increase in hospital expenses compared to the previous year.

On the other hand, private hospitals without vocation for public healthcare services directly billed the health insurance on a per act principle. The price list was determined following negotiations with the regional hospital agencies on a historical basis with geographical variations.

FIGURE 2.1: French Social Security Mechanism



The disparities created between public, private non-profit and private profit centers made their monitoring extremely challenging and any attempt to compare costs between the public and private sectors were proven to be difficult. The government was no longer able to maintain a global budget system which they therefore soon sought to gradually replace with an activity based model (T2A), as presented in Figure 2.1.

2.2 Introducing the T2A and PMSI principles

The activity based model (T2A) aims at providing a more coherent method for reimbursing care as well as monitoring, reporting and financing each hospital's activities. To reach these objectives, the French government established in 2005 an information system "Programme de Médicalisation des Systèmes d'Information" (PMSI), see Appendix A, to systematically collect data on particular diseases and types of medical or surgical care for each patient while also enabling a classification of each care pathway.

2.2.1 T2A reimbursement mechanism: GHM vs GHS

When a patient is admitted in acute care, denoted as "Médecine Chirurgie Obstétrique" (MCO), his personal information (sex, age, postal code etc.) as well as any diagnosis, tests and medical/surgical acts are registered by the hospital's PMSI base in one or several "Résumé d'Unité Medicale" (RUM). The combination of the latter form the standardized discharge abstracts, "Résumé de Sortie Standardisé" (RSS), that are patient specific and are used after anonymization as a database for non-medical professionals and a mean of communication with the Social Security.

Depending on the information presented in his medical summaries, each patient is then classed under a "Group Homogène de Malades" (GHM) similar to Boston's "Diagnosis Related Groups". The French medical classification of clinical procedures, "Classification Commune des Actes Médicaux" (CCAM), summarizes the characteristics of each act by associating it with one specific code. These codes are then used by an algorithm, at the hospitals' disposal, to identify the major diagnosis categories, associated surgical or medical acts and determine the output GHM.

For each coded GHM in the PMSI, the hospital receives a nationally determined reimbursement amount labeled "Groupe Homogène de Séjour" (GHS) that should, theoretically, cover their healthcare expenditure. To illustrate how this reimbursement system works, we take a look at laparoscopic Sleeve Gastrectomies and Gastric Bypass procedures coded under the GHM 10C131 "Interventions on the digestive track for obese patients other than gastroplasty". The last number in this code defines the complexity (from 1 to 4), or level, of the medical/surgical care with higher numbers being associated with a higher reimbursement; while the letter (C or M) indicates whether it is a surgical or medical act.

TABLE 2.1: Extract from the Public Hospital GHS List - 2014

GHM	Libellés	GHS	SB	SH	EXB	EXH
10C131	Interventions digestives autres que les gastroplasties, pour obésité, niveau 1	4 687.95	0	17		315.42
10C132	Interventions digestives autres que les gastroplasties, pour obésité, niveau 2	6 120.88	0	18		293.07
10C133	Interventions digestives autres que les gastroplasties, pour obésité, niveau 3	11 316.72	0	31		315.42
10C134	Interventions digestives autres que les gastroplasties, pour obésité, niveau 4	20 774.22	11	68		569.39

Data source: ATIH - *http* : *//www.atih.sante.fr/*

As table 2.1 demonstrates, several factors other than the severity level impact the reimbursement value. While we only present an extract, the full list of GHS values is provided by the "Agence Technique de l'Information sur l'Hospitalisation" (ATIH), which publishes a freely accessible yearly updated list on their website.

"Seuil Bas" (SB) and "Seuil Haut" (SH) define the minimal and maximal length of stay between which the reimbursement value does not change. In other words, whether a patient coded under 10C131 has a length of stay of 0, 5 or 17 days, the hospital would still be reimbursed 4 687.95 Euro.

For the fourth severity level, a SB is defined to impose a minimal length of stay of 11 days for any patient registered under 10C134. If the hospital discharges the patient before the SB, the reimbursement is devalued to that of the GHM of lower level (10C133 in this case). When a patient's length of stay exceeds the upper bound (SH), the hospital receives a supplementary EXH amount for each additional day.

To determine and adjust these parameters, the ATIH conducts yearly national cost studies during which a group of voluntary hospitals share some elements from their

financial records in exchange of a compensation. The objective being threefold:

- Construction of a national cost range which forms the foundation for determining the reimbursement values;
- Publishing of a mean cost per GHM to which each healthcare provider can compare their own cost;
- Creation of a database useful for analyzing potential changes to the GHM classification.

2.2.2 ICR as a tool for cost management

The PMSI does not only concern itself with the definition of reimbursement categories and values but also provides French hospitals with a method for calculating the cost per surgical operation using what they call "Indices de Coût Relatif" (ICR). To be more precise, the ICR are a tool for calculating the average cost per procedure by allocating to every patient admission a portion of the total annual expenses of some of the hospital's centers.

To determine the number of ICR points per procedure, the French social security approached doctors, accounting experts and biomedical engineers to evaluate resource use for each type of intervention. A laparoscopic Sleeve Gastrectomy (CCAM code: HFFC018), for example, was valued at 322 operating blocks and 167 anesthesia ICR (ATIH - Tables des ICR CCAM V22) while a laparoscopic Gastric Bypass (CCAM code: HFCC003) was valued at respectively 516 and 200 points.

The described numbers, however, are based on several principles that demonstrate their lack of precision [Finances Hospitalières]:

- Optimal conditions in terms of resource availability and use are considered (no shortage of personnel nor instruments);
- Only a part of the direct cost is taken into account (disposables are not always taken into account);
- Data only compiles estimations of main cost parameters: working hours, mobilised personnel, instrument use;

- Analysis based on experts feedback and opinion, not on an actual retrospective database.

While the number of ICR points per procedure is nationally determined, each hospital has its own set of cost per point needed to complete the analysis. To better understand how such calculations are made, we take a closer look at Strasbourg's University Hospital's organization and how the PMSI influence their cost management and calculation process.

Beginning 2008, the adoption of an activity-based payment model altered every hospital's organization, Strasbourg included, to form a mix of activity centers called "Pôle d'Activité". Every center is managed by one medical officer mandated to fix objectives of medico-economic, care provision, teaching and research efficiency along with the hospital's top management.

To comprehend the usefulness of ICR points, an important distinction should be made between activity centers that have a hospital ward, and therefore receive the GHS (reimbursement), from those that do not in which case they are considered medico-technical centers. Examples of the latter include anesthesia, imaging and operating blocks which possess their own individual cost per ICR used to allocate their expenses to centers that use their services.

Strasbourg's University Hospital is divided into a total of 22 activity centers among which the "Pôle Hépato-Digestif" (P.4190) that manages all procedures related to the digestive system. The center itself is divided into a Digestive (S.2210) and a Hepato-Gastroenterology (S.2215) service each with their own set of specialized surgeons and functional units, "UF", mainly used for resource allocation and cost tracking.

At the lowest level, the Digestive service is divided into 11 functional units that regroup costs according to whether they can be traced back to the operating blocks (UF.2118), hospital wards (UF.2211/2212/2213), outpatient consultations (UF.2073), functional explorations (UF.2074) or other cost drivers. For example, the UF.2118 regroups the total yearly operating room expenses such as instruments, medical personnel and medical devices specific to digestive procedures.

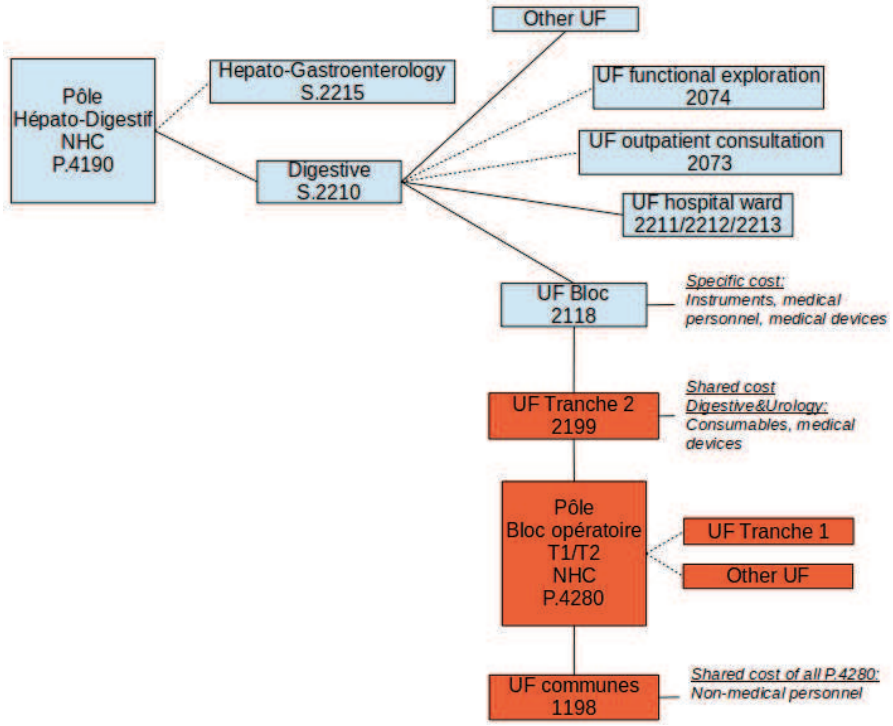
Other operating room expenses are shared by different specialties and do not figure in these specific UFs but appear instead in a medico-technical center, "Pôle Bloc Opératoire"

(P.4280). More precisely, the UF "Tranche 2" (UF.2199) of the aforementioned center traces all operating room costs shared by digestive and urology surgical procedures. These costs include, but are not limited to, consumables (exp: gloves, syringe etc.) and medical equipment (exp: operating table).

The calculation of a cost per ICR point for the UF.2118 is done through a series of accounting treatments that aim at providing a method for calculating the cost per procedure attached to this functional unit (such as sleeve gastrectomy or gastric bypass). At the same time, using the cost per ICR point serves as a mean for the hospital to distribute the expenses of its medico-technical centers.

We provide an example for the "Pôle Bloc Opératoire" but a similar analysis can also be applied to anesthesia, imaging and other medico-technical centers. The method is as follows:

FIGURE 2.2: Example of Strasbourg University Hospital's Organization



1. Determine the total number of ICR points in P.4280 (Number of procedure times ICR points per procedure);

2. Determine the total number of ICR points in UF.2199 (which includes both digestive and urology surgical procedures)

   Suppose that the ICR UF.2199 represents 70% of the ICR in P.4280;

3. Allocate 70% of UF.1198's total annual expenditures to UF.2199;

4. Determine the total number of ICR points in UF.2118 and divide it by the ICR points in UF.2199
   Suppose that the ICR UF.2118 represents 60% of the ICR in UF.2199;

5. Allocate 60% of UF.2199's total annual expenditures (including the value from step 3) to UF.2118;

6. Identify whether patients were admitted in UF.2211,2212 or 2213 and determine the total number of ICR points for each group of patients
   Suppose 50% of the ICR UF.2118 are due to patients who were admitted into UF.2211;

7. Divide 50% of the total annual expenditures of UF.2218 (including the value from step 5) by the total number of ICR points of patients admitted into UF.2211;

8. Repeat steps 6 and 7 for UF.2212 and 2213. You now have a cost per ICR point for each patient according to the whether they were admitted in UF.2211,2212 or 2213.

After applying the first five steps, every medico-technical center will have its expenses distributed between activity centers that use them. From an accounting point of view, the balance sheet "Pôle Bloc Opératoire" should therefore be at equilibrium.

In 2013, after adding a portion of the hospital's overhead cost, the application of the eight steps for the "Pôle Hépato-digestif" yielded the following results:

Table 2.2: Cost per ICR point 2013 - Digestive Service

ICR	UF	Allocated Cost	ICR points	Cost per point
Block	2211	1 363 709.14	238 663.00	5.71
	2212	1 180 316.91	207 482.00	5.69
	2213	1 323 369.15	230 963.00	5.73
Anaesthesia	2211	579 027.76	118 930.00	4.87
	2212	567 880.69	116 650.00	4.87
	2213	549 678.33	112 911.00	4.87

Source: Strasbourg's University Hospital - Department of Medical Information

Using the values presented in Table 2.2, a laparoscopic Sleeve Gastrectomy of a patient admitted into UF 2211 with 322 operating blocks and 167 anesthesia ICR would cost 2 651.91 Euro (1 835.40 from the operating room, 813.29 from anesthesia) while a laparoscopic Gastric bypass costs 3 920.36 Euro (2 941.20 from the operating room, 974.00 from anesthesia). Both procedures have a reimbursement of 4 687.95 Euro at the first severity level, making Sleeve Gastrectomies more cost-advantageous for the hospital if we consider an identical length of stay.

Note that since the GHM mainly depends on major diagnosis categories, the more exams the hospital performs on a patient during the same admission, the higher the cost without any change in the reimbursement. It is therefore in the hospital's interest to promote the use of precise (effective) techniques as to limit wasteful practice.

2.3 Limits of the PMSI methodology

The current methodology used for cost calculation at the "Centre Hospitalo-Universitaire" (CHU) Strasbourg has several limits that makes it undesirable to the activity of the IHU Strasbourg. Any institution with the aim of developing or acquiring innovative surgical technologies will be faced with a number of obstacles that highlight the existing methodological weakness.

The first relates to the fact that new developments are not systematically evaluated to determine a specific CCAM code and thus ICR points. To evaluate the cost per operation of an innovative procedure, the hospital would need to base their analysis on the most similar procedure while artificially varying the cost per ICR point (such as adding the purchase price of the medical device).

Such a method would prove inefficient as innovations usually tend to replace existing tools or alter the operation in other manners, which would not be captured, such as:

- Increase or decrease in the operation duration;
- Change in the number of personnel, for example if an additional assistant is needed or no longer required;
- Replacement of existing instruments with technology specific ones.

The second obstacle lies in the method of defining the hospital service's cost per ICR as the total yearly expenditure divided by the total points. When a surgical technology replaces an existing one with an expected reduction in the cost per operation, the impact would be translated as a decrease in the yearly expenditure of the entire service meaning that:

- in a context of continuous innovation and rapid changes, the impact of one technology or event can be overshadowed by the impact of another;
- for the same number of ICR points for the existing and new technology, the cost per operation of all procedures attached to the service is reduced translating a lack of transparency regarding the impact of an innovation.

From a revenue standpoint, as innovative procedures need to be evaluated by the HAS before being registered on the list of reimbursable products and having an associated GHM, hospitals can only code them under an existing group and thus be reimbursed at a possibly unfitting value. This is especially bothersome, particularly for the IHU, when defining the amount to charge foreign patients as such surgical institutes will have a dual objective: competitiveness and profit maximization.

When focusing on medical tourism, even public hospitals are placed in a competitive market context as many countries attempt to project the image of a medical haven. To be competitive, healthcare institutes ought to present patients with the highest quality at the lowest price possible for each procedure. However, to have a sustainable business model, these institutes also need to avoid charging prices lower than the cost of each service.

As the ICR method yields average costs for different procedures combined, it is unable to fill both objectives simultaneously and will tend to favor procedure that are undercharged. By construction, an average value of a data set is lower than the highest points, thus some procedures will be undercharged, and higher than the lowest ones, thus some procedures will be overcharged.

The observation of the ICR method's effects goes beyond medico-economic evaluations as their impact can be expected at both a hospital and national level. Institutes that base their investment choices, i.e. whether to acquire/continue using a technology or

technique, on this tool either risk missing out on good opportunities or mistaking bad ones for good deals.

Missing out on good opportunities to either decrease healthcare costs or increase care quality would be felt by both the Social Security and the patients. Adopting toxic practices would further increase the hospitals' deficit forcing them to increase their debt and compromising both their patients' future as well as theirs.

The presented weaknesses in the currently used methods for evaluating surgical costs are a clear indication of the hospitals' need for a more comprehensive and adaptable methodology. The IHU should be particularly desiring of such a method as to maximize its ability to demonstrate the usefulness of developed hybrid surgical technologies.

3 Cost approaches in health economics: definitions and recommendations

Before providing a literature review of the existing methods for cost evaluations, we present the reader with a few definitions of economic terminology and underline an important distinction between the French and English languages. During the thesis, we noticed many differences in the definition of commonly used terminologies by both economists and health economists, which rendered discussions quite confusing.

The next subsections will also go over the methods for assessing the cost of production as highlighted in the economic literature which, we hope, will give the reader the tools necessary to better apprehend our work.

3.1 Economic definitions

In a general sense, economics is a social science that concerns itself with the behavior and interaction of economic agents such as individuals, firms, markets or countries. The field itself is broken down into two branches: Macro-economics and Micro-economics.

The first branch only deals with entire economies (production, consumption, savings, and investment) and measures (unemployment, growth, public policies) affecting it on a national level. The second focuses on the behavior of individual economic agents and their interactions with the market.

Among the topics of micro-economics is "Costs of production", our point of interest for this section, which discusses the necessity and possibility of measuring the cost of an object or service as the sum of the value of resources needed to make the output available[1]. To conduct such a study, defining the distinction between *cost* and *charge* is essential for any analysis to have any utility.

Cost is the price paid by the producer for resources consumed (input) during the production process. Charge is the price of the output, usually defined by the producer but also influenced by regulations and the market, that usually covers the need for the institution to break-even and be solvent [Finkler, 1982] or make profit. While both terms

[1] In micro-economics, we also consider *opportunity costs* which reflect the gains that had been foregone from the best alternative use of resources committed to a studied activity or technology.

reflect a cost, they do so from different perspectives and therefore should not be used interchangeably.

We also draw the reader's attention on the difference between the French and English terminology as to avoid any misunderstandings. In French, the notion of "charge" means the sum of expenditures for the ongoing accounting year. In English, it is the sum paid by the consumer (the amount he is charged) for a product or service.

A second distinction should be made between cost and *expense*. An expense is a payment from a budget that reflects, for example, the purchase price of an equipment or the salary of an individual. The cost, however, represents the act of consumption (or draw on resources) and is thus only initiated when the resource is used [Kristensen and Sigmund, 2007].

In accounting, another distinction is made between *direct* and *indirect* costs. A direct cost reflects the value of resources that are accurately traced to a cost object (a department, a project, etc) whereas indirect costs benefit multiple cost objects and cannot be accurately attributed to each. In surgery, for example, a glove's value is a direct cost induced by the production of the surgical act whereas the hospital manager's salary is an indirect cost distributable over all the hospital's activities.

Every direct or indirect cost can either be categorized as *fixed* or *variable*, a distinction particularly common in cost of production studies and useful for determining the break-even point. A cost is considered fixed if it does not vary according to the level of activity, in a certain "capacity range", while a variable cost does vary with the output. In our surgery example, the glove is a variable cost as the production of one additional surgical act requires several additional pairs. The operating room, however, is a fixed cost as the extra unit of output would not require the investment in a room unless it is already working at full capacity in which case we exceed the "capacity range".

We often stumble upon the term "overhead cost", or simply *overhead*, which can either be direct or indirect, fixed or variable. In both economics and accounting, it refers to expenses that must be covered on a regular basis independently of whether the activity is at its peak or non-existent. Infrastructure maintenance and amortization, for example, can be considered as indirect fixed overheads while electricity consumption can be regarded as a direct variable one.

3.2 Health economic definitions

In health economics, particularly for the evaluation of immunization programs, the World Health Organization (WHO) has expressed the need to differentiate between costs born by the health sector from those born by patients/families (including lost productivity), and future costs as a consequence of the intervention. Although it refers to medical treatment and not medical devices, the guide [WHO, 2008] provides several principles that are common to innovations in both fields namely the involvement of several players in the care process: healthcare providers, patients and society.

Traditionally, for the assessment of medical devices, the health economic literature suggests a distinction between *direct healthcare*, *direct non-healthcare* and *indirect* costs [Gold, 1996].

Direct healthcare costs refer to the resource consumption needed for providing the intervention. Resources include, for example, the cost of medical devices, hospital stay, pharmaceuticals and outpatient visits.

Direct non healthcare costs vary in nature and their consideration largely depends on the analysts' viewpoint. When a societal perspective is adopted, for example, all resources used to provide care such as travel/waiting time as well as lost earnings and all expenses avoided due to the treatment are to be included. However, when a narrower viewpoint is adopted, such as that of the Ministry of Health, changes that occur outside of the healthcare sector are no longer pertinent for the analysis.

Indirect costs (or productivity losses) combine both the cost associated with lost, or impaired, ability to work or to engage in leisure activities due to morbidity as well as lost economic productivity due to death. Note that the time a patient spends seeking care, participating in or undergoing an intervention is considered part of the intervention itself; lost productivity during this time-frame is thus considered a direct cost.

In both economics and health economics, the terms *average*, *marginal* and *incremental* are used to describe the method for reporting studies' endpoints. Average costs reflect the costs per unit of output in both fields.

In economics, both marginal and incremental are used interchangeably and describe the additional cost of producing one extra unit of output, i.e. one additional patient treated

or one additional unit of intervention produced. It is important to note that while average costs take both fixed and variable costs into account, the marginal approach is derived solely from variable costs (when in a certain "capacity range").

In health economics, the term incremental designates the difference between two alternative technologies and is thus completely different from the marginal concept. Incremental costs comprise a part of the core result of health economic evaluations, i.e. cost-effectiveness, cost-utility and cost-benefit ratios.

3.3 Methods for cost analysis: recommendations

3.3.1 Choice of perspective

Depending on each nation's healthcare system and the recommendations formulated by its healthcare agency, the distinction between direct health care, direct non healthcare and indirect costs is likely to be modified. The Danish Center for Health Technology Assessment's (DACEHTA) handbook by Kristensen and Sigmund [2007], for example, uses this classification but adapts the measures with regard to three levels of analysis: society, healthcare sector and hospital.

TABLE 2.3: DACEHTA - Cost perspective in economic evaluations

Perspective			Cost type	Resource
Society	Healthcare sector	Hospital	Direct costs: in hospital	Health personnel, medicine, utensils, tests, capital equipment (plant & buildings), in-patient stay(hotel), outpatient visits, overheads (food, lighting, heat, etc.), (research & training)
			Direct costs: in the primary healthcare sector	consultation with general practitioner, practicing specialist, physiotherapist, etc., prescription medicine (the danish national Health Insurance service's share), public surveys
			Direct costs: in other sectors	Home care & home nursing, social events, including support for medicine (municipal grants), aids
			Direct costs: for patients and families	User payment (medicine, dentist), transport, time spent on investigation/treatment, (unpaid) time spent by family or friends in caring for patients
			Productivity loss/gain in society	changes in patients' temporary absence through sickness, reduced ability to work due to sickness and disability, or lost production in the case of premature death
			Future costs	Future unrelated costs including health costs generated as a result of a patient's lifetime being extended or shortened

Source: DACEHTA - Health technology assessment handbook - Table 9.2

The Canadian Agency for Drugs and Technologies in Health (CADTH) [CADTH, 2006] provides a similar approach that emphasizes the role of a publicly financed healthcare with a distinction between three perspectives: societal, public payer and publicly funded health care system. When compared to the Danish presentation in Table 2.3, the Canadian approach is near identical with a public payer interested in all direct health and non-healthcare cost, and a publicly funded healthcare system interested in all cost categories except direct costs in other sectors.

Note that the WHO [WHO, 2008] recommends that future costs, such as increased consumption of healthcare services due to a life extension, not be taken into account considering that there has been no professional consensus in the literature over the measurement methodology to be used. The CADTH recommends only including these costs in a sensitivity analysis if data are available and their impact is expected to be substantial. They also recommend excluding resources for which there is identical use between the intervention and its alternative.

The French high authority for healthcare (Haute autorité de santé - HAS) chose to adopt a direct vs indirect cost definition without distinguishing between direct medical (health) and direct non-medical (non-healthcare). Their objective being the evaluation of production costs whatever their nature and whoever funds the intervention.

Their direct cost relates to all resources needed for the production of the analyzed interventions including patients' time. From their point of view, indirect costs refer to the impact of the intervention on patients' time devoted to work or leisure [HAS, 2012].

Both the Danish and Canadian guidelines recommend the adoption of the broadest and most extensive societal perspective for economic evaluations. The National Institute for Health and Care Excellence (NICE) [NICE, 2013] indicates that the perspective on outcomes should include all direct health effects whether for patients or not. All cost related analysis should be done from the national health service (NHS) as well as personal and social services point of view. The HAS, however, only states the need for a collective perspective that is sufficiently broad to take into account all stakeholders involved in the treatment.

3.3.2 Costing approach

In a general sense, as suggested by Larsen *et al.* [2003], cost evaluations can be broken down into three steps:

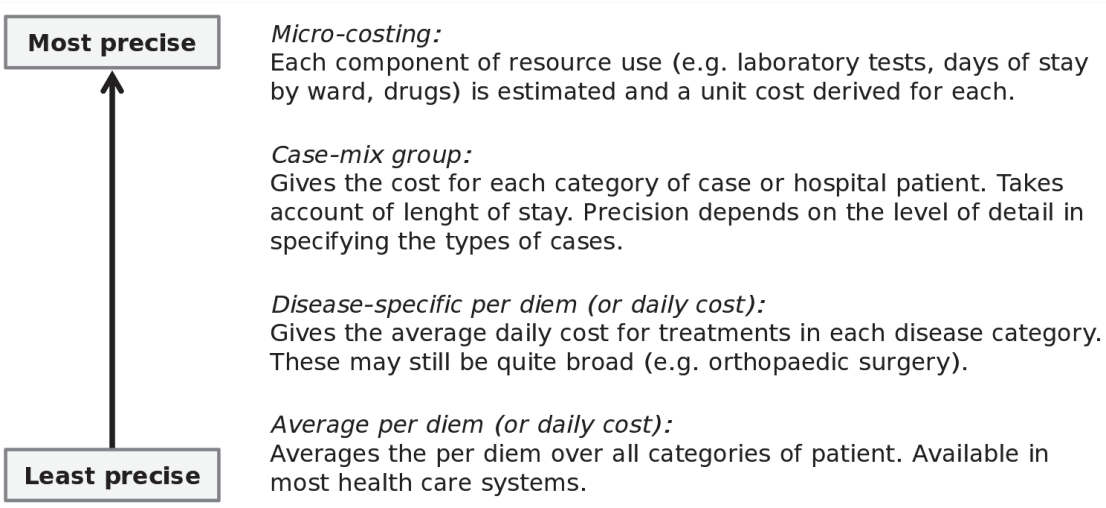
1. Identification of the relevant resource use involved in the health technologies under comparison;

2. Measurement of resource use in physical units, i.e. the determination of the quantities of resources;

3. Valuation of the unit costs of the resources used.

The identification of relevant resources largely depends on the perspective adopted by the analyst conducting the study. Nevertheless, the analysis of treatments' cost (or direct healthcare cost) is common to all viewpoints and its estimation therefore plays an important role in economic evaluation. Focusing on the correct estimation of the aforementioned cost type should pose solid foundations for any study.

FIGURE 2.3: Types of hospital costing methodologies



Perspectives aside, the measurement and valuation steps can be done using distinct approaches with variable precision and implementation difficulty as presented in Figure 2.3 from Drummond *et al.* [2005].

Micro-costing (bottom-up) approaches favor the direct assessment of unit costs for each resource used in the treatment process of a particular type of patient. While such methods provide a high degree of detail and precisions, they require a significant investment in both time and resources as such detailed data are not always systematically collected.

Macro-costing (or gross-costing, top-down) approaches tend to use national average data for large categories of input or output such as hospital bed days or GHM. While the level of detail using these methods is lower, they are also less time consuming.

Several other types of costing methodologies (case-mix group, disease specific daily cost or average daily cost) exist as they try to balance the trade-off between accuracy and the time/effort needed to apply them. Sometimes less precise measurement is sufficient,

especially for resources that are less central for the analysis. As Kristensen and Sigmund [2007] note in their handbook, micro-costing and macro-costing approaches can also be used simultaneously:

> *"Micro-costing and macro-costing approaches can even both be used in the same analysis for costing the various forms of resource consumption. For example, in an analysis of minimally invasive hip arthroplasty compared with traditional hip arthroplasty, it will be essential to measure resource consumption in connection with the operation at a highly detailed level as it is primarily here that there will be a difference. On the other hand, a bed day rate may be "good enough" in determining costs in connection with admission as this parameter is not so central to the analysis."*

Even though the importance of clearly reporting which approach is used along with a justification of the choice, neither the DACEHTA, CADTH nor HAS recommends the general use of a specific costing method. Nevertheless, the HAS states that micro-costing techniques are particularly suitable for innovative surgical procedures/technologies, especially for those that have not yet been documented on their list of reimbursable products or for which there is no specific GHM.

None of the guides explicitly recommends the reporting of either average or marginal costs in economic evaluations. Nevertheless, the DACEHTA points out that the use of marginal costs is useful when the assessment focuses on the changes in a given activity. Average costs, on the other hand, are useful where comparison of two technologies with different infrastructure needs is involved, or if one wants to generalize about costs at a national level.

4 Costing in the surgical literature

As an institute specialized in the development and use of innovative hybrid surgical technologies, the IHU will require a detailed costing method to decide which technologies are most cost advantageous[2]. We therefore seek to adopt the institutes' perspective for determining the cost of production, where a unit of output is a healthy patient.

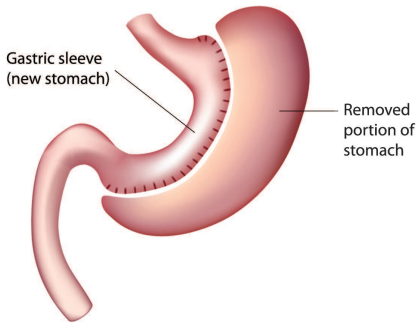
As several costing methods exist, we were interested in identifying the most prevalent ones in the surgical literature as to align our analysis or improve upon them to fully and correctly evaluate the cost of minimally invasive surgery. We focus our analysis on computer-assisted and laparoscopic techniques, with an emphasize on Gastric Bypass, as the IHU maintains a prospective database on all bariatric surgeries.

4.1 Bariatric surgery and techniques

When individuals reach a body mass index of over 35 kg/m^2 they have the option of undergoing a bariatric surgical procedure as they are considered severely obese (if BMI $\geq$ 35) or morbidly obese (if BMI $\geq$ 40). The term "bariatric surgery" refers to procedures that aim at reducing the size of the digestive pouch as to help these patients lose weight by decreasing their capacity to ingest food.

The reduction of the stomach's size can be achieved with a gastric band, removal of a portion of the stomach (sleeve gastrectomy) or by resecting and re-routing the small intestine to a small stomach pouch (gastric bypass surgery). The latter adds a component of malabsorbtion of the gastric restriction.

FIGURE 2.4: Sleeve Gastrectomy

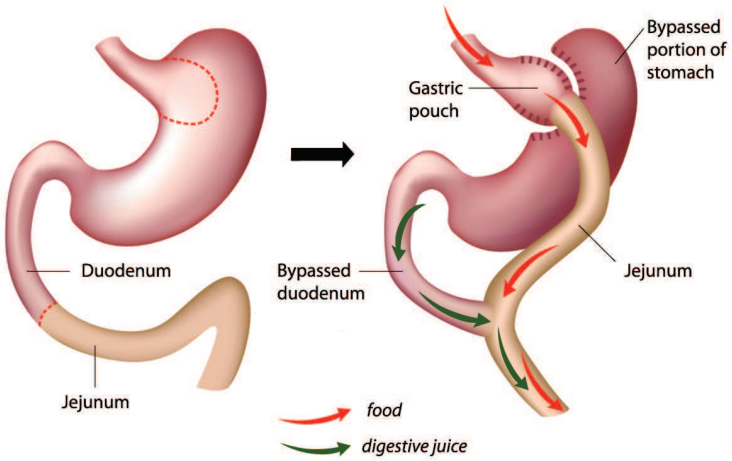


[2] At this stage of the analysis, we will not look into the effectiveness as our interest lies in understanding how the cost of an innovative surgical procedure can be determined.

Sleeve gastrectomy, or gastric sleeve, is a non reversible procedure that reduces the stomach to about 15% of its original size by surgical removal of a large portion of the greater curvature. The open edges of the new stomach, as shown in figure 2.4, are attached together typically with either surgical staples, sutures, or both, to leave the stomach shaped more like a tube, or a sleeve.

Gastric Bypass (GBP) surgery, initially developed in the 1960s by Mason [ASMBS], involves reducing the size of the stomach as well as bypassing part of the small intestine. The consequence for the patient is a reduction in the amount of food ingested and a lower absorption of nutrients thus leading to weight reduction. To prevent malnutrition, these patients are usually prescribed vitamins and mineral supplements.

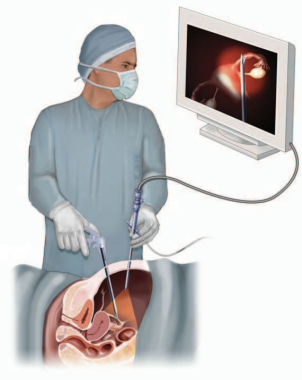
FIGURE 2.5: GastricBypassRouxenY



The Roux-en-Y (RYGBP) is one of the most common forms of gastric bypass surgery during which a small gastric pouch is created with a stapler device and connected to the distal small intestine (jejunum). The upper part of the small intestine (bypassed duodenum), as shown in Figure 2.5, is then reattached to the rest in a Y-shaped configuration.

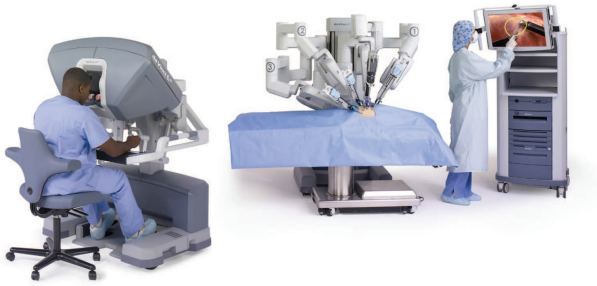
Both procedures can be done using several techniques and a variety of instruments. The open surgical approach was most prevalent until 1994, when Drs. Wittgrove and Clark reported the first case series of laparoscopic RYGBP, thus proposing an alternative method of access and exposure [ASMBS].

FIGURE 2.6: Laparoscopic surgery



Open RYGBP is an invasive procedure usually performed by creating a large incision and using abdominal wall retractors for exposure. Laparoscopic RYGBP, as shown in Figure 2.6, is a minimally invasive procedure performed through 5 or 6 small abdominal incisions and a carbon dioxide gas based insufflation of the abdomen (peritoneal cavity) to create a space within which to work.

FIGURE 2.7: Robotic surgery



The introduction of robotics offered surgeons an innovative minimally invasive alternative for conducting surgical operations. To date, Intuitive Surgical is the only company that offers a sufficiently developed system to be used on a clinical and daily basis. Their product, the da Vinci® robotic system, was approved by the US Food and Drug Administration (FDA) in 2001 and has been used in various specialties among which: Head&Neck, Colorectal, General Surgery, Gynecology, Cardiac, Thoracic and Urology.

The latest in the series, the da Vinci® Si, is composed of four elements [Intuitive Surgical]: surgeon console, patient-side cart, surgical instruments and a 3D HD vision system.

The purchase price of such a system ranges from $1.0M to $2.3M with a yearly maintenance cost of around $100K to $170K (Intuitive Surgical Investor Presentation Q1 2013).

The console allows the surgeon to operate while being seated, viewing a high definition 3D image of the surgical field. His hand movements are transmitted from the master controls situated at the console to the 4 robotic arms that are part of the patient-side cart.

The vision system is equipped with a high definition 3D endoscope and image processing equipment that provide the entire operating room (OR) team with a view of the operating field on a large monitor. Through this system, one can observe the surgical instruments' movements. A major perceived benefit of the robot is the increased maneuverability of the instruments - many offering several degrees of freedom - which makes complex actions such as suturing easier for the surgeon.

As one of the "hot topics" in minimally invasive surgery, we focused on the da Vinci® robotic system and its comparison to laparoscopy for our cost analysis example. As both techniques are used in several specialties, we chose to not constrain ourselves to bariatric surgery for our review and instead compared the costing methodologies used in the evaluation of Prostatectomies, Cystectomies, Hysterectomies, Gastric bypass and Fundoplications [Ismail et al., 2014].

4.2 Surgical literature cost comparison

We conducted a Pubmed search using the Mesh terms *("Surgery, Computer-Assisted"[Mesh] OR "Robotics"[Mesh]) AND "Costs and Cost Analysis"[Mesh]* and manually selected the 19 most relevant articles[3] to our study. Each article was then analyzed with respect to the following criteria that, from a surgical institute's perspective, constitute the basis for determining a cost per operation:

- Cost, not charge, data is used;
- Operating room costs can be calculated separately from hospital admission and exams;

[3]We excluded articles that only analyze the cost of complications and those for which we did not have access to.

- Medical equipment's (Robot included) cost and maintenance are taken into account;
- Personnel cost is identified;
- Re-usable instruments' cost are calculated;
- Disposables' cost are reported.

Six papers [Hagen et al., 2012; Park et al., 2011; Pasic et al., 2010; Venkat et al., 2012; Wright et al., 2013, 2012] did not meet the first two criteria, making the operating room cost analysis, separately from the hospitals', impossible. For an economist, the segmentation of costs is essential for analyzing the cost-effectiveness of decisions or policies. Considering that policies affecting the operating room also indirectly affect the rest of the hospital, decision makers should have the correct tools to reallocate resources from one segment to another depending on the desired direct and indirect effects.

Out of the thirteen remaining articles, the robot's purchase and maintenance costs were only accounted for in seven [Bolenz et al., 2010; Costi et al., 2003; El nakadi et al., 2006; Lau et al., 2012; Lee et al., 2011; Lotan et al., 2004; Smith et al., 2010]. Published articles that do not take these costs into account [Broome et al., 2012; Delaney et al., 2003; Dennis et al., 2012; Hubens et al., 2007; Morino et al., 2004; Sarlos et al., 2010], even if the robot was a donation, introduce a significant bias in the surgical literature. Conclusions on cost-effectiveness ratios, or comparative analysis, either become more favourable towards adopting the new technology or lack in evidence for any reliable decision.

None of the articles took into account all medical equipment that are shared among different specialities (monitors, surgical pendant, etc.). Sarlos *et al.* [2010] and Huben *et al.* [2007] did not consider the cost of any medical equipment, whether shared or not. The introduction of new technologies render other ones obsolete and the changes that are thus incurred affect both shared and procedure specific devices. If we are to identify these changes, our cost analysis must cover the entire operating room without making exceptions.

Three articles [El nakadi et al., 2006; Lee et al., 2011; Smith et al., 2010] demonstrated an intriguing variability in calculating the personnel cost. While Smith *et al.* [2010] took into account OR personnel and excluded surgeons' fee, Lee *et al.* [2011] only took the

latter into account. El nakadi *et al.* [2006] preferred to include only the OR nurse cost. Two articles [Costi et al., 2003; Hubens et al., 2007] did not take into consideration the personnel cost at all. Whereas all other direct expenses are determined as a per operation expense, the personnel cost defines the cost per minute of the operating room. This element is essential if surgeons wish to identify the cost of an additional minute of operation.

Further variability is observable in the study by Dennis *et al.* [2012] which, even though only considered the cost of the anaesthesia machine in the medical equipment's category, was the only article to fully integrate the cost of re-usable instruments and disposables with the sterilization and anaesthetic agent costs taken into account. It was also the only article to provide the cost of the entire OR personnel.

Costi *et al.* [2003] took into account the cost of medical equipment, re-usable and disposable instruments only incompletely, whereas Bolenz *et al.* [2010] took partial consideration of each criterion.

Overall, the reviewed surgical literature shows that when cost is reported, it is frequently done in a haphazard and non-rigorous way. Due to missing information on what is included in each calculation, we were neither able to compare results nor use weighted scoring methods, for the weight of each cost vary from one procedure to another. If we are to correctly identify the role and potential of innovative surgical technologies, the development of a comprehensive method for assessing and reporting costs is essential. Such a method is currently lacking in the surgical literature.

5 Costing method proposal for surgical technologies

As a proposal for answering the lack of harmony in the surgical literature's cost calculation and reporting, we suggest the use of a micro-costing methodology as recommended by the HAS. In a simple form, the method calculates the average cost per operation using four equations to which we have made small changes that improve their coherence since their initial publication in 2014 [Ismail et al., 2014].

In this section, we start off by proposing a costing method focused on evaluating the use of minimally invasive surgical technologies. To validate our proposition, we establish a benchmark value using French national data and method to which we will compare our applications' results.

5.1 Cost methodology

5.1.1 Fixed Cost - Medical Equipment

To avoid any confusion over the terms "medical device" and "medical equipment", we outline and use the definitions given by the WHO in their guide for the health technology assessment of medical devices [WHO, 2011].

The term medical device refers to articles, instruments, apparatus or machines that are used during an intervention, diagnosis/treatment of diseases or for detecting, measuring, restoring, correcting, or modifying the structure of the body for some health purpose. It is a wide definition that include both heavy machinery (such as monitors, endoscopic columns etc..) and small instruments (staplers, needles, etc.) alike.

The term medical equipment refers to medical devices that require calibration, maintenance, repair, user training and decommissioning all of which are usually done by biomedical engineers. Examples include operating tables, surgical lights, ceiling supply units which possess a "service life" expressing the average replacement cycle (in years) for the technology based on mechanical failure and obsolescence. Note that the initial purchase price of surgical equipment needed to perform the procedure is only part of the financial investment required as each require some type of routine maintenance or upkeep which is usually covered by "maintenance/service contracts" with the company or third party vendors.

The cost of a particular medical equipment for a procedure can thus be considered as a fixed cost dependent on several parameters. If we consider an operating room equipped with m medical equipment (anaesthetic machine, monitors, endoscopy video column, etc.), the Medical Equipment Cost (MEC) per minute can be calculate using the following equation (see Appendix B for details):

$$MEC = \sum_{i=1}^{m} \frac{1}{E_i \times T_i}(P_i + M_i \times \frac{1-(1+r)^{-E_i-1}}{1-(1+r)^{-1}}) \tag{2.1}$$

Where P_i, M_i, E_i and T_i are, respectively, medical equipment i's:

- Purchase price;
- Maintenance fee per year;
- Service life expressed in years;
- Total duration of operations per year (in minutes) during which the equipment was used.

The discount rate r, nationally fixed at 2.5% for France, reflects the time value of money. In other words, money that is available today is worth more than the same amount of money available in the future since it could be earning interest.

If T_i is unknown, it is possible to calculate a cost per operation using the mean number of operations per year for which each equipment has been used. The use of such a measure, however, is not unproblematic as it reduces the accuracy of marginal calculations, i.e. when trying to determine the cost of an extra minute of operation.

5.1.2 Fixed Cost - Personnel

The term "robotic" or "robot-assisted" leads the imagination to a semi-automatic operation partially conducted by a robot. In reality, a robot-assisted surgery requires as many or more personnel as a laparoscopic operation and results, in most cases, in an increase in operative times.

These longer surgical operations translate into an increase in surgery cost with respect to the personnel cost, which can be determined using Equation (2.2). The per minute Personnel Cost (PC) of a number p of personnel present during surgical operations is expressed as (see Appendix C for details):

$$PC = \frac{1}{12} \sum_{i=1}^{p} \frac{W_i \times t_i}{L_i \times Ewd_i} \tag{2.2}$$

Where W_i, L_i, Ewd_i and t_i are, respectively, personnel i's:

- Annual loaded salary;
- Weekly paid working hours;
- Effective working days per year; as in *(working days - paid leave)*;
- Time spent in surgery operations, expressed in minutes.

5.1.3 Variable Cost - Re-usable Instruments

Hospitals today are faced with many management choices that affect operating costs. The choice of reusable versus disposable operating room supplies used to be clear-cut: re-usable supplies were less expensive but disposable supplies were more convenient. Today, with patient safety concerns, increasing regulations, labor costs and increasing disposable costs, this simplified view no longer holds. Both reprocessing expenses and disposable costs must be taken into account when evaluating the cost of a procedure.

Equation (2.3) can be used to identify the Instrument Cost (IC) per operation during which n re-usable instruments were needed. It takes into account the sterilization cost with respect to the fact that once the instrument has used up its last life then it would not require sterilization.

$$IC = \sum_{i=1}^{n} N_i \times \frac{P_i + (E_i - 1) \times S_i}{E_i} \tag{2.3}$$

Where P_i, E_i, N_i and S_i are, respectively, instrument i's:

- Purchase price;
- Maximum possible number of uses;
- Number of units used;
- Sterilisation cost.

The additional cost (S_i) reflects the resources needed to sterilize instrument i as in labour (based on technician/nurse's time), rinsing, disinfection, packaging, and steam

autoclaving [Yung et al., 2010]. Due to data unavailability, the sterilization cost was determined through a literature survey.

In our search, Apelgre *et al.* [1994] were the only authors to address this issue in detail. By considering the time and resources needed for cleaning, sterilization and packaging of reusable instruments, they determined a total cost of $0.80 (or 1.06 Euro) per instrument per case.

5.1.4 Variable Cost - Disposables

Depending on the procedure, number of complications and other factors, various consumables (anaesthetic agent, implants, units of blood, etc.) will add to the operation cost. Integrating this element into our equation is an easy task. The challenge, however, lies in the time-consuming process of collecting such detailed data.

Hospitals that successfully manage to identify all disposables used during surgical operations need only to multiply the number of units used by their purchase price to obtain the Disposable Cost (DC). Mathematically, for a number d of disposables:

$$DC = \sum_{i=1}^{d} (N_i \times P_i) \tag{2.4}$$

Where N_i and P_i are, respectively, disposable i's:

- Number of units used;
- Purchase price.

5.2 Benchmark for Validation

During the thesis, the IHU suggested that an internship be proposed focusing on the medico-economic evaluation of technological innovation in bariatric surgery. In 2015, Silviu Necoara was subsequently hired for a period of 3 months under the supervision of the PhD student Imad Ismail.

The internship's objective consisted in analyzing the cost-effectiveness's evolution of Laparoscopic Gastric Band (LGB) vs Laparoscopic Gastric Bypass (LGBP), in France

and the United States. We hypothesized that, despite the higher surgery cost, length of stay and convalescence time, the choice of LGBP over LGB is overall more economically viable for the healthcare system.

To perform this study, the intern was asked to determine a French average cost per LGBP operation using national data. Hence, all calculations were based on the French "Étude Nationale des Coûts" (ENC) 2013 database, updated every year by the ATIH, which provides an average cost per GHM by aggregating all hospitals.

The publicly accessible ENC database contains detailed cost information for each GHM, divided into six expenses categories: clinical activity, medico-technical, logistics and general management, medical logistics, direct cost, and structure. Each category is further divided into subcategories as follows:

- Clinical activity: *personnel, maintenance and amortization in reanimation, intensive care, and continued monitoring*;
- Medico-technical: *total expenses in anesthesia, OR, dialysis, radiology, functional exploration, imagery, etc.*;
- Logistics and general management: *maintenance, "hotel services", transportation*;
- Medical logistics: *other logistics expenses*;
- Direct: *pharmaceuticals, implants, other consumables, blood, personnel, etc.*;
- Structure: *real-estate*.

TABLE 2.4: ENC base OR Cost for GHM 10C131

Expense Category	Sub-category	Total (Euro)
Medico technical	Anesthesia	712
	OR	813
	Other	134
Direct	Disposables	643
	Implants	278
	Pharmaceuticals	114
	Personnel	81
	Other	50
Total		2 826.05

Source: ENC 2013

By construction, the medico-technical and direct expenses should represent the average value of resources consumed in the OR. For the GHM 10C131, corresponding to LGBP of the first severity level, these values amount to a national average of 1 659 and 1 167 Euro respectively, as presented in Table **??**.

Hence, if our proposed cost methodology is to be validated, its application should indicate an average cost per LGBP operation of approximately 2 826.05 Euro. This value will therefore serve as a benchmark for our results.

6 Application 2012

During our thesis, we performed two applications of our methodology according to the quality and availability of the data. For the first application (2012), we tried to position ourselves from the surgeon's point of view recognizing that detailed data is not always accessible nor even recorded.

Due to a certain lack of data and information exchange with the hospital, we base our analysis on several assumptions. We list those in an attempt to minimize their impact on our application:

- Past their life expectancy, medical equipment have a null value;
- Medical equipments' maintenance fees are fixed;
- Hospitals should consider investing in a new surgical robot when volumes exceed 400 robot-assisted operations per year[4].

6.1 Data collection

As a first application, we used retrospective data collected from 1/01/2012 to 31/12/2012, partially by the IHU team, for patients that underwent computer assisted gastric bypass operations at Strasbourg's university hospital. For each operation, the IHU's clinical research technician manually recorded the presence of medical staff, duration of each phase of each operation as well as the number and name of some instruments used.

In total, at the time of analysis, our database contained 44 Gastric bypass operations done by the same surgeon using the da Vinci robotic system. While we could've extended our dataset to operations done by other surgeons, we preferred to restrict our analysis as to reduce the bias due to the operator's characteristics (experience, agility, etc.).

6.1.1 Fixed Cost - Medical Equipment

The first step in determining the cost of medical equipment is the identification of relevant resources present in the OR where the da Vinci surgical system is installed.

[4]Based on an expert's feedback and supported by Intuitive Surgical's recommendations

Since our database did not contain such details, we contacted the hospital's biomedical engineers who were able to provide us with a list of most medical equipment along with their purchase price, maintenance cost and service life.

The second step consists in determining the duration of operations per year during which each equipment was used as to amortize the purchase price and maintenance cost. We were unable to retrieve the total room occupation time for 2012 due to confidentiality, but were able to identify the total number of operations done in the OR by contacting the operating bloc's manager.

TABLE 2.5: Medical equipment data 2012

Equipment	Purchase price	Maintenance	Service life	Yearly use
DaVinci Si Robot	900 000	135 000	5	147
DaVinci Si Optic	17 000	850	5	147
Anaesthetic machine	60 000	3 000	12	528
Endoscopy Column	50 000	2 500	7	528
Operating Table	50 000	2 500	15	528
Four Syringe Pumps	32 000	1 600	10	528
Surgical Light	25 000	1 250	15	528
Two Monitors	20 000	1 000	7	528
Electro-surgical unit	15 000	750	10	528
Ceiling supply unit	13 000	650	15	528
Surgical Pendant	9 000	450	15	528

All medical equipment presented in Table 2.5, except the daVinci Si Robot and Endoscope, are bought by the hospital and shared among all 528 operations taking place in the same OR. The da Vinci equipment, bought by the IHU at preferential and confidential prices, were effectively used in a total of 147 operations.

6.1.2 Fixed Cost - Personnel

Collected data on operating room occupation time was broken down into 5 sets corresponding to the 5 phases of a computer assisted gastric bypass. To determine the time

spent in surgical operations from which to derive the personnel cost, we analyzed whom of the medical personnel were present in the OR during each phase.

Note that these operations were **not** done entirely using the robot system as the needed instruments were not available. Each operation therefore contained a coelioscopic phase to prepare the patient (Phase 3), followed by a robot-assisted phase to perform the jejunojejunal (JJ) and/or gastrojejunal (GJ) anastomosis (Phase 4) and a second coelioscopic phase to finish the operation (Phase 5).

1. Room preparation : switching on electronic devices and preparing instruments
   Personnel: circulating nurse, scrub nurse;
2. Anesthesia: patient arrival, preparation and induction of anesthesia
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, anesthesiologist;
3. Surgery preparation: incision/trocar placement, robot drape covering
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, surgeon, 2 interns/assistants;
4. Surgery: robot docking, robotic surgery operation, robot parking
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, surgeon, 2 interns/assistants;
5. Surgery completion: closure, patient exit
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, anesthesiologist.

Due to missing data for a number of patients, we proceeded to calculated an average duration for each phase as well as an average room occupation time for our entire sample. We recognize that such detailed data on phase duration is rarely recorded.

Our proposal, when using this version of our methodology, is to base the time spent in the OR by each personnel on a percentage of total room occupation time. For example, according to our study, surgeons have an estimated presence representing 70% of an operation's total room occupation duration while anesthesiologists are present 24% of the total duration.

Financial data presented in Table 2.6 were communicated by contacting the head of the hospital's digestive department and are confidential. Information on both work days

TABLE 2.6: Personnel data 2012

Personnel	W_i	L_i	Paid leave	t_i
Surgeon	110 324	48	44	221
Anesthesiologist	110 324	48	44	76
Nurse anesthetist	61 563	35	48	297
Circulating nurse	60 613	35	48	314
Scrub nurse	60 613	35	48	314
Intern1/assistant1	37 693	48	30	221
Intern2/assistant2	37 693	48	30	221

and paid leave were deduced from the hospital's internal rules relative to the medical presence's organization. We assume that the surgeon is a hospital practitioner with no university-related activity, his salary is therefore fully paid by the hospital.

6.1.3 Variable Cost - Re-usable Instruments

While our database contained detailed information on the use of each robot specific instrument, it was highly unlikely that the hospital would possess such information for all instruments and operations. Similar to the personnel approach, we started by calculating an average use for each instruments. Instruments that were used in over 50% of operations were considered to be essential and their cost taken into account.

We identified that, typically, computer assisted Gastric Bypass operations require the use of 4 re-usable instruments along with their associated disposable accessories. Whether computer-assisted or laparoscopic, every gastric bypass operation also requires a "coelioscopic box" which contains a set of commonly used laparoscopic instruments. It was not possible to go into detail as to what the box actually contains and how much of its contents is used during each operation. Discussions with biomedical engineers and the manager of the operating blocs allowed us to estimate the box's value at 9 000 Euro and a maximum use of 150 operations.

TABLE 2.7: Re-usable Instruments 2012

Instruments	Maximum Uses	Purchase Price
Bowel Grasper	20	4 600
5 mm Needle Driver	20	4600
Monopolar curved scissors	10	3 600
Fenestrated Bipolar Forceps	10	2 700
Coelioscopic box	150	9000

Data presented in Table 2.7 on robotic instruments were gathered using Intuitive Surgical's commercial catalog. The latter contains the reference, maximum number of uses and purchase price information for each instrument, all of which are considered confidential.

6.1.4 Variable Cost - Disposables

During data collection, the IHU team was primarily interested in recording the use of robot specific instruments and disposables they bought. Each operation, however, uses both robotic and laparoscopic disposables which are rarely recorded in detail by the hospital.

TABLE 2.8: Robot specific disposables 2012

Consumables	UnitsUsed	PricePerUnit
Drapes 3 arms	1	200
Drapes Instrument arm	1	45
Tip Cover for 420179	1	20
Canula seal 5mm	1	20

Table 2.8 presents robot-specific disposables typically used in our sample and as recorded by the IHU. To estimate the number and type of non-robot specific disposables, we asked for the help of the operating blocs manager who was kind enough to create a list of all disposables used for one operation. To verify the list's exhaustivity and accuracy, we reviewed it with the help of several IHU fellows and surgeons.

TABLE 2.9: Most expensive common disposables 2012

Consumables	UnitsUsed	PricePerUnit
Ligasure 5mm	1	508
EndoGIA	1	281
Manchons de contension (paire)	1	269
Recharge endoGIA brune 60	3	153
Recharge endoGIA violette 60	3	1523

Table 2.9 presents the five most expensive non-robotic specific disposables used in a computer-assisted Gastric Bypass operation. Other disposables taken into account in our application include needles, antiseptic, urine collector, gloves, syringe, etc..

6.2 Results

The following Table 2.10 presents the total cost per operation for the 44 robot-assisted Gastric Bypass with regard to each element of both fixed and variable costs.

TABLE 2.10: Total cost per Gastric Bypass operation 2012

Element	Cost (€)	Weight
Medical equipment	2 012.76	0.29
Personnel	1 075.52	0.15
Re-usables	1 153.75	0.17
Disposables	2 719.78	0.39
Total per operation	6 961.81	1

The amortized value of medical equipment amounts to a total of 2 012.76 Euro, exclusive of taxes, per operation. Considering that the da Vinci® Si System was used in a total of 147 operations, its amortization value amounts to 1 932.74 Euro which represents 96.02% of all medical equipment's cost.

By determining the mean duration each personnel spends in the operating room, we are able to integrate the total payroll cost data provided by our hospital into Equation (2.2).

With a mean occupation time of 314 minutes, we determine a per minute personnel cost of 3.43 Euro.

The cost of re-usable instruments, tax excluded, sums up to 1 153.75 Euro. However, we must take into account that we did not perform fully robot-assisted operations and it is thus likely that some robotic instruments were not needed or were replaced by traditional laparoscopic instruments.

While the disposables' cost accounts for 39% of the total cost per operation, we have little control over it. This value can vary greatly from one procedure type to another especially if implants are needed or if complications occur. However, we can try to reduce it by limiting wastefulness and preferring basic over new high-technology disposable instruments with the same functionality.

7 Application 2013

Several values were either unknown or confidential when we made the first analysis in 2012 and therefore could not be used for the 2012 application and publication [Ismail et al., 2014]. In this section, we seek to update the application of the methodology using the additional information collected in the last 3 years after gaining permission from the hospital to access their data.

In particular, we adapt our approach to a highly detailed dataset that is usually part of clinical studies' protocol. The presentation of the data is done in a more informative way with an emphasize on the comparison between two surgical techniques.

To compensate for the lack of some information that were not collected by the hospital or are too difficult to access, and render the analysis feasible, we had to make several assumptions similar to what was done in 2012:

- Past their life expectancy, medical equipment have a null value;
- Hospitals should consider investing in a new surgical robot when volumes exceed 400 robot-assisted operations per year[5];
- All operations, laparoscopic and computer assisted are done in the same operating room;
- The overhead cost for laparoscopic and computer assisted surgery are equal.

Theoretically, the care pathway of patients that undergo Robotic Gastric Bypass (RGBP) and those that undergo Laparoscopic Gastric Bypass (LGBP) should be relatively identical as they share similar characteristics and needs. In a comparative analysis, one implication of such an assumption is the non-necessity of including common procedures such as scans, blood tests or other exams that are not impacted by the introduction of the new technology.

7.1 Data collection

We focus on the data of a protocol written by the IHU clinical team, late 2012, for the comparison of the clinical and medico-economic impacts of computer-assisted versus

[5]Based on an expert's feedback and supported by Intuitive Surgical's recommendations.

laparoscopic gastric bypass. The study, approved by the different comities (scientific, ethical, etc.), spans a 1 year period (2013) and includes 134 patients with a BMI of over 35 randomized to either a laparoscopic or robotic group with the surgeon being blinded to the randomization.

Considering that it is the patient's decision to participate in the protocol, several individuals changed their minds before the operation date while others preferred to undergo a sleeve gastrectomy instead of a gastric bypass. Two additional patients were excluded from the analysis as they were randomized to the robotic group but were deemed too difficult to operate on, they were therefore operated on using the laparoscopic technique.

Another two patients were excluded due to decisions and events planned by the hospital/surgeon but not the protocol. For the first patient, the surgeon decided to perform an additional procedure (on top of the gastric bypass) considering that the patient was already in operation. For the second patient, an electricity outbreak was planned (to test the robot's restoration mechanism) which happened during the robot's working time thus blocking its mechanism.

In total thirteen patients did not undergo an operation in the context of the protocol and were therefore excluded. Of the 122 remaining patients, 58 were randomized to the robotic group and 64 to the laparoscopic one.

7.1.1 Fixed Cost - Medical Equipment

Our protocol data did not contain any information on medical equipment present in the OR where the operations took place. We therefore base our analysis on the list provided by the hospital's medical engineers in 2012, which we completed by manually surveying the OR with the help of the operating blocs manager and re-contacting the engineers for additional financial information.

To determine the duration of operations per year during which each equipment was used, we contacted the hospital's management controllers ("contrôleurs de gestion") who were able to provide us with a list of all operations done per month in UF 2199 (see Figure 2.2), for 2012 and 2013, along with their total duration. After extraction of the OR specific data, we determined a room occupation time of respectively 1732:22 and 1658:09 hours or, equivalently, an average of 101 715 minutes over the two years.

The da Vinci Si robot, optic and container are bought by the IHU Strasbourg at preferential prices and used only during computer assisted operations. As the use of the robotic equipment is relatively recent, we based our analysis on an estimated number of 150 computer assisted operations per year, as suggested by the IHU. As for the duration, data from the protocol estimate an average operation duration of 255.33 minutes (standard deviation 35.37) and therefore an average yearly room occupation time of 38 299 Minutes.

All other medical equipment are bought by the hospital and shared among all operations taking place in the OR. Their purchase price and maintenance costs are therefore amortized over the average yearly room occupation time previously determined at 101 715 minutes.

The coelioscopic optic is used in both laparoscopic and computer-assisted operations as the needed instruments to do full robotic surgery are not available. We assume that it was only used in the OR containing the robotic system as we did not have access to equipment specific data, i.e. average yearly duration of operations that used the optic all ORs included.

TABLE 2.11: Medical equipment data 2013

Equipment	Purchase price	Maintenance	Service life	Yearly use
DaVinci Si Robot	900 000	135 000	5	38 299
DaVinci Si Optic	17 000	850	5	38 299
Robotic Container	900	45	7	38 299
Coelioscopic Optic	3 000	150	5	101 715
Anaesthetic machine	60 000	3 000	12	101 715
Endoscopy Column	50 000	2 500	7	101 715
Operating Table	50 000	2 500	15	101 715
Fixed table pilum	33 143	1657	15	101 715
Four Syringe Pumps	32 000	1 600	10	101 715
Surgical Light	25 000	1 250	15	101 715
Two Monitors	20 000	1 000	7	101 715
Electro-surgical unit	15 000	750	10	101 715
Ceiling supply unit	13 000	650	15	101 715
Surgical Pendant	9 000	450	15	101 715
Mattress	5 660	283	7	101 715
Aspirator	3 354	168	10	101 715
Storage carts	3 235	162	10	101 715
Closet	2 697	135	10	101 715
Tables	2 000	100	10	101 715
Chairs	528	26	7	101 715

Source: HUS - Biomedical engineers

Table 2.11 summarizes the data as they are imported by the **R** [R Development Core Team, 2011] algorithm and used in our cost analysis. As a rule, the hospital fixes the maintenance cost at 5% of the medical equipment's purchase price.

7.1.2 Fixed Cost - Personnel

Collected data on operating room occupation time was broken down into 4 sets corresponding to 4 phases of a computer assisted gastric bypass with different personnel presence. To determine the time spent in surgical operations, from which we derived

the personnel cost, we analyzed whom of the medical personnel were present in the OR during each phase.

1. Anesthesia: room preparation, patient arrival and induction of anesthesia
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, anesthesiologist;

2. Robot preparation: robot drape covering
   Personnel: circulating nurse, scrub nurse, nurse anesthetist;

3. Surgery: incision/trocar placement, coelio 1, robotic docking, robotic surgery, robot parking, coelio 2
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, surgeon, 2 interns/assistants;

4. Surgery completion: wound closure, patient exit
   Personnel: circulating nurse, scrub nurse, nurse anesthetist, 2 interns/assistants.

Each operation contains a coelioscopic phase (coelio 1) to prepare the patient, followed by a robot-assisted phase to perform the jejunojejunal (JJ) and/or gastrojejunal (GJ) anastomosis and a second coelioscopic phase (coelio 1) to finish the operation. However, since the personnel present in the OR are the same for the three surgical steps, we merged them into Phase 3.

We noticed a certain "Idle time" between the end of Phase 1 and the start of Phase 2 which the clinical team was unable to explain. We assume that only the circulating nurse, scrub nurse and nurse anesthetist are present during this interval.

TABLE 2.12: Personnel data

Personnel	W_i	L_i	Paid leave
Surgeon	110 324	48	44
Anesthesiologist	110 324	48	44
Nurse anesthetist	61 563	35	48
Circulating nurse	60 613	35	48
Scrub nurse	60 613	35	48
Intern1	37 693	48	30
Intern2	37 693	48	30

Source: Chief of the Digestive department

Table 2.12 summarizes the data as they are imported by the **R** algorithm and used in our cost analysis. We assume, as done for 2012, that the surgeon is a hospital practitioner with no university-related activity, his salary is therefore fully paid by the hospital.

7.1.3 Variable Cost - Instruments

During data collection, no distinction was made between disposable and re-usable instruments which reflect the realistic difficulties of manual on-site data collection. While it is possible to create a methodology that distinguishes between disposable and re-usable instruments, we have chosen to merge both under the same formula. Since the **R** algorithm applies the formula for each instrument individually, it would simply consider disposables as re-usables with a maximum number of uses of 1, thus not influencing the results.

Information on purchase prices were retrieved from the IHU bills since all instruments included in the protocol are bought by the institute. Robotic instruments' maximum uses were determined using Intuitive Surgical's commercial catalog.

TABLE 2.13: Re-usable and Disposable Instruments

Instrument	Purchase Price	Maximum Uses
Maryland Dissector 5mm	5 409	20
Needle Driver 5mm	5 392	20
Bowel Grasper 5mm	5 392	20
Monopolar Cautery Instrument 5mm	4 852	18
Monopolar Curved Scissors 8mm	3 751	10
Curved Scissors 5mm	3 751	12
Maryland Bipolar Forceps	3 175	10
Precise Bipolar Forceps 8mm	3 165	10
Fenestrated Bipolar Forceps 8mm	3 165	10
ProGrasp Forceps	2 587	10
Large needle driver 8mm	2 587	10
Permanent Cautery Hook 8mm	2 352	10
Cadiere Forceps 8mm	2 344	10
Harmonic ACE Curved Shears 5mm	1 294	20
Harmonic ACE Curved Shears 8mm	1 294	20
Harmonic ACE Curved Shears Insert	504	1
ligasure 5mm	500	1
ligasure 10mm	334	1

Source: IHU Protocole

Table 2.13 summarizes a portion of the data as they are imported by the **R** algorithm and used in our cost analysis. Note that, disposable instruments such as antiseptic, urine collector, gloves, syringe, etc. were not included in the protocol and were therefore not taken into account, which might cause our results to underestimate the cost per operation.

7.2 Results

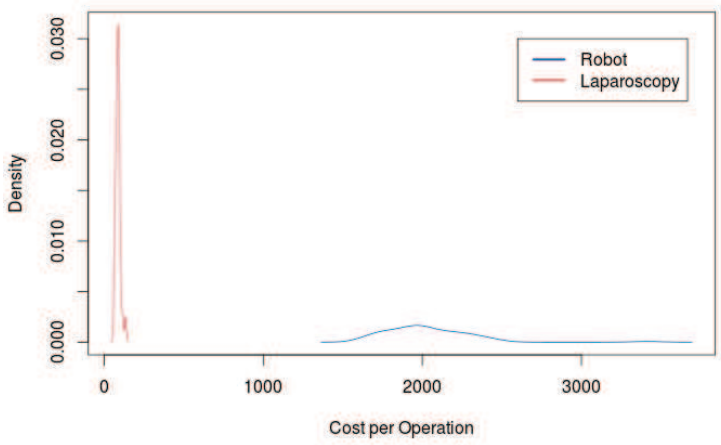
Based on the presented assumptions and using the data collected during the protocol, we were able to determine the average cost per operation for Robotic Gastric Bypass

(RGBP) and Laparoscopic Gastric Bypass (LGBP). All analysis was made using the free open source **R** [R Development Core Team, 2011] statistical software.

7.2.1 Fixed Cost - Medical Equipment

The mean medical equipment's cost per operation for RGBP and LGBP are respectively 2 031.34 (sd 281.41) and 87.76 (sd 14.90) Euro. A Welch Two Sample t-test indicates a statistically significant difference with a p-value $< 2.2e-16$.

FIGURE 2.8: Kernel Density of Medical Equipment Cost



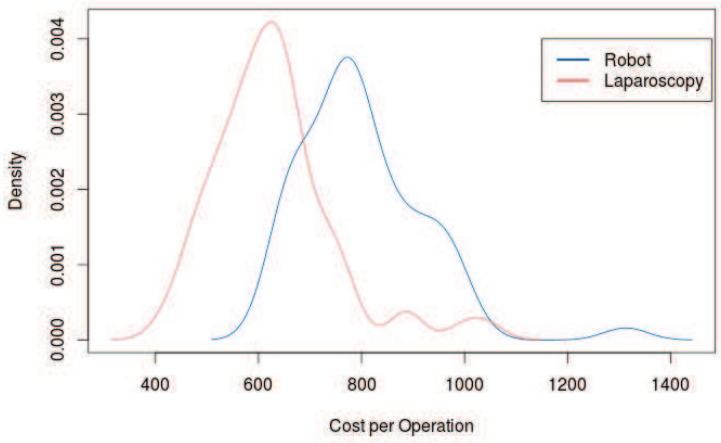
According to Figure 2.8, the cost per LGBP presents a normal distribution with weak standard deviation. The distribution of the cost per RGBP, on the other hand, is near flat indicating a very high variability.

According to our analysis, 55.20% of the incremental cost is due to medical equipment specific to the robotic system. The robot purchase price and maintenance amortization alone represent 95.61% of the medical equipment's cost per RGBP. In other words, with an average cost of 1915.45 Euro (sd 277.51) per operation, the robotic system is responsible for most of the variability in the distribution.

7.2.2 Fixed Cost - Personnel

The mean personnel cost per operation for RGBP and LGBP are respectively 800.79 (sd 121.69) and 627.72 (sd 119.30) Euro. A Welch Two Sample t-test indicates a statistically significant difference with a p-value $= 1.453e - 12$.

FIGURE 2.9: Kernel Density of Personnel Cost



According to Figure 2.9, both RGBP and LGBP durations present a right-skewed log-normal distribution. The presence of outliers in both medical equipment and personnel cost can be explained by their calculation as a cost per minute.

TABLE 2.14: Personnel average presence as percent of operation duration

Personnel	RGBP	LGBP	Mean
Surgeon	55.81	55.37	55.59
Interns/assistants	61.10	60.95	61.02
Scrub nurse	99.99	99.68	99.84
Circulating nurse	98.30	99.68	98.99
Anesthesiologist	4.31	6.19	5.25
Nurse Anesthetist	99.99	99.68	99.84

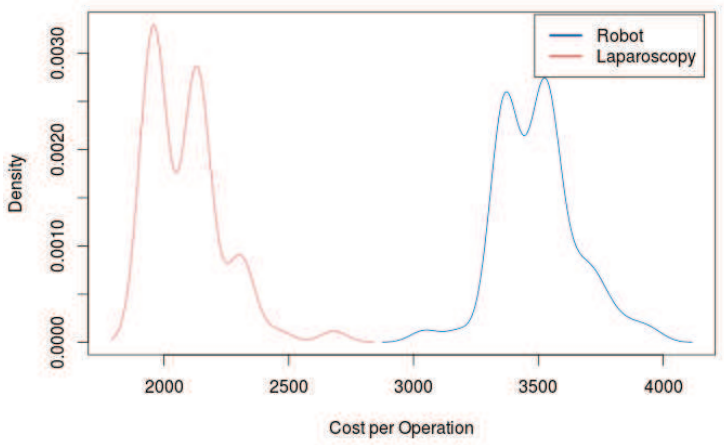
The personnel cost represents 4.91% of the incremental cost. Our data suggests that, on average, surgeons and interns/assistants are present during three-fifth of the total duration of a gastric bypass operation while the nurses are practically present the entire

time. Anesthesiologists only participates during an average of 5.25% of the total duration as it is common for each to follow several operations at the same.

7.2.3 Variable Cost - Instruments

The mean instruments' cost per operation for RGBP and LGBP are respectively 3 493.49 (sd 159.23) and 2 089.26 (sd 149.64) Euro. A Welch Two Sample t-test indicates a statistically significant difference with a p-value $< 2.2e - 16$.

FIGURE 2.10: Kernel Density of Instrument Cost



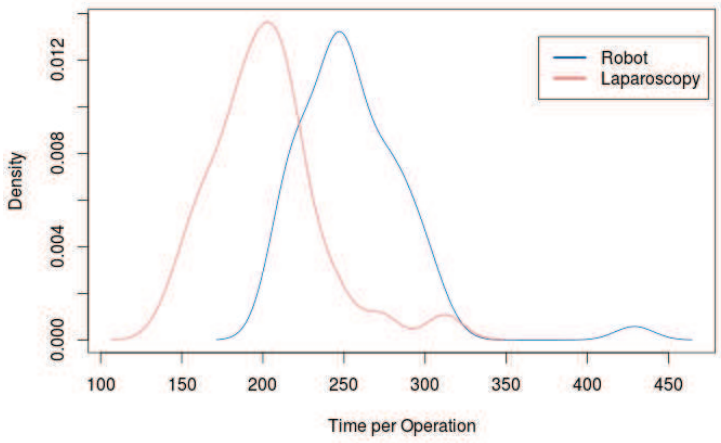
According to Figure 2.10, both RGBP and LGBP costs per operation present a bimodal distribution, an indication of the presence of two groups in each dataset. We can hypothesis that obese patients with co-morbidities require different/more instruments than patients without. The outliers indicate a malfunction in some instruments, which were replaced, or a malfunction in the robotic system avoiding the use of certain instruments.

Our analysis shows that a significant part of the incremental cost is due to the variable instruments' cost (39.88%). However, we must take into account that the surgeon did not perform fully robot-assisted operations as it was not possible. Both laparoscopic and robotic instruments were used during RGBP possibly leading to wastefulness as they are replaced by one instrument in LGBP.

7.2.4 Cost per Operation

The mean room occupation time for RGBP and LGBP are respectively 255.33 (sd 35.37) and 201.98 (sd 34.29) minutes. A Welch Two Sample t-test indicates a statistically significant difference with a p-value $= 9.291e - 14$.

FIGURE 2.11: Kernel Density of Room Occupation Time



According to Figure 2.11, both RGBP and LGBP's average operation durations present a right-skewed log-normal distribution. While a large number of data points are close to the mean, several outliers are observable which are likely to impact the cost per operation of both medical equipment and the personnel. Observing the data in more detail indicated that the additional room occupation time for 3 patients was due to complications.

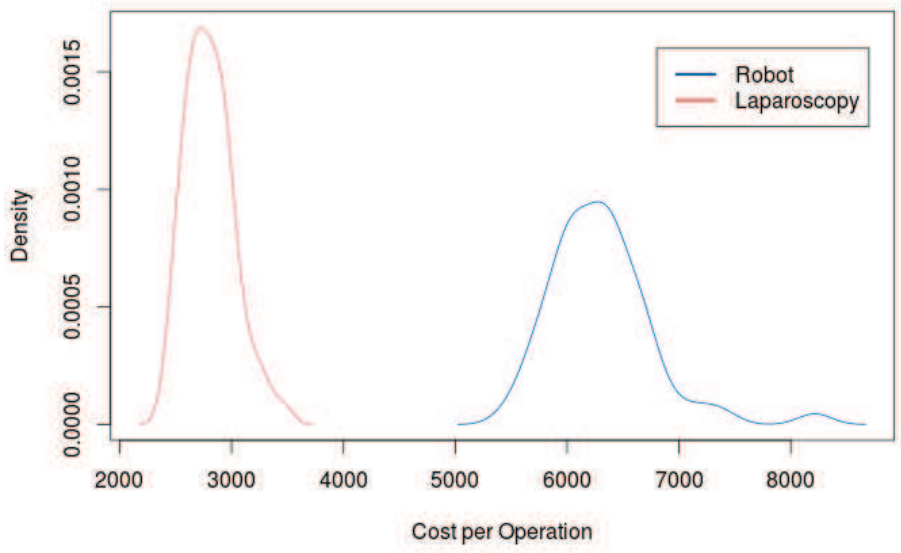
The average cost per minute of medical equipment can be determined at 7.96 and 0.43 Euro for RGBP and LGBP respectively. The personnel's average cost per minute largely depends on which phase of the operation is extended. Nevertheless, if we consider the operation as a whole, we can estimate a cost per minute of 3.14 and 3.10 for RGBP and LGBP, or an average of 3.12 Euro.

TABLE 2.15: Average cost per Gastric Bypass operation (Euro)

	RGBP	LGBP	p-value
Equipment	2 031.34 (281.41)	87.76 (14.90)	$< 2.2e-16$
Personnel	800.79 (121.69)	627.72 (119.30)	$= 1.453e-12$
Instrument	3 493.49 (159.23)	2 089.26 (149.64)	$< 2.2e-16$
Average per operation	6 325.62 (464.96)	2 804.74 (217.94)	$< 2.2e-16$

Table 2.15 indicates that the average cost per RGBP and LGBP are respectively 6 325.62 and 2 804.74 Euro. With a p-value $< 2.2e-16$, the difference in the cost per operation is statistically significant.

FIGURE 2.12: Kernel Density of Average Cost per Operation



Analyzing the average cost per operation's distribution shown in Figure 2.12 further shows the high degree of variability between the two techniques with two distinct normal distributions.

7.3 Sensitivity analysis

Considering the high purchase price of the robotic system and its maintenance cost, any healthcare institute that decides to acquire it should, theoretically, use it to its full

capacity. Instead of the IHU robotic system's estimated use of 150 operations per year, we modeled its use for 400 operations with an average operation duration of 255.33 minutes.

Under this assumption, the mean medical equipment's cost per operation for RGBP and LGBP are respectively 837.90 (sd 127.32) and 87.76 (sd 14.90) with an average total cost per operation of 5 227.14 and 2 804.74 Euro. A Welch Two Sample t-test indicates a statistically significant difference for both variables with a p-value $< 2.2e-16$.

Published studies focused on robot-assisted surgery either choose to amortize the purchasing price over 5 years [Breitenstein et al., 2008; El Nakadi et al., 2006; Morgan et al., 2005; Smith et al., 2010] or 7 years [Bolenz et al., 2010; Hagen et al., 2012; Lotan et al., 2004; van Dam et al., 2011]. The choice mainly seems to depend on the hospital's policy for medical devices' amortization with no consensus over the service life of the surgical system.

Assuming a service life of 7 years, instead of the 5 years we used in our analysis, for an estimated use during 150 operations per year, the average equipment cost per RGBP operation amounts to 1 736.73 (sd 263.89). Under this assumption, the average total cost per operation are 6 037.65 (sd 457.79) and 2 804.74 (sd 217.94) for RGBP and LGBP respectively. A Welch Two Sample t-tests indicates a statistically significant difference with a p-value $< 2.2e-16$.

Aside from the mentioned fixed and variable costs, surgical operations require extensive facility modifications for a sterile environment, a large ancillary labor force to conduct high risk interventions in a safe and effective manner, and increasingly, a high cost of the enabling technology needed for the procedure. All these elements can be distilled into an institution specific per-minute cost for using the operating room - and any supplementary expense would be added on to this baseline "overhead". As we did not include the overhead cost in our applications, we attempt to determine its value through a comparison to the hospital's ICR methodology.

Using the hospital's ICR technique, we were able to determine a cost per LGBP of 3 920.36 Euro that includes both fixed and variable expenses as well as a portion of the overhead cost; compared to 2 804.74 Euro using our own method. We hypothesis that the difference of 1 115.62 Euro per operation (5.51 per minute considering an LGBP

operation duration of 202.64 minutes) is mainly due to the inclusion of overhead costs, i.e medical and management logistic expense as well as infrastructure amortization, and the inclusion of common disposables such as gloves or syringes otherwise not included in the IHU protocol. As we use both the Anesthesia and Block ICR, the cost per LGBP should also reflect expenses of the anesthesia medico-technical center.

Assuming that the 5.51 per minute overhead cost value is precise, applying it to RGB for a mean operation duration of 255.33 minutes yields an average total cost per operation of 7 731.32 Euro. The incremental cost of using the da Vinci during gastric bypass procedures, when compared with an LGBP cost of 3 920.36 Euro, increases to an average of 3 810.96 Euro per operation all resources included.

8 Discussion

French healthcare has evolved into a system in which hospitals have little insight over the impact of innovations on their activities. The tools (T2A, PMSI, ICR) that have been put at their disposable by public institutions are at most convenient to use but imprecise and could therefore hinder progress as the uncertainty, especially during an economic crisis, is undesirable.

The risk that accompanies the adoption of innovation is even less desirable considering that there are no financial incentives to take the leap. As we have seen through the description of the T2A system, innovative procedures, or techniques that are based on innovative technologies, do not have a specific reimbursement and are therefore likely to run at a deficit.

To justify the choice of investing in an innovative minimally invasive technology whether to the health authority or the payer, hospitals will need to present reasonable arguments that are adapted to their specific situation. It is more convenient, for example, for business institutions to acquire technologies with low fixed costs because, in case of low activity, the losses would be limited. However, for high volumes of activity, it is more advantageous for a company to invest in technologies with low variable costs as to increase the return on investment in the long term.

In other words, hospitals that estimate their activity will be higher than the level needed to reach the break-even point would be wise to focus primarily on controlling their variable costs. If the activity is expected to be lower, then decreasing the fixed costs should be the primary concern. Adopting technologies with a high fixed cost is therefore equivalent to taking more risk. In case of a change in the number of operations, the hospital would either make a high profit or take high losses.

Health technology assessment institutions whether in Canada, Denmark, United Kingdom or France, have taken great care in providing methodological guides for the assessment of innovative technologies. By following their recommendations, we were able to build a micro-costing method that allows the systematic assessment of the financial impact of minimally invasive surgical technologies on surgical operations.

Throughout this chapter, we mainly focused on the cost of surgical operations by positioning ourselves from the hospital's point of view. The fixed versus variable differentiation allows users to identify whether the investment in a new minimally invasive technology would yield positive or negative financial returns.

Results' comparison

Our 2012 application uses an estimation approach based on average use data which allows hospitals to calculate a cost per operation using their current information collection system. Results show that the cost per computer-assisted gastric bypass amounts to an average of 6 961.81 Euro without taking into account the overhead cost nor adding the cost of hospital stay and other exams. The comparison to the corresponding GHM with a reimbursement of 4 687.95 Euro [6] that include the entire patient care pathway marks a difference of 2 273.86 Euro. Current use of the da Vinci robotic system in Gastric Bypass therefore appears to present little financial incentive when only the operation's cost is taken into account.

In a more detailed estimation, our 2013 application uses a cost per operation approach based on a detailed database whose collection usually requires dedicated staff or a modern information collection system. Results show that the incremental cost of using the da Vinci, compared to laparoscopy, during gastric bypass procedures amounts to an average of 3 520.88 Euro. Our sensitivity analysis demonstrates that even when used at full capacity or to its maximum life service, the robotic system still does not present a financial advantage compared to its laparoscopic alternative.

When the 2013 LGBP results are compared to the benchmark determined in Sub-section 5.2, we notice that both values are nearly identical. Indeed, the 2013 application yielded an average cost per LGBP operation of 2 804.72 Euro while the benchmark value was set at 2 826.05 Euro. We can safely consider that our 2013 approach correctly estimates the average cost per operation.

When compared together, both the 2012 and 2013 approaches yield similar results for RGBP (6 961.81 vs 6 325.62) even though they do not take into account all resources.

[6] As mentioned earlier in this chapter, both LGBP and RGBP are coded under the same GHM and are therefore reimbursed at the same value.

As the 2013 approach has been determined to be correct, when compared to the ENC method, we can also validate the 2012 application.

Method and approaches' advantages

One major advantage of our method, compared to ENC, is our ability to calculate the cost per operation for innovative surgical technologies that do not possess a GHM[7]. While both the 2012 and 2013 approaches can be used, we recommend that the choice be made depending on the analyst's objective keeping in mind each one's advantages and disadvantages.

One advantage of the 2012 approach, compared to the 2013 one, is the ability to prospectively estimate the cost per operation and perform a break even analysis before investing in an innovative technology. Another advantage is the ability to prospectively estimate the selling price of a technology that the IHU is developing for a certain expected GHM reimbursement value. Data collection mostly depends on surgeons, engineers and managers' feedback for the identification of resources *typically* used during operations.

One advantage of the 2013 approach, compared to the 2012 one, is the ability to calculate standard deviations, present kernel density plots and perform statistical significance tests when conducting comparative clinical studies. Another, essential, advantage is the fact that this second approach is required when conducting studies in a protocol setting and has more scientific validity when publishing in the literature. Data collection, currently, mostly depends on dedicated staff in charge of attending each operation and manually recording resource use.

Limits of the methodology

One of the limits of our methodology was the inability to go into deeper detail for the overhead cost even though we convinced the hospital of the method's utility and gained permission to conduct the analysis using their data as a case-study. The work we started with the management adviser of the Hepato-Digestive department had to be put to a stop as the hospital's management appears to give low priority to cost analysis.

[7]Reminder: if a reimbursement is desired, innovative surgical technologies need to be evaluated by the national health authority before obtaining a GHM. The request document's construction, submission and evaluation could take several years.

We chose to determine an overhead cost per minute using both Anesthesia and Block ICR since we already took the anesthesia personnel into account in our calculation. Using only the Block ICR would underestimate the overhead cost and was therefore not advised.

We were able to determine a maximum number of uses for robotic re-usable instruments using data from Intuitive Surgical as they impose such a limitation. Non-robotic instruments from other companies do not have a pre-defined limit and are therefore used until broken or considered unusable. The hospital neither tracks these instruments' use nor the number of sterilization and, therefore, does not know what their service life is further dampening the accuracy of our assessment - through probably not to a great degree .

Considering these weaknesses, we try to be as transparent as possible so that users and readers can judge the relevance, precision and reliability of the cost data and method by themselves. We feel that compared to the widely variable approaches used in most of the cost/benefit peer reviewed literature, both our approaches have sound economic foundations and are validated by the real-life examples we used.

Currently, the biggest obstacle to the implementation of our second more detailed approach on a wider scale is the data collection system used at the hospital. Every patient has a "fiche patient" in which we find the patient's characteristics, operation duration (divided into anesthesia and surgery phases) as well as the present medical personnel and instruments used. The hospital ought, however, to concentrate on using modern electronic tracking and information management systems as to build automatically updatable database at the lowest cost possible.

9 Conclusion

In the past, the adoption of innovative technologies into hospital practice was guided by the practitioner's preference and the patient's desire for one treatment or another. Hospitals and the government used to pay little attention to the economic implications of financing and using surgical technologies.

Today, the introduction of innovative minimally invasive hybrid surgery in French operating rooms is bound to face two strong barriers. The first, methodological, relates to the current French medical information collection and analysis system's inability to determine the cost per operation of innovative surgical technologies. The second, economical, imposes having any additional incurred costs be justified through significant socio-economic benefits.

In this chapter, we started out by searching for a solution to the first barrier by studying how the current French healthcare system and cost calculation work. After highlighting the weaknesses in the existing method, we proceeded to conduct a literature review of potentially applicable costing methodologies for surgical technologies.

Through our review, we were able to highlight an important lack of a common nomenclature for analyzing the cost of surgical operations. The variability in calculation and reporting drove us to establish our own method, which we sought to apply and validate using the example of da Vinci robot-assisted surgery.

Using data from the IHU Strasbourg, we presented two different approaches to applying our costing methodology according to whether the studied technology is adopted and whether detailed data is available. The first 2012 approach proves to be most pertinent for ex-ante calculations, or when detailed data is unavailable, while the second 2013 approach is most suited for ex-post analysis, or when data is abundant.

Further developments, or at least applications, are still needed to demonstrate our method's practicability when applied to the entire patient care pathway or including a precise calculation of the overhead costs. The restriction of our analysis to the surgical act itself was not done by choice, but was rather a consequence of the hospital's relationship with the IHU.

While being able to determine the cost of using innovative hybrid surgical technologies represents a great step forward to fulfilling our thesis' goal, we have yet to break the second (economical) barrier. In the next chapter, we attempt to address this question through a detailed analysis of methodologies for assessing the socio-economic benefit of hybrid surgical technologies.

Chapter 3

Extended health economic evaluation for medical devices

1 Introduction

As a French institute specialized in the development and use of innovative surgical technologies, the IHU will possibly have to face some of the many constraints that the French healthcare system has erected over the years. Difficulty of assessing the cost of innovations, lack of data collection and access, and even the lack of methods for evaluating the outcomes altogether, are but a few examples of such obstacles.

Historically, the methods for evaluating a treatment's effectiveness focused on the physician's point of view with an emphasis on symptoms, cure and mortality. With the increase in technology leveraged medicine and the diversification of patient care, the focus gradually shifted towards the patient's point of view emphasizing the impacts of a treatment on his life expectancy and quality of life.

Recent years have seen hospitals experience yet another shift in the focus of decision making, and politics more generally. With a financial crisis sweeping all sectors of the economy, healthcare discussions were no longer centered on the patient but more on the hospital and, more generally, the social security/government's expenditures.

Advancing technologies that "only" improve patients' quality of life is no longer the main focus for public reimbursement agencies and hospitals. What is considered as a

good opportunity, however, is an innovation that can also be proven to present a positive economic impact be it through cost reductions or an increase in revenue.

In the previous chapter, we strongly emphasized the importance of estimating the impact of innovations in minimally invasive surgery on the cost of surgical operations. The method we proposed, however, is not sufficient as most technology leveraged innovations in this field tend to increase the cost instead of controlling it.

Traditionally, health economic evaluations have mainly focused on the benefits for the patient and shied away from the impacts that innovations could have on surgeons, hospitals and the region more generally. The development of minimally invasive surgery, however, is motivated by its potential contribution to an increase in the surgeon's performance, the hospitals' efficiency and the region's attractiveness.

In this chapter, we therefore try to widen our previous chapter's analysis by including the entire patient's care pathway and the impacts that such innovations could have on all actors. We hope to show that there may be gains with a broader view of patient care that could possibly offset the additional investment cost, such as with computer assisted surgery, at least from the government's perspective.

The first section will be dedicated to describing and analyzing the particularities of medical devices (in general) as we try to identify whether current established economic evaluation methodologies can be applied to our study. Through a comparison of established methodological guidelines, we also try to identify key points that could help us create a list of outcome points of relevance to our objective.

The second section provides analysts with a list of measures that we consider of relevance for the economic evaluation of minimally invasive surgery, and medical devices more generally. After defining and justifying the inclusion of each variable, we also discuss the available methods, or tools, to measure their impacts.

The third section of this chapter is an example of these methods' application meant to give the reader an idea of what kind of conclusions, or results, can be achieved using the discussed evaluation measures. We try to provide a full example using the IHU's da Vinci Surgical System's data and, where the protocol's database is lacking, using data from other innovative surgical procedures.

The discussion section concentrates on interpreting our application's results as well as providing an overview of the difficulties that analysts could encounter using the methods discussed in this chapter. We conclude by summarizing our findings and suggesting a course of action that, for the next years and from our point of view, should be the focus of economic evaluations for minimally invasive surgery and the IHU Strasbourg.

2 Economic evaluation approaches for medical devices: a literature review

To perform any economic evaluation of minimally invasive surgery, we must first understand the nature and characteristics of the object being analyzed. As medical devices, for example, minimally invasive technologies present a number of particularities (detailed below) that the health economic literature has yet to take into account. Such a lack of consideration appears to be due to medical devices' inferior weight in the global healthcare expenditure compared to that of pharmaceutical products in general.

In this section, we start off with a description of medical devices highlighting the challenges that they pose when performing economic evaluations. We try to address each particularity either by proposing an evaluation approach or by pointing out the existing obstacles to be bypassed.

We then provide an overview of the health economic evaluation literature and recommendations, albeit created with pharmaceutical products in, and how they apply or can be adapted to innovative surgical technologies. As the methodology for cost analysis has already been addressed in Chapter 2, we will mainly focus on the outcome side of the economic evaluation equation.

2.1 The particularities of medical devices

The economic evaluation literature has proven to be quite abundant in the pharmacoeconomics sub-discipline with 38 countries each having created its own recommendations [ISPOR]. In comparison, the medical devices' literature is noticeably rarer even though their evaluation raises a number of questions that are frequently overlooked by the more generic pharmacoeconomic guidelines [Barkun et al., 2009; Ergina et al., 2009; Kirisits and Redekop, 2013].

Drummond *et al.* [2009] took interest in analyzing these differences through a study of medical devices' characteristics and their comparison to pharmaceutical products. Their conclusions, summarized below, should shed some light on the difficulties that analysts encounter and will have to overcome when analyzing hybrid innovations:

- Medical devices are often used in different indications. Being indivisible, their value must be a weighted average of their use in multiple applications;
- The implementation of a new device may require organizational changes such as combining diagnosis with surgery. Training is another factor specifically required for innovative technologies that introduce fundamental changes in patient care;
- Innovations, especially in the case of diagnosis, are only an element in the entire patient care pathway. Patient outcomes cannot always be attributed to the introduction of the medical device as the improvement can be due to subsequent treatments;
- Most devices undergo modifications during their lifetime which may impact their efficacy. A device with low efficacy at introduction may prove to be highly effective after further development;
- Use of medical devices, particularly in surgery, is associated with a "learning curve". Innovative devices have an intrinsic disadvantage when compared to existing tools due to the user's skills and experience.

The first point has been previously addressed in this thesis through our cost calculation methodology by taking into account the use of each medical device over the year. The second point has also been taken into account to some extent for, while our costing method identifies all organizational changes that occur in the operating field and care pathway, it does not systematically evaluate the changes in the institution's overhead.

While the third point presents a major obstacle to economic evaluations, it can be bypassed by correctly establishing a clinical trial protocol. Outside the boundaries of a protocol driven database, various econometric methods could be used to isolate the effect of a technology. French healthcare institutes, however, do not currently possess the kind of data necessary to conduct such complex studies.

The authors correctly address the fourth and fifth points by stating that clinical and economic evaluation of devices should be viewed as an iterative approach with revisions being made to the estimates as more evidence is gathered on effectiveness in actual use. The obstacle, again, lies in the current data collection mechanism used in French healthcare institutes that render these approaches difficult and costly to perform.

Yet another particularity is discussed by Taylor *et al.* [2009] who point out that the evidence requirements to the licensing of medical devices are much lower than for drugs. Regulators seem to mainly base their decisions on studies of safety and effectiveness that are not necessarily based on randomized designs. What is more, they do not typically demand long-term efficacy data.

Kingkaew *et al.* [2014] and Ergina el al. [2009] further discuss the importance of randomized control trials which, they state, are often not feasible for medical devices. Their argumentation revolves around the impracticability of concealment, blinding and randomization which require the consent from subjects because of ethical issues. Furthermore, the analysis results of randomized control trials are often limited in terms of target population, sample size as well as time scale of monitoring and evaluation. The cost of such trials also forms a third barrier as new technologies are often not reimbursed for pending their regulatory approval - which requires prospective studies.

Even taking into account these particularities, the authors [Drummond et al., 2009; Ergina et al., 2009; Kingkaew and Teerawattananon, 2014; Taylor and Iglesias, 2009] agree that the requirements (i.e. use of cost per quality of life measure) for the policy making component of the Health Technology Assessment (HTA) process are similar for both pharmaceutical products and medical devices. While pharmacoeconomic guidelines can theoretically be used in both cases, the particularities of medical devices require some adjustments to the proposed approaches.

2.2 Evaluation guidelines: a focus on outcomes

The effects of a treatment, or the impacts of an innovative hybrid medical device, can be defined in various ways and using different methodologies. The analyst's first role is to select and justify, in advance, his choice of both cost and outcome parameters with respect to the research question, indication, available data and national recommendations.

In that sense, the comparison of economic evaluation guidelines is essential to identify methodological principles that potentially maximize the scientific validity of economic evaluations, especially when considering reimbursement agencies. However, as Mathes *et al.* [2013] point out, a number of differences exist in cross-country recommendations due

to the structure and regulation of health care systems; to which they add the observation of conflicting recommendations that cannot always be rationally explained.

Masseti *et al.* [2015] published a topic-by-topic comparison of French and British guidelines for the economic evaluation of health technologies in order to bring out their key differences and similarities. Their findings show that both governments recommend the use of Cost-Utility Analysis (CUA) with health related quality of life (HRQoL - See section 3.2) measures considered as the preferred method for outcome evaluation. A high preference is also expressed for the use of Quality Adjusted Life Years (QALY - See section 3.2), especially when trying to register a product for reimbursement in which case this measure becomes mandatory.

Both the French and British agencies reject the use of Cost-Benefit Analysis (CBA) most notably due to the debate regarding the ethical implications of assigning a value to patients' lives. Nevertheless, the French "Haute Autorité de Santé" (HAS) considers CBA relevant only as an additional source of information if its application is feasible for the studied intervention [HAS, 2012].

Randomized clinical trials are the favored methods for data collections with non-randomized studies being recommended only as a supplement to add value to the results, limit bias or provide additional information. According to the French and British guidelines, both positive and negative effects of a technology are to be taken into consideration.

In terms of impacts on workplace productivity, the UK explicitly indicates that this factor is to be excluded from the analysis as they adopt the National Health Service's (NHS) perspective. As such, the government mainly takes interest in analyzing the impacts of innovations on the national health system's expenses which exclude productivity related ones. France, on the other hand, allows the study and reporting of such impacts in a separate analysis in the form of indirect costs.

The Canadian Agency for Drugs and Technologies in Health [CADTH, 2006] provides similar recommendations with a focus on CUA and HRQoL outcomes. As with French guidelines, they also accept the use of CBA as a secondary type of analysis provided that the steps taken to convert the outcomes into monetary terms is thoroughly explained.

The Danish Center for Health Technology Assessment [Kristensen and Sigmund, 2007] does not provide a fixed standard for how health economic evaluations should be performed. Instead, they provide analysts with a detailed overview of all health economic methodologies with recommendations as to what to include in each cost and outcome parts.

In terms of outcome assessment, the authors did not express a preference for any specific measure. In the case of CUA, however, attention should be given to the fact that the impact of reduced income is already included in QALY measures which poses a potential risk of double counting the cost of productivity loss.

As Kirisits *et al.* [2013] note, the use of QALYs can be somewhat complicated for the evaluation of medical devices given that the efficacy or effectiveness of such technologies is usually reported in the form of intermediate outcomes (complication rate, procedure duration, diagnostic performance etc.). Consequently, to capture the impacts of an innovative medical technology, the analyst ought to evaluate the costs and benefits during the entire care pathway taking into account both successful and failed treatments as well as short and long term outcomes.

Stepping outside the care pathway, the analyzed guidelines do not appear to take interest in the previously discussed effect that innovative medical devices have on hospital attractiveness and efficiency nor its impact on the region's economy. This is most probably due to the recommendations' focus on pharmaceuticals, as signaled by Masseti *et al.* [2015], which do not present such impacts.

In terms of productivity loss, reviewed guidelines discuss in sufficient detail the measurement methods for absenteeism but little to no attention is given to the impact on presenteeism. As the latter has only become a study subject around the year 2000 [Johns, 2009], few reliable results have yet to be published in the literature.

3 Review of economic evaluation measures

In the previous section, we highlighted the weaknesses in current economic evaluation guidelines as they have been created mainly with pharmaceutical products in mind. Since we demonstrated that medical devices present many fundamental differences, it

is now more clear that the use of these published recommendations require certain modifications.

In this section, we provide a literature synthesis of the variables that can potentially be included in a medico-economic evaluation of innovative surgical technologies. For each variable, we also perform a literature review as to identify which methods could, or should, be used for the measurement of its effects.

3.1 Direct and indirect costs

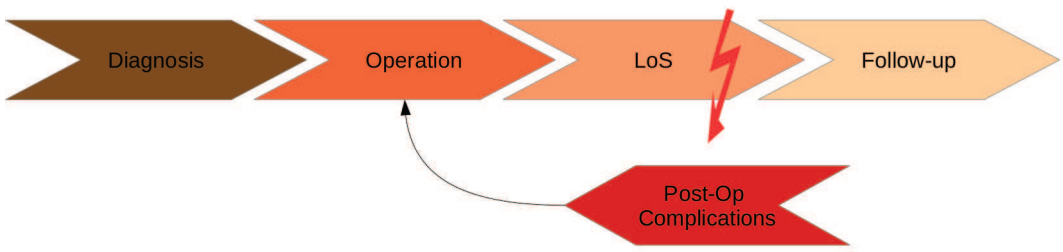
The introduction of minimally invasive procedures such as laparoscopy or endoscopy has known rapid success mainly due to their effectiveness and patient friendliness. However, they were also responsible for a substantial increase in the cost of operations due to their reliance on complex instrumentation. If analysts were to only look at the cost per operation, their studies would have, without a doubt, hindered the adoption of these innovative surgical innovations.

3.1.1 Length of Stay and Complications

Technology leveraged innovations in minimally invasive surgery, although expensive, are characterized by their ability to significantly reduce patients' recovery time, complication rates and length of stay. When analyzing the cost of using a minimally invasive technology, it is therefore essential to take the entire patient care pathway into account.

From a purely economic standpoint, the treatment of diseases can be considered as a complex production process during which a sick patient (input) is transformed into a healthier individual (output). In the surgical care setting, this production process is equivalent to the patient care pathway including all activities needed for the input-output transformation: Diagnosis, Surgical Operation, Length of Stay (LoS) and Follow-up.

FIGURE 3.1: Patient care pathway



Generally, the cost of surgical operations represents only a part of the entire process's (Figure 3.1) and its increase is, more often than not, counterbalanced by a decrease in resource use during the other phases. Depending on the type of care, however, some phases would be more affected than others in which case it is the analyst's choice to either restrict the analysis or include the entire pathway.

In outpatient care[1] (Ambulatory), for example, patients receiving treatment usually also receive a same day discharge as their recovery is considered to not need continuous monitoring. In such cases, hospital length of stay plays a minor to no role in patient's care when comparing surgical innovations.

In inpatient care[2], the effect of introducing a new technology is often observable through a variation in the number of hospital days needed for recovery and, consequently, the cost of care. However, the use of this measure in economic evaluations seems to be ambiguous as to its consideration as either a cost or an outcome. It is not uncommon in cost-effectiveness analysis, for example, to consider LoS as the outcome measure while cost-utility and cost-minimization analysis automatically include this variable in the cost part.

In the particular case of Minimally Invasive Surgery (MIS), when compared to more invasive approaches, not only should we observe a reduction in hospital LoS but also in the amount of care that the patient needs. The premise of MIS is a reduction in surgical trauma [Desborough, 2000] which in turn facilitates the patient's recovery, who would, theoretically, require less medical attention. Such a change could potentially reduce the work load on both the nurses and hospital staff more generally, thus reducing the cost per hospital bed day.

During the care pathway, it is possible for the patient to experience unexpected complications that disrupt his recovery in different ways. Theoretically, an advance in surgical technologies will result in fewer or less sever complications. Methodologically speaking, the distinction between intra-operative and post-operative complications therefore plays a simplifying role in an economic evaluation as their consequences affect different steps of the care process and can be treated differently.

[1] Outpatient care definition: admissions that do not require patients to be hospitalized.
[2] Inpatient care definition: admissions that require patients to be hospitalized.

On the one hand, the immediate consequences of intra-operative complications (surgical site infections, bleedings, etc.) are usually translated though an increase in surgical resources' use and possibly length of stay. On the other hand, consequences of post-operative complications can vary between the need for supplementary medication, a longer hospital stay or even a re-operation in which case the impact is considerable.

The cost of intra-operative complications is usually harder to discern from the surgical operation's cost as it is not common to identify complication specific resource use (other than disposables). Their cost is therefore usually integrated into the cost per operation.

Whether patients were admitted into inpatient or outpatient care, the impacts of surgical technologies on post-operative complications can be evaluated, from our point of view, following a two step analysis. First, the added cost of complications should be defined taking into account surgical/medical resource use and length of stay. Second, the variation in the complication rate-of-occurrence following the introduction of a new technology should be determined.

Translating these values into an expected cost for each type of complication is then only a matter of multiplying both numbers. However, this also implies possessing the necessary data to perform such a calculation.

3.1.2 Absenteeism

The premise of Minimally Invasive Surgery is a significant reduction in surgical trauma allowing patient to recover faster and thus reduce absenteeism (time off work). The inclusion of this measure as an economic impact in the evaluation of innovative minimally invasive technologies is therefore logical and necessary.

Patient recovery naturally includes a transition phase from a sick to a healthy state during which they are unable to fulfill many of their daily activities be it personal (leisure) or professional (work). When adopting a societal perspective in economic evaluations, the time patients spend off work can be expressed in two parts as both a direct and indirect cost.

A treatment in pharmacotherapy often consists in patients acquiring, then consuming, a drug without necessarily interrupting their daily work-flow. In the case of surgical

treatment, however, the patient is a direct participant in the "production process" during which they are considered as an "input" from an economic standpoint. The time patients dedicate for diagnosis, surgery, hospitalization and follow-up can therefore be considered as a direct absenteeism cost of a treatment.

In both pharmacotherapy and surgical treatment, the patient is sometimes required to stay at home to rest and heal as part of the treatment process. In economic evaluations, this time off work can be expressed as sick leave and included as an indirect absenteeism cost of a treatment.

The valuation of absenteeism in monetary terms is the center of debate in health economics with two methods being suggested, Human capital and Friction cost, each offering a different level of precision and measurement difficulty. The human-capital method takes the patient's perspective and counts any hour not worked as an hour lost. By contrast, the friction-cost method takes the employer's perspective and only counts as lost those hours not worked until another employee takes over the patient's responsibilities [Hout, 2010].

The human capital approach is based on the logic that gross wages reflect the minimal value of production [Hout, 2010]. In other words, loss of production is at least equal to the gross earnings of patients before deductions, plus employer-paid benefits. To cover the cost of those that are in unemployment, the decision maker may choose to use national average wages.

The friction cost method provides more precise estimates, and is usually lower than with the human capital approach, by considering loss of productivity as the time-span organizations need to restore the initial production level [Hout, 2010]. However, results are very likely to vary by location, industry, firm and category of worker meaning that decision makers must rely on previously established cost estimates.

Consideration should therefore be given to whether the loss in production is compensated by the employee, or colleagues, upon his return to work or whether the employer has hired a replacement worker. On one hand, Drummond *et al.* [2005] argues that evaluations using the human capital approach tend to overestimate the true cost to society if the individuals were to be taken out of the workforce. On the other hand, assuming full employment, Pauly *et al.* [2002] indicate that the average wage per day can either be a

reasonably accurate measure or substantially underestimate the cost of lost work time depending on both the work and the firm's characteristics.

3.1.3 Presenteeism

Certain health and disease conditions impose a cost burden to the employer not only due to absenteeism but also to on-the-job productivity losses. Dealing with these conditions should naturally imply the restoration, or even amelioration, of a normal productivity level. Minimally invasive surgery, like any other therapy, deals with the treatment of such physical ailments that burden individuals and would, therefore, directly impact presenteeism. As with absenteeism, the inclusion of this measure as an economic impact in the evaluation of innovative minimally invasive technologies is therefore logical and necessary.

The literature points out two different types of presenteeism according to whether it is due to an acute illness or a chronic condition [Johns, 2009]. In the first case, the patient would have a choice as to either attend work or take a sick day. In the second case, employees may be required to work in spite of their health condition.

Health technology assessment guidelines have paid little to no attention to the impact of treating diseases on the level of productivity aside from absenteeism. The comparison of pharmacoeconomic guidelines [CADTH, 2006; HAS, 2012; Kristensen and Sigmund, 2007; NICE, 2013; WHO, 2008] reveals a complete lack of consideration for this variable.

A literature review by Schultz *et al.* [2009] on the magnitude of presenteeism costs demonstrates the relative lack of evaluation of this variable as either a cost or an outcome in economic evaluations. It is only in recent years that authors appear to have started taking interest in this question with most of the research focusing on measurement methods.

To date, randomized control trials were the most commonly used and accepted methods estimating the impact of presenteeism. Alternatives such as patient diaries, surveys or single-group repeated measures studies were also suggested even though their use appear to be less common [Burton et al., 2003].

Attempts to estimate the daily impact of health status on productivity remain limited in numbers. We only know of two studies, Goetzel *et al.* [2004] and Collins *et al.* [2005],

that provide the number of hours lost per day as well as their financial value for different diseases and impairments.

TABLE 3.1: Daily hours lost and economic impact per impairment

	Goetzel *et al.*		Collins *et al.*		Average	
	Hours	Dollar	Hours	Dollar	US	FR
Allergy	0.9	20	1.5	33.7	26.8	27.6
Any Cancer	0.7	16	–	–	16.0	16.5
Arthritis	0.9	21	1.6	36.5	28.7	29.6
Asthma	0.9	20	1.4	33.2	26.6	27.4
Back/Neck disorder	–	–	1.7	40.2	40.2	41.5
Depression/mental illness	1.2	28	2.9	67.4	47.7	49.2
Diabetes	0.9	21	1.4	33.0	27.0	27.8
Heart disease	0.5	13	1.6	36.9	24.9	25.7
Hypertension	0.6	13	–	–	13.0	13.4
Migraine/headache	1.6	38	1.9	43.3	40.6	41.9
Musculoskeletal	–	–	1.7	39.8	39.8	41.1
Respiratory disorders	1.4	32	1.9	44.1	38.0	39.2
Stomach/bowel disorder	–	–	1.7	40.2	40.2	41.5

Table 3.1 summarizes the findings of the two studies by presenting the average daily amount of hours lost as well as their monetary equivalent in US dollars. In both studies, the average daily dollar impact was obtained by multiplying the average lost hours per day by the average hourly wages and benefits ($23.15) of all U.S. Companies for 2001. Using the French average hourly wage of 17.90 Euro ($23.88) for 2010, as reported by the INSEE, and the average lost hours per day as reported in the studies, we are able to deduce an average daily dollar impact for France [INSEE].

Note however, that the authors use different methodologies and approaches. The measurement of presenteeism and its estimated cost can therefore be highly variable especially considering that they combine results from different methods.

3.2 Outcome measures

In economic evaluations, the health outcome taken into consideration largely depends on data availability and the chosen type of analysis. Cost-effectiveness, for example, focus on single program specific and unvalued (in terms of preference) measures such as episode free days, life years gained or lives saved. Many other possibilities are offered to the analyst who, in principle, bears the responsibility of choosing the right outcome measure all the while justifying his choice.

3.2.1 Unvalued outcomes

The first choice that analysts will have to make consists in either evaluating the technical efficacy of an innovative technology or adopting a more patient centered approach. Bariatric surgery studies, for example, have often focused on efficacy outcomes related to either short or medium term weight reductions [O'Brien et al., 2006], expressed as a mean percentage of excess weight loss. Other studies include the impact of treatments on disease specific co-morbidities such as diabetes, hyperlipidemia, hypertension, or obstructive sleep apnea [Buchwald et al., 2004].

As most interventions, Minimally Invasive Surgery included, seek to improve patients' well-being, Health Related Quality of life (HRQoL) [3] has been increasingly used as the primary outcome in treatments' economic evaluations. The measurement of this improvement, however, present high variability as different tools exist in the form of either disease specific or generic questionnaires.

Disease specific questionnaires focus on the evaluation of dimensions that are potentially affected by a certain treatment. The Functional Digestive Disorders Quality of Life (FDDQL) self administered questionnaire [Chassany et al., 1999], for example, contains 43 items that measure the physical, psychological, and perceptual impact of dyspepsia and irritable bowel syndromes.

Generic questionnaires, in their raw form, attempt to reflect the patients' physical, psychological and social well-being in a comprehensive manner. The Short Form 36 (SF-36) [Brazier et al., 1992], for example, is a self administered questionnaire containing

[3] HRQoL definition: A measure of the impact health status has on several dimensions, such as positive emotions and life satisfaction, of an individual's life.

36 items that measure health on eight dimensions covering functional status, well being and the overall evaluation of health.

The use of generic questionnaires allows for the comparison of different treatments and diseases as responses are not particularly sensitive to the nature of the sickness. However, as Preedy *et al.* [2011] point out, the use of condition specific instruments provide higher precision and validity:

> *"The use of condition specific instrument provide better psychometric properties, namely, content validity. In addition, the attribution factor is better in condition-specific instrument. This concept can be explained by the following example: When using generic instruments, obese patients will rate their general health, sleep, social activity, etc. without direct reference to obesity, which will make the rating susceptible to external influence from other conditions or factors. However, the use of obesity-specific instruments will filter out external influences as it will only rate the impact of obesity"*

A common problem with both types of Quality of Life (QoL) questionnaires is the absence of the notion of preference for the various possible outcomes. It is therefore not clear whether a higher score is associated with a preferred outcome. The existing solution comes in the form of preference based QoL measures calibrated onto a scale of [0,1] with 0 being dead and 1 being perfect health [Drummond et al., 2005], as we describe in the following subsection.

3.2.2 Preference based QoL measures

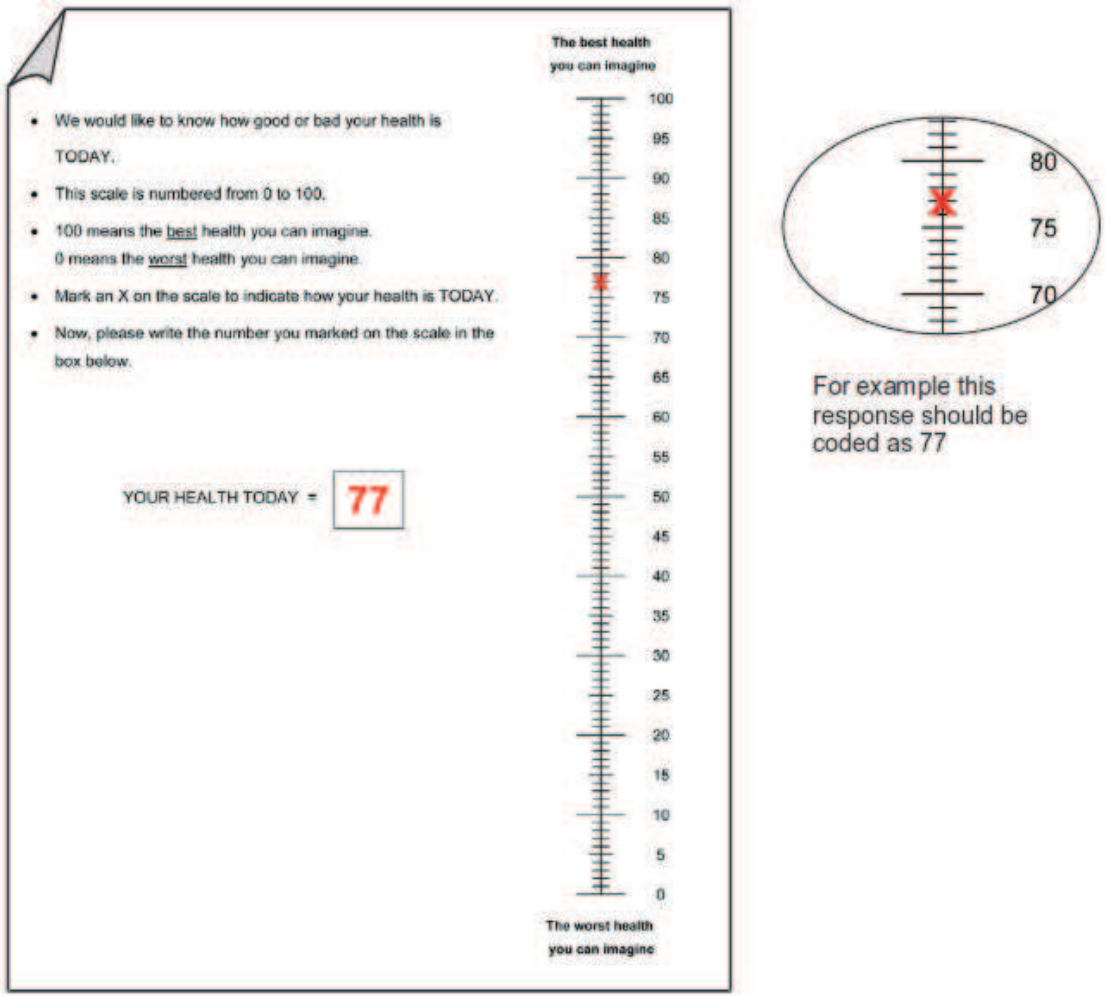
Cost-Utility Analysis (CUA) is a full economic evaluation that focuses on morbidity and mortality related outcome measures that integrate the notion of preference. Disability Adjusted Life Years (DALYs) and Quality Adjusted Life Years (QALYs) are two of the most known outcomes to have been taken into account in the published CUA literature.

Considered as the gold standard in health economic evaluations, QALYs are a common measure that combine both life expectancy and health-related quality of life (HRQoL). The former is typically measured using disease specific life tables [Fontaine et al., 2003;

Peeters et al., 2003] while the latter is measured through generic surveys for which utility functions have already been determined (such as the EQ-5D).

The EuroQoL group, established in 1987, comprises a network of international multidisciplinary researchers who are at the origin of one of the four most renowned preference based HRQoL questionnaires[4]. Their product, the EQ-5D, is basically a 2 pages document (Figures 3.2 and 3.3) with one page presenting a visual analogue scale (EQ VAS) and a descriptive system based on time trade-off on the other.

FIGURE 3.2: EQ-5D Visual Analogue Scale



***NB: Missing values** should be coded as '999'.*

***NB:** If there is a discrepancy between where the respondent has placed the X and the number he/she has written in the box, administrators should use the number in the box.*

[4]The other HRQoL surveys being the Short Form 6D (SF-6D), Quality of Wellbeing (QWB) and Health Utility Index (HUI) [Furlong et al., 2001]

Figure 3.2 presents an example of the EQ-5D visual analogue scale which records the respondent's self-rated health. This information is mostly used as a quantitative measure of health outcome, as perceived by the patient, in cost-effectiveness studies. The VAS is often used as a way to prepare the patient for a more detailed evaluation as it allows him to become more aware of his current health state.

While practical to use, the VAS has several weaknesses due to known measurement biases previously reported by Torrance *et al.* [2001]. Context bias reflects the idea that a VAS score for one state depends on the number and type of better or worst states apparent to the patient at the time. End aversion is another bias that reflect the reluctance of patients to use the extreme values of a measurement scale.

FIGURE 3.3: EQ-5D-5L Descriptive System

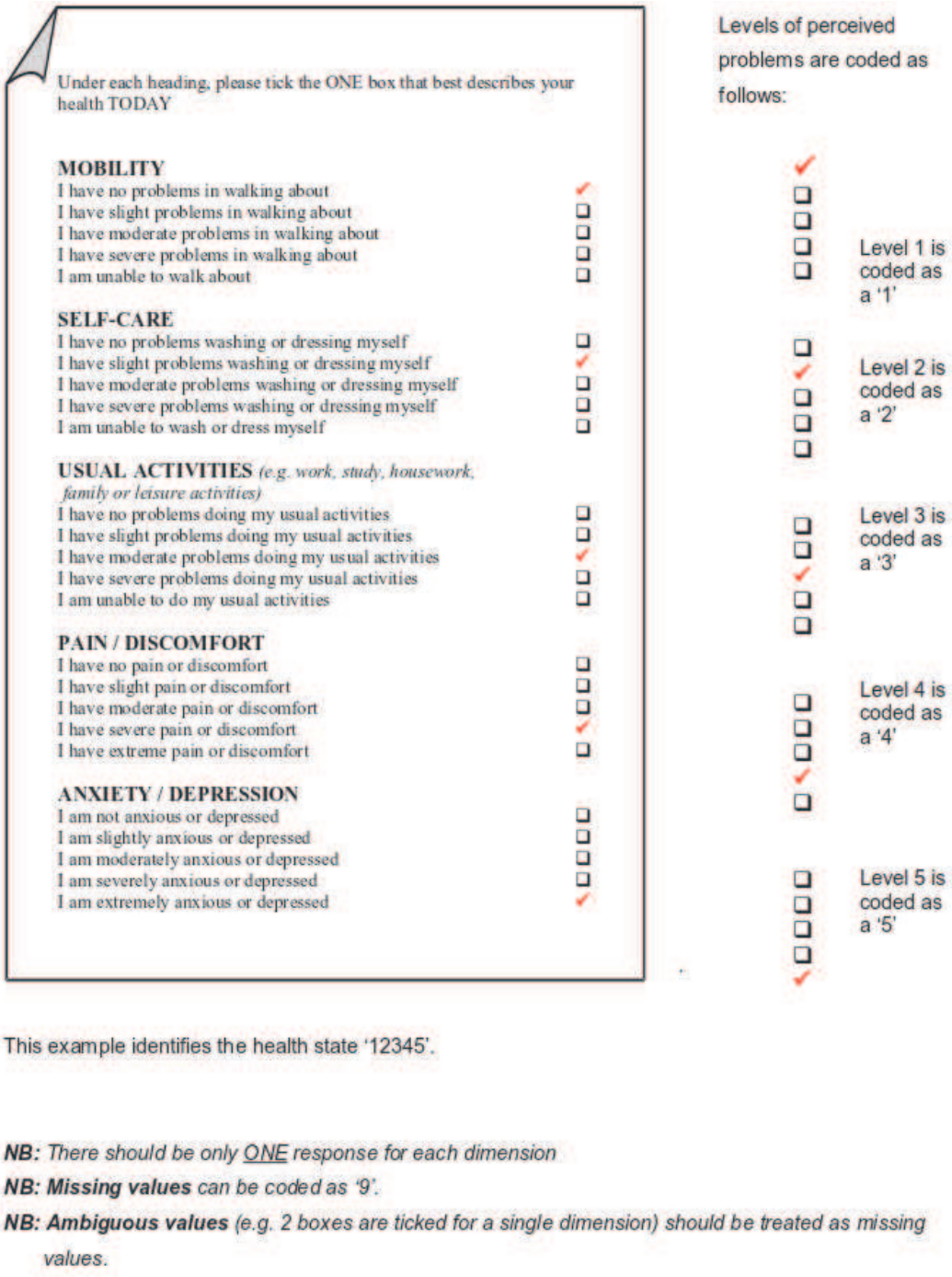


Figure 3.3 presents one possible outcome of the 5 levels EQ-5D descriptive system covering the five traditional dimensions: mobility, self care, usual activities, pain/discomfort and anxiety/depression. Patients presented with this survey are first asked to choose, for each dimension, one of five levels: no problems, slight problems, moderate problems, severe problems, and extreme problems.

For example, state 11111 indicates no problems on any of the 5 dimensions, while state 22222 indicates some problems walking about, some problems washing or dressing self, some problems with performing usual activities, moderate pain or discomfort and moderately anxious or depressed. Each patient's answers are translated into a "health state", or profile, of the possible 3125 combinations from which a utility value can be generated. For example, an extra year in state 11111 would be valued at $1 * 1.000 = 1\,QALY$ and an extra year spent in state 22222 would be valued at $1 * 0.516 = 0.516\,QALY$ [Phillips and Thompson, 2009].

The translation of each health state into an utility value depends on country specific utility functions defined by the EuroQol Group. Using econometric modeling and large sample databases, these functions supposedly estimate the preference of each population for one dimension or another. Being able to walk about and care for one's self, for example, might have more importance than the absence of pain or discomfort in countries where mutual assistance is uncommon.

Analysts looking to create their own preference based HRQoL measuring methodologies may choose to apply one of two existing methodologies [Drummond et al., 2005; Morris et al., 2007]: Standard Gamble or Time trade off.

The Standard Gamble (SG) method consists in presenting patients with a choice between two possibilities: a health state (State 1) that can be chosen with certainty but include a disease or impairment, and a gamble with one state (State 2) being better and another (State 3) being worse. Respondents are then asked to determine the probability of State 2 which would make them indifferent between being in State 1 with certainty and taking the risk of finding themselves in State 2. The utility of State 1 is then equal to the probability given by the respondent.

The Time Trade Off (TTO) has been suggested as an easier method to use than SG and consists in giving respondents a choice between two health profiles: a particular health state (State 1) for a number of years (X) or full health for a shorter period of time. The respondent is then asked how many years would they be willing to sacrifice in order to live in full health instead of X years in State 1. Let's assume the respondent prefers to live 5 years in full health instead of 10 in State 1, State 1's utility value in this case would be $5/10 = 0.5$.

The inclusion of QALY measures into an economic evaluation is traditionally done through one of two approaches. The first, specific to cost-utility analysis, considers the QALY as the sole effectiveness measure by integrating it in the cost-utility equation as is. The second, specific to cost-benefit analysis, converts the QALY into a financial value (using Willingness to Pay) which is then integrated into a more general "benefit" equation.

3.2.3 QALY Willingness To Pay

Compared to CEA and CUA, Cost-Benefit (CBA) methods attempt to include a large number of outcomes under a single monetary value which offers decision makers with much higher flexibility in including different measures. Combining treatment changes to the patient's productivity, absenteeism and even QoL becomes possible; provided the analyst succeeds in translating all impacts in monetary terms.

From the patients' perspective, the value of a QALY should theoretically translate the benefit they derive from a medical intervention taking into account its impact on their work-related functionality/productivity, social life as well as speed and quality of recovery since all these items are measured in surveys such as the EQ-5D. Note that unless specifically told to ignore the impact that return to work would have on their income, patients may factor this effect into their response in which case analysts must be careful as to avoid double-counting productivity gains.

The most challenging task for decision makers conducting CBAs resides in finding the monetary value of a one point gain in QALYs. The health economic literature commonly put forth Willingness to pay (WTP) as one option for indicating the amount of resources patients are willing to sacrifice in order to avoid an undesirable loss in, or seek an amelioration of, their quality of life.

Three methods have been suggested for measuring patients' WTP: human capital [Johannesson, 1996], revealed preference and contingent valuation (or stated preferences of WTP) [Healey and Chisholm, 1999]. The latter appear to be the most commonly used method as it yields a theoretically correct measure of "strength of preference" otherwise expressed as the value of a commodity under standard welfare economics.

In Europe, the EuroVAQ project attempted to estimate the WTP values per country using a chained and a direct approach of contingent valuations based on the EQ-5D questionnaire [Donaldson et al., 2010]. Their findings provide a set of WTP per QALY depending on the method used, QALY gain and initial health state.

In the time variant chained approach, each respondent is asked to complete a utility assessment to evaluate a given health state on a scale between 0 and 1. Next, they are asked to estimate their WTP to avoid a given duration of that current health state with the duration being variable as to keep the QALY gain constant across respondents.

For example, for a respondent with a health state's utility value of 0.90, avoiding 6 months in that state with certainty would amount to a gain of 0.05 QALYs (0.10 * 6/12). The respondent with a health state's utility value of 0.8 would need only avoid three months in that health state with certainty to gain 0.05 QALYs [Donaldson et al., 2010].

TABLE 3.2: EuroVAQ - Value of a QALY trimmed time variant chained approach (US Dollars)

0.10 increase	Green	Yellow
Netherlands	18 623	15 738
UK	15 897	13 228
France	16 613	11 317
Spain	33 789	26 299
Sweden	19 287	18 292
Norway	26 399	24 757
Denmark	31 456	24 796
Poland	22 434	18 601
Hungary	13 222	10 938

Table 3.2 summarizes the findings for the trimmed time variant chained approach based on two initial health states, Green (22222 profile) being worse than Yellow (21121 profile), and assuming an increase of 0.10 QALYs. Analysts have the possibility of utilizing these values to either model outcomes or conduct sensitivity analysis.

Perhaps the most intriguing finding in this report is the fact that there is no one value per QALY for any one country. In France, for example, a patient in a bad health state

is willing to pay 16 613 per QALY but a patient with a better initial health state would pay 11 317 Euro. This observation is also valid for all other countries presented in table 3.2.

Monetizing QALY gains appears to be a delicate issue due to the existence of different measurement methods and a high variability in the results. Nevertheless, the values presented in this section can serve to form hypothesis, model estimations and conduct sensitivity analysis until a more general consensus is reached by international health economists.

3.3 Medical tourism

The term "medical tourism" has been given more importance in recent years with the emergence of healthcare destinations or "paradises" such as India or Thailand. The OECD defines medical, or health, tourism as when consumers elect to travel across international borders with the intention of receiving some form of medical treatment. This definition excludes wellness tourism which refers to visiting spas, homoeopathy treatments or traditional therapies.

Heath technology economic evaluation guidelines have yet to become aware of the fundamental difference in the mechanism that governs medical devices compared to pharmaceutical products for which medical tourism, from our point of view, is a mostly irrelevant point. It is therefore not surprising to see that the analysis of the medical tourism's impact is very rarely mentioned in HTA guidelines.

To elaborate, in case of pharmaceutical therapy, the patient only needs to visit a doctor then acquire and consume a drug marking a clear distinction between him and the product that can be offered in any pharmacy or even ordered from abroad. In surgical or medical care, the patient takes full part in the treatment by being physically present, often unconscious, for a certain duration thus becoming both the consumer and part of the product itself.

Particularly for technology leveraged surgery, the requirements for an innovative treatment are often high in terms of both financial and human capital which cannot be met by all healthcare facilities. While a drug can be ordered from the internet, it is obviously not possible to order a skilled surgeon along with his team and medical devices.

As a direct participant, patients seeking affordable top-of-the-line surgical treatments therefore need to be mobile.

3.3.1 Market view

Several studies have attempted to analyze the medical tourism market size with variable methods and precision leading to a number of, sometimes contradicting, estimations. Horrowitz *et al.* [2007] provide an interesting overview of this literature by pointing out claims for a total market size of 80 Billion Euro in 2008, with a 20% annual growth, while others estimate it to 50 Billion in 2010. Even if these findings appear inconsistent, we hypothesize that the 2010's market size is somewhere between 50 and 110 Billion Euro.

Table 3.3: Number of medical tourists 2012 - in thousands

Country	Patients	Country	Patients
Thailand	2 000	Costa Rica	250
Hungary	1 500	Brazil	150
India	1 000	Mexico	100
Singapore	1 000	South Korea	100
Malaysia	550	Colombia	80
Poland	500	Belgium	60
Philippines	400	Turkey	60
United States	250	**Total**	**8 000**

Sources: Patients beyond borders and Deloitte Center for Health Solutions [Deloitte, 2008]

In terms of tourist numbers, it was estimated that over 8 Million patients (Figure 3.3) traveled to more than 15 destinations for medical care in 2012. Even though it appears that no consensus exists, and the data is therefore unreliable, we can at least hypothesize that the top three destinations (Thailand, Hungary and India) represent more than half of the market size with France not having any visible presence.

3.3.2 Drivers of medical tourism

Few studies have been able to fully explain the factors that drive medical tourism and the reasons that incite patients to travel abroad. The weakness of this literature is due in a large part to the absence of routine data collection and the fact that most trade occurs within the private sector [Smith et al., 2011].

Traditionally, medical tourists were mainly from wealthy economies where the cost of medical care was too high or access to newer treatments and technologies was restricted. Increasingly, however, the availability of cheap transportations and accommodations is extending the market to the middle classes.

The available evidence suggests five main drivers behind the upsurge of demand for medical health services overseas [Lunt and Carrera, 2010]: cost, availability, familiarity, quality and bioethical legislation. Economic evaluations should allow hospitals to increase their international presence by communicating on both the cost and quality dimensions of care.

Economic benefits have been presented as the central focus of medical tourists since Thailand, India and Hungary are known to offer less expensive care than other destinations. Waiting lists for non-essential surgery, such as knee reconstruction, also influence patient choices as they can be as long as 18 months in some countries but only a week in others [Connell, 2006].

Distance also offers privacy to patients since their medical needs can be confounded, or disguised, as traditional tourism. Sex change procedures, for example, comes to mind as an obvious example of a surgical operation for which patients would appreciate the distance from standard daily life. Less obvious examples include any operation considered as taboo or which would change the community's view towards the patient, such as cosmetic surgery.

Medical travel also opens up a number of possibilities for patients who are presented with alternatives that do not necessarily exist in their home countries whether it is due to legislation, such as ban of abortions, or unavailability due to high skill requirements or slow regulatory pathways. Even though the latter are in place to mainly protect patients, they also serve to slow the introduction of the newest technology or therapy. It

is particularly the case for hybrid minimally invasive surgery and institutes considered as pioneers as they develop new technologies or procedures.

Smith *et al.* [2011] highlights the importance of medical tourism as a source of income, and foreign exchange, for exporting countries as well as a mean to reverse the "brain drain" for developing countries. However, they also draw attention to the dangers of developing a two tiered system in which the local population does not possess the means to benefit from high quality healthcare services or even benefit from the revenue generated by medical tourism.

3.3.3 Impact measurement

The current approaches to assessing the impact of medical tourism have been limited to either discussions, based on systematic reviews, or analysis of a macro-economic nature based on case studies. All the more, the quality of information presented in these studies have been repeatedly criticized for their lack of empirical evidence [Johnston et al., 2010; Lunt and Carrera, 2010].

As Connell *et al.* [2013] point out, the whole infrastructure of the tourism industry (travel agencies, hotels, restaurants, etc.) benefit from patients' stay during their convalescence period. In the case of Thailand, for example, NaRanong *et al.* [2011] explored both the positive and negative effects of medical tourism on the economy, health staff and medical costs. According to their findings, every year, medical tourism generates around 0.4% of the country's GDP amounting to 36.8-41.6 billion baht (1.7 Billion Euro) in added-value.

Historically, the analysis of this "tickle down" effect has been done using one of three methodologies [Jackson et al., 2005]: Computable General Equilibrium (CGE) models, Input-Output models or Cost-Benefit analysis.

CGE models are a set of equations, derived from economic theory, that describe the national economy and the interactions that exist between its components. The simultaneous solving of these equations allows analysts to determine an equilibrium in which the quantities of supply and demand are equal in every market, for a certain set of prices [Burfisher, 2011]. In that sense, CGE models are especially adapted to evaluate the effect of economic and policy shocks on the economy as a whole.

Country specific Input-Output models describe relationships between sectors and actors of an economy through the sale and purchase transactions that take place within. Input-Output tables, published by the Organization for Economic Co-operation and Development (OECD), allow the analyst to track the effect that every Euro spent in hotels, for example, would have onto their suppliers, their employees and even infrastructure used to access their services (i.e. roads).

Impact measurement using Cost-Benefit analysis consists in comparing the resource use and the impact, in terms of economic gain, of a project or event. When addressing public institutions, whether to ask for public funding or registering a new surgical product for reimbursement, the impact assessment ought to demonstrate that the benefits to society or the economy are greater than the costs.

Burgan *et al.* [2000] argue that the cost-benefit method is particularly suitable for evaluating public expenditure on special events such as tourism; and more particularly medical tourism. As such, and taking into account the low amount of data we possess, we will be adopting this approach as a first application to the IHU's case.

3.4 Intangible factors and innovation opportunity

Some benefits of innovations are always hard to discern: for instance, the use of high definition laparoscopes and monitors certainly increases cost without any proven benefit to patients' safety or outcome. Yet anyone who has used or witnessed a high definition operating room environment would practically refuse to work in a standard environment.

Other benefits might be less challenging to measure but cannot be easily translated into monetary terms. The use of computer-assisted surgery, for example, has perhaps allowed surgeons not trained or proficient in laparoscopy to develop their skills in minimally invasive techniques and thus improve patient care. Using econometric methods combined with survey-based data collection, it is theoretically possible to assess the impact of new technologies on learning curves and skill transferability. To a lesser extent, we can translate this impact into monetary terms through an analysis of the effect on more traditional measures such as operation time, number of operations or patient outcome.

On a wider scale, innovations tend to increase the acquiring institute or user's renown not only towards international patients but also professionals. The ensuing increase in

attractiveness towards international experts, industry, patients or even venture capitalists presents opportunities to develop new scientific collaborations, industry partnerships and the institute's activity as a whole. The health economic literature does not take these factors into consideration therefore potentially underestimating the effect of innovative technologies.

The short shelf life of medical devices imposes a need for constant innovation as to change, adapt or improve their functionality and renew the market's interest. Several terms are known by the economics community to describe this dynamic: disruptive, radical and incremental innovation. The differentiation between these terms has been subject to extensive discussions and variability specific to each discipline as pointed out by Koberg *et al.* [2003] and, more generally, by Baregheh *et al.* [2009] regarding the definition of "innovation" as a whole.

As Professor Clayton Christensen explains[5], a disruptive innovation is not a breakthrough innovation that improve upon an existing product, but one that transforms products that historically were so expensive or complicated that only a portion of people had access to. Disruptive innovations render the product much more affordable or accessible by a much larger population thus extending the market from the bottom, to people that were not initially considered as customers.

A simple way to look at the difference between radical and incremental is by considering, on one hand, radical innovation as either improvements that mark a significant shift from existing performance, or as solutions to complex problems that existing products do not solve. Incremental innovation, on the other hand, aims at enhancing an existing technology by adding a series of small improvements. Admittedly, some products present a higher potential for improvement than others, a characteristic that cannot be easily measured *ex ante*.

Current practice in health economics focus on the measurement of cost and effect of health innovations without taking into account the nature of the technology itself. It is essential to recognize that even if a product is proven to not be cost-effective at adoption, it might present enough opportunities to develop other innovations or even small improvements that potentially would shift the cost-effectiveness ratio (A more detailed

[5]See interview with Prof. Clayton Christensen: *http : //www.claytonchristensen.com/key − concepts/*

discussion on this point will be had in the next Chapter).

Minimally invasive surgery have the potential to impact both the economy and the society in numerous ways whether by affecting care efficiency, workplace productivity, quality of life, medical tourism, or the less straightforward measure of practitioners' and patients' view of surgical care. However, taking any such measures into account depends on the availability of reliable data, which is often problematic outside of clinical protocols.

4 Application: evaluation method

In Chapter 2, we based our cost analysis on resource use data from a protocol written by the IHU clinical team, in late 2012, for the comparison of the clinical and the medico-economic impact of computer-assisted versus laparoscopic gastric bypass. The same protocol's database contains information on each patient's quality of life, number of complications, number of days off work and length of hospital stay which form the base for our outcome analysis.

We remind the reader that our choice for these minimally invasive surgical procedures is driven by two reasons. The first relates to the hospital's and the IHU's consideration of computer-assisted surgery as their most innovative hybrid technique currently in possession. The second reason is a direct consequence of health economic principles dictating that any economic evaluation of a given technology should be performed by comparing it to the most cost-effective and widespread alternative, which in our case is laparoscopy.

4.1 Length of stay and complications

During our talks with Strasbourg's University Hospital over the cost calculation methodology developed in Chapter 2, they insisted on their desire to apply our method only to the surgical operations and not hospital LoS. While they did not explain the logic behind such a decision, they gave their "Pôle Hépato-Digestif"'s management adviser permission to evaluate the cost of a day of hospital ward using their own methodology.

As explained in Chapter 2, the hospital's costing method is not well suited to determine the impact that an innovative surgical technology could have on the cost per operation. However, if we consider that the only impact an innovative technology could have on hospitalization is a decrease in Length of stay, and not in the medical attention that patients need, then their cost per hospital bed day (i.e. resources consumed to provide the medical attention) is applicable.

The adviser's calculation method is based on a "Compte de Résultat Analytique" report, called CREA, produced annually and describing year $N-2$'s activity. The report, introduced as part of the activity-based model (T2A - See Chapter 2) of reimbursement,

is a tool that the hospital uses to compare each department's expenses (after allocating a part of other departments' expenses) with its revenue.

The expenses that are allocated to the "Pôle Hépato-Digestif" are typically divided into three categories: Direct, Logistics/Structure and Medico-technical. The Direct expenses correspond to resource uses that can be accurately traced to the hospital ward's activity including personnel, drugs, catering, maintenance and amortization.

The Logistics and Structure expenses relate to common resources that are shared among the hospital's different departments and activities. Therefore, only a portion of these expenses are allocated to the "Pôle Hépato-Digestif"'s hospital wards including logistics fees, administrative salaries and structure amortization/maintenance.

Originally, the Medico-technical (MT) category included expenses from eight MT centres: OR, Pathology, Biology, Dialysis, Anaesthesia, Imaging, Exploration and other. However, the application of our costing methodology is meant to take into account the expenses of OR, dialysis, anaesthesia and exploration MT activities which should therefore be excluded from the hospital stay analysis.

To derive a cost per day of hospital ward in the "Pôle Hépato-Digestif", we had the option of using the total number of hospital bed days, for 2013, as defined either by the government or by our analysis. From the government's point of view, the number of hospital bed days corresponds to the "journée PMSI" which does not count outpatients' stay[6].

From our point of view, resources are consumed for every day the patient is admitted into a hospital ward whether following outpatient or inpatient procedures. The number of hospital bed days, which we call "journée administrative", would therefore be higher than the "journée PMSI" as most outpatient procedure infer one bed day.

By its definition and construction, the cost per hospital bed day automatically covers resource use due to post operative complications, such as bedside medical examination or medication. The cost of both post-operative and intra-operative complications can be determined using our cost methodology presented in Chapter 2, especially in the case of re-operation following post-operative complications.

[6]For outpatient care, patients are discharged the same day before midnight.

4.2 Absenteeism and Presenteeism

At the time of establishing the protocol, the only known method for collecting surgery related absenteeism data consisted in directly asking patients for an estimation of time spent off work after receiving care. The IHU clinical technician was designated as the person in charge of questioning patients at follow up and filling the corresponding database.

During collection, a high number of missing data was pointed out since patients who do not have a professional activity did not report a time off work. The clinical technician also highlighted the fact that the data, for those who do work, was highly unreliable for two main reasons. First, when asked at different time periods about their time off work, many patients gave contradictory approximate answers ranging from one week to one month. Second, reports from patients who were on sick-leave following surgery do not distinguish between absenteeism due to the surgical act itself and other factors.

TABLE 3.4: Hourly employee cost

Sector	2012	2013	2014
Commerce	34.9	35,0	35,2
Industry	36.6	36,8	37,0
Construction	30,7	30,6	30,4
Market service	34,7	34,8	35,1
Average	34.225	34.3	34.425

Source: INSEE

In a first step, we analyze whether the difference in reported time off work between the computer assisted and laparoscopic group is statistically significant using a welsh t student. In a second step, we use the human capital approach to estimate the economic impact of absenteeism based on the average hourly employee cost of 34.43 Euro, equivalent to 275.44 Euro per day (Table 3.4) assuming a 35 hours shift per week.

Our database did not contain any information on presenteeism as its impact analysis was not included as an objective of the clinical protocol. We therefore cannot include this impact measurement in our analysis aside from discussing it.

4.3 Quality of life

4.3.1 Data collection

At the writing of the protocol, the IHU decided that obesity specific questionnaires were to be used for the evaluation of patients' QoL. To make sure all aspects of obesity surgery were covered, two questionnaires were put forth: "GastroIntestinal Quality of Life Instrument" (GIQLI) and updated "Bariatric Analysis and Reporting Outcome System" (BAROS).

An English version of the GIQLI was created and published in 1995 due to the unavailability of any other instrument for measuring the QoL of patients with Gastrointestinal diseases [Eypasch et al., 1995]. The result, presented in Appendix D, is a questionnaire containing 36 questions each with five response categories.

The patient is asked to give answers for each of the 36 questions, which are then processed by a specific algorithm to deduce a numerical score of QoL. Although QIQLI is a general gastrointestinal index not specific to obesity, it is less generic than the EQ-5D, SF-6D, QWB or HUI and should theoretically be more representative of the impact of weight loss surgery.

The BAROS was created and published in 1998 in response to the lack of a standard of comparison for the surgical treatment of sever obesity [Oria and Moorehead, 1998]. The questionnaire is mainly aimed at patients who undergo weight loss surgery and allows the assessment of several outcome measures considered as specific to this type of procedure.

The initial result covered three areas of interest (weight loss, improvement of medical conditions, and QoL) spanning five dimensions: self-esteem, physical activity, social life, work conditions and sexual activity. To assess patients' QoL, a questionnaire "Moorehead-Ardelt Quality of Life Questionnaire" (M-A QoLQ) was specifically created as part of the BAROS.

In 2009, Oria *et al.* [2009] saw fit to update their questionnaires using their users' feedback collected during the last 10 years. The updated result of the M-A QoLQ, presented in Appendix E, integrates the patients' relationship to food as it was found to

be a critical factor in clinical trials. The 6 dimensions forming the resulting questionnaire are equally valued with a score of 0.5 points for each.

The patient is asked to fill out the M-A QoLQ presenting a description of each item's state as in not at all or very much, for example. The system then defines five outcome groups (failure, fair, good, very good, and excellent) based on a scoring table that adds or subtracts points to determine the patient's QoL.

In the initial protocol, no measure of QoL before the surgical operation was programmed and only a post-operative assessment was planed. After explaining that it is impossible to analyze an impact of surgery without a pre + post intervention data, we suggested that every patient's QoL should be measured at least once when he gives his accord as to his inclusion in the protocol and then four additional times at one, three, six and twelve months after surgery.

For a number of patients, the decision to integrate the measurement of their QoL at inclusion came a bit late which introduced several missing observations in our analysis. For patients who did not yet undergo an operation, their QoL measurement came the day before the operation which, theoretically, may introduce a bias in their results due to pre-operative fear or excitement.

4.3.2 Data analysis: T.test vs 2X2 ANOVA vs HLM

Our data structure follows a repeated measurement design on each individual randomly assigned to either a robotic or laparoscopic group. We can therefore identify two factors that are likely to influence the change in QoL: Time and Group. Such type of data, or studies, are described as "longitudinal" in which the entity under study is observed, or measured, over two or more time points [O'Connell and McCoach, 2004].

The analysis of statistical methods used in the surgical literature [Kurichi and Sonnad, 2006] demonstrate an important variability, and weakness, in their application and reporting. T-tests and ANOVA appear to be increasingly popular among surgeons and clinicians even though their use is not always adapted to the data format.

The temptation when analyzing longitudinal data may be to compare observations using a series of t-tests, or one of its variants. This poses two problems:

- T-tests cannot compare more than two groups of patients, or more than 2 set of observations, at the same time;
- Every time we conduct a t-test on the same data, we increase the chance of committing a Type-1 error. In other words, we increase the probability that any one comparison will be found significant due to chance [McDonald, 2009].

As a consequence, the use of multiple t-test comparisons reduces our confidence that a study result can be generalized to independent data [Wikipedia, a]. To put it simply, consider that a p-value of 0.05 means that there's a 5% chance of getting our observed results if the null hypothesis was true. If you perform 100 t-tests you would expect 5 of them to be false positives; which are to be preferably avoided. It is therefore recommended to first use general comparison tests such as the Analysis of Variance (ANOVA) followed by post-hoc tests such as Tukey's, Scheffé's or the Bonferroni method to provide more precise details.

The first method that was thought to be correct for the evaluation of this data structure was a two-way repeated measures ANOVA. The "two-way" term reflects the fact that there are two factors in the experiment, different treatments (i.e. group) and different conditions (i.e. time). The "repeated measures" term indicates that the same patient was subject to more than one condition, in our case it means their QoL was measured at different time periods.

When only one of the two factors is a repeated measure, the analysis is often called a mixed-design ANOVA with one factor being a between-subjects variable and the other a within-subjects variable. A "subject" in this case can be viewed as the patient and the between-subjects variable considered as what differentiates some patients from others, which is the type of surgery in our case.

In the same manner, the within-subjects variable can be considered as what differentiates one observation from another for each patient, and in our case that is the time period. As we measure the QoL for each subject before and after surgery, this means that the subject is serving as his or her own control and the repeated measures analysis also controls for this fact.

The use of a two-way repeated measures ANOVA is conditional to several assumptions regarding the data structure. First, it requires observations to be normally distributed

with variance homogeneity and, second, it relies on a balanced design in which we have the same number of observations in both groups. In a clinical trials setting, the second assumption is likely to be violated as missing observations and randomization often lead to unbalanced data [O'Connell and McCoach, 2004].

Another requirement of the ANOVA model is that the times of measurement during the course of the study must be equivalent for all patients. For example, all patients must be surveyed at intervention and every two months after. If a patient was unable to provide an answer at the fourth month, it is not possible to use the collected data, for example at five months, without decreasing the model's precision.

To bypass the problem of unbalanced design, we can base our analysis on a Hierarchical Linear Model (HLM) [Liang and Zeger, 1986] which, although demonstrated to be highly suited for longitudinal research in health economics [O'Connell and McCoach, 2004], has been significantly underused in the surgical literature. Aside from handling unbalanced data, these multilevel models have the advantage of controlling for the variability in measurement periods across individuals. In other words, HLM is capable of treating time as either a fixed or random effect.

As a fixed effect, data collection is required to be had at fixed time periods for all patients in the sample. As a random effect, measurement can be done at any time from an established reference point for all patients. Note, however, that similarity in collection periods allows for a better reflection of the effects and that, to fit a linear trend, three or more time points must be available for the majority of patients [O'Connell and McCoach, 2004].

While many of the initial assumptions imposed for the ANOVA models are relaxed for HLM, the normality and homogeneity of variance are still required as to ensure unbiased estimations. In **R** [R Development Core Team, 2011] software, normality of residuals can be tested using the *qqplot* function.

4.3.3 Focus on hierarchical linear modelling

Finch *et al.*'s book [2014] on multilevel modeling using **R** has been a great inspiration for writing this section as well as applying these models to our data. Following their recommendations, we start by taking a look at the basic linear regression model presented

in Equation 3.1 to fully understand the principles behind multilevel modeling.

$$y = \beta_0 + \beta_1 x + \varepsilon \tag{3.1}$$

The dependent variable y, which holds the observations of our subjects, is described as a function of an independent variable x (or level 1 predictor), such as age or time, multiplied by a "slope" coefficient β_1. The β_0, described as an "intercept", serves as the conditional mean of y, when $x = 0$, and is common to all individuals . The error term ε is different from one subject to another and is meant to reflect the variation that our model has failed to explain through the inclusion of our dependent variable x.

In multi-centre medical studies, we often observe a clustering phenomena in which patients belong to groups, which in turn are clustered in one hospital or another. It would therefore be wise to suggest the existence of a different intercept β_0 for each cluster. The same observation can also be made for the slope β_1 which would potentially take different values for each cluster. Based on this fact, Equation 3.1 can be re-written as follows:

$$y_{ij} = \beta_{0j} + \beta_{1j} x_{ij} + \varepsilon_{ij} \tag{3.2}$$

As Equation 3.2 indicates, the i'th observation of the j'th individual is expressed as a function of an intercept, that is common to all observations of an individual but different across individuals, and an independent variable x_{ij} whose impact, or "slope", is also common to observations of the same individual.

In that sense, the intercept β_{0j} is described as "random" for it is a combination of a fixed effect, constant across individuals, and a random effect that is individual specific. The same applies to the slope which we could qualify as random when the independent variable's effect is assumed to be different across individuals.

$$\beta_{0j} = \gamma_{00} + U_{0j} \tag{3.3}$$

$$\beta_{1j} = \gamma_{10} \tag{3.4}$$

$$Score_{ij} = \beta_{0j} + \beta_{1j} Time_{ij} + \varepsilon_{ij} \tag{3.5}$$

$$\beta_{hj} = \gamma_{h0} + \gamma_{h1} Treatment_j + U_{hj} \tag{3.6}$$

Mathematically, based on a random intercept (Equation 3.3), a random slope (Equation 3.4), a level 1 time predictor (Equation 3.5) and a level 2 treatment predictor (Equation 3.6), our model can be expressed as follows:

$$\begin{aligned} Score_{ij} = \gamma_{00} + \gamma_{10} Time_{ij} + \gamma_{10} Treatment_j + \gamma_{1001} Time_{ij} Treatment_j \\ + U_{0j} + U_{1j} Time_{ij} + \varepsilon_{ij} \end{aligned} \tag{3.7}$$

In our case (Equation 3.7), we propose to explain the relationship between Quality of Life scores (y_{ij}) and both Treatment ($Treatment_j$) and Time ($Time_{ij}$), called a level-1 predictor. Treatment, called a level-2 predictor, takes a single value across time for each subject. As a level 2 predictor, the treatment variable's slope will tell us whether the variations in score over time occur faster for one group or another.

The cross-level interaction term $\gamma_{1001} Time_{ij} Treatment_j$ represents, as the name implies, the interaction between time and treatment. The coefficient γ_{1001} indicates the extent to which the relationship between the measurement period and Quality of life score is dependent on the treatment group.

We also model a different slope and intercept for each subject to express individual differences in score changes over time allowing us to control for the inter-dependency between multiple responses from the same individual. In that respect, $U_0 j$ represents the random variation for the intercept across subjects, and $U_1 j$ represents the random variation for the slope across subjects.

4.4 Medical tourism

As a young institute, the IHU has not yet constructed a database neither wide nor detailed enough to analyze the impact of its emerging medical tourism activity. A difficulty that is exacerbated by the fact that foreign patients currently pay two separate bills: one for the hospital to cover medical costs and a second for the IHU to cover organization costs.

Unfortunately, information exchange between the hospital and the IHU regarding foreign patients spending is very limited. What we do know is that the hospital currently bills patients, that are not insured by the French Social Security, 1 500 Euro per day spent in their facilities without differentiating between the types of operations.

4.4.1 Impact calculation

According to the IHU, at the time of analysis, their strategy would consist in offering foreign patient a "package" that covers their entire stay from transportation to medical care. Patients would only pay one bill to the IHU who then is charged by the hospital, hotels and other providers.

To provide estimates of what the potential impact of minimally invasive surgery could be in terms of medical tourism, we had to build our package based on two different scenarios of care offers. In the first, we assume that the hospital would charge the IHU the same way as it would have charged the patient, i.e. 1 500 Euro per day. In the second, we assume that the hospital would bill the IHU based on a detailed cost calculation of the patient's care pathway.

We take both Laparoscopic Gastric Bypass (LGB) and Peroral Endoscopic Myotomy (POEM) as examples of applications since data is available for both procedures. Each "package" contains the following:

- 2 pre and 3 post operation consultations;
- 1 blood test;
- 1 surgical operation;
- 4 hospital bed days;
- 15 hours needed for organisation (administration staff time);
- 1 two-way transportation from and to Zurich airport (considered as the preferred arrival point by the IHU);
- 6 hotel nights;
- 4 hours of interpret service.

Cost of consultations, blood test and hospital bed days were determined by the hospital as they did not wish for us to go into detail. Transportation, hotel and interpret service costs were based on market prices currently billed to the IHU. Administration staff time's cost was calculated by using our costing algorithm developed in Chapter 2.

Cost of LGB was calculated using the 2013 micro-costing methodology and data collected through the IHU protocol comparing laparoscopic and computer-assisted Gastric Bypass. We assume that all laparoscopic Gastric Bypass operations are done in the same OR, or set of ORs, in which a total of 600 laparoscopic operations are done per year. No other type of procedures, i.e. open or endoscopy, are done in these operating rooms.

The cost per POEM operation is determined using the 2012 micro-costing methodology and personally collected data. Calculation details are provided in the following subsections.

4.4.2 Case Study: POEM

To analyze the impact of medical tourism, we based our analysis on available data at the IHU at the time of the study. As the only procedure for which foreign patients data was collected, our analysis focused on Peroral Endoscopic Myotomy (POEM) performed between 2013 and 2014.

Peroral Endoscopic Myotomy (POEM) is an endoscopic procedure used to treat patients presenting swallowing disorders and most commonly for Achalasia. As an endoscopic procedure, it is done without the need to perform any incisions on the patient since the flexible instrument is either passed through the mouth or rectum.

Figure 3.4: POEM

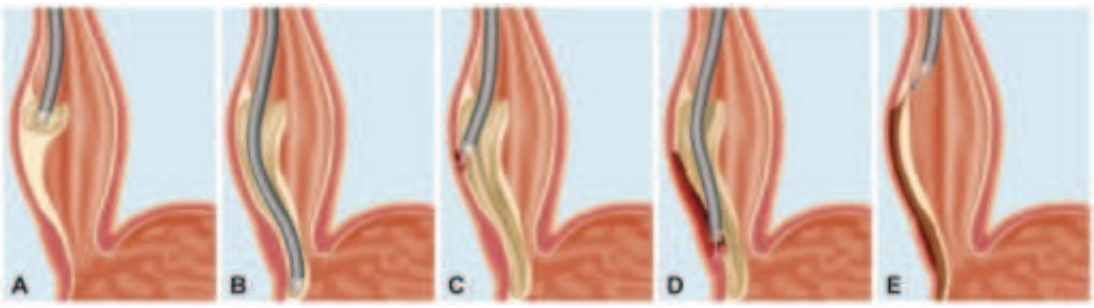


Figure 3.4 provides a graphical representation of a POEM which can be described as a 4 steps procedure [Swanstrom et al., 2011]:

- A submucosal "lift" is performed by liquid injection, followed by a longitudinal incisions of the elevated mucosa;
- Insertion of the endoscope through the submucosal space and creation of an endoscopic tunnel;
- Dissection of the inner circular muscle layer and sling fibers of the lower esophageal sphincter;
- Withdrawal of the endoscope and closure by standard endoscopic hemoclips.

As neither the hospital nor the IHU possess a detailed enough database, POEM costs were calculated using our 2012 micro-costing methodology developed in Chapter 2.

TABLE 3.5: Medical equipment data PEOM

Equipment	Purchase price	Maintenance	Service life	Yearly use
Anaesthetic machine	60 000	3 000	12	96 000
Endoscopy Column	50 000	2 500	7	96 000
Operating Table	50 000	2 500	15	96 000
Fixed table pilum	33 143	1657	15	96 000
Four Syringe Pumps	32 000	1 600	10	96 000
Surgical Light	25 000	1 250	15	96 000
Two Monitors	20 000	1 000	7	96 000
Electro-surgical unit	15 000	750	10	96 000
Ceiling supply unit	13 000	650	15	96 000
Surgical Pendant	9 000	450	15	96 000
Mattress	5 660	283	7	96 000
Aspirator	3 354	168	10	96 000
Storage carts	3 235	162	10	96 000
Closet	2 697	135	10	96 000
Tables	2 000	100	10	96 0005
Chairs	528	26	7	96 000

Table 3.5 provides a list of medical equipment present in the OR upon which our cost calculation is based. To conduct this analysis, we assume that all POEM operations are done in the same OR, or set of ORs, in which a total of 600 endoscopies are done per year for an average room occupation time of 165 minutes. We assume that no other type of procedures, i.e. neither open nor laparoscopy, are done in these rooms as we do not possess the total yearly room occupation time all procedures included.

TABLE 3.6: Personnel data POEM

Personnel	W_i	L_i	Paid leave	t_i
Surgeon 1	110 324	48	44	120
Surgeon 2	110 324	48	44	120
Anaesthetist	110 324	48	44	105
Nurse anaesthetist	61 563	35	48	165
Circulating nurse	60 613	35	48	165
Scrub nurse	60 613	35	48	165

Table 3.6 presents the personnel related data collected using experts feedback with whom we attempted to estimate the time spent in the OR for each personnel. In terms of re-usable instruments, only the clip applier, with a purchase price of 1 130 Euro, was reported to be used during POEM. We assume that the clip applier can be used a maximum of 20 times before being replaced.

TABLE 3.7: Most expensive disposables POEM

Consumables	UnitsUsed	PricePerUnit
Triangle tip knife	1	381
Manchons de contension (paire)	1	269
Guardus overtube oesophageal	1	236
Extraction balloon	1	116

Table 3.7 presents four of the twenty-five disposables reported to be used during POEM. Note that even though the data exists in a more detailed format, we were unable to retrieve it due to confidentiality.

4.5 Intangible benefits

In an attempt to develop a method for measuring the intangible benefits of introducing innovative minimally invasive technologies, we take the da Vinci surgical system as an example of application. Our choice is based on its widespread success which should, theoretically, provide us with a wide range of data sources (surgeons) to interrogate.

Although expensive, the da Vinci surgical system has seen particular commercial success even in a context of financial crisis. The reason behind the proliferation of the surgical system in both private clinics and hospitals does not only relate to its effectiveness in terms of patient outcome but must also be correlated to other factors.

To identify the reasons behind this success, we developed a 1 page survey that focus on analyzing the utility of the da Vinci robotic system from the surgeons' perspective. The resulting survey, presented in Appendix F, is divided into 11 questions pertaining to patient, surgeon and hospital related benefits. We emphasize the comparison with laparoscopic techniques since they currently represent the most common, and most effective, alternative.

The first four questions aim at identifying the surgeon's characteristics which mainly reflect his experience and knowledge in surgery. We hypothesize that experienced surgeons are more likely to be rational about their view of technologies' utility while younger surgeons are more eager to explore innovative routes.

Question five measures the innovation's impact on both the patient and the surgeon. We are especially interested in knowing whether surgeons learn faster using the da Vinci robotic system than using laparoscopy. While it is also possible to conduct such an analysis through a learning curve assessment, we did not have the necessary resources to go forward with it.

Question six focus on analyzing the impact of the robotic system on the surgical operation and surgical field compared to laparoscopy. While such evaluations can be done using real life data, it is interesting to see how the user perceives the innovation's effectiveness.

Questions seven, eight and nine attempt to evaluate the importance of advantages put forward by Intuitive Surgical, the creators of the da Vinci surgical system, and disadvantages published in the literature. We take interest in the users' view on the restriction in the maximum use for da Vinci instruments as it can either be perceived as an advantage, with a possible reduction in complications related to instrument breaking, or disadvantage due to an increase in cost.

Question ten considers the innovation's effect on the surgeon's professional career through his teaching and research activities. We recognize that surgical innovations' role is not restricted to improving surgery management and outcome but also includes stimulating collaborations and skill acquisition.

Finally, the last question provides the survey analyst with a tool to evaluate the importance of all variables, measured previously, from the surgeon's viewpoint. Intuitively, we expect that if answers that put forward the robotic system's disadvantages are predominant, the respondent will not view the system's future positively.

5 Results

To apply the concepts discussed in the previous sections, we base our analysis on several databases from the hospital, IHU and the literature. In this section, we present the results of our applications with the hope that they will give the reader a better view on the kind of conclusions that can be made in economic evaluations of medical devices. The main objective being to identify the possibility of creating an all inclusive cost-benefit methodology.

We also use this opportunity to evaluate the cost-effectiveness of the Da Vinci surgical system since it is considered, by the IHU, as the currently best example of a hybrid minimally invasive surgery. Furthermore, a relatively large IHU database is at our disposable to apply several, even if not all, of our previously discussed methodologies.

5.1 Length of stay

The analysis of length of stay is based, first, on the hospital's database for the calculation of a cost per hospital day and, second, on the IHU's protocol for the comparison of computer assisted and laparoscopic Gastric Bypass's length of stay.

5.1.1 Cost per day of hospital ward

Based on the 2013's CREA, the hospital's management adviser calculations allows for the estimation of a cost per hospital ward day. While the precision of the values presented in this section is criticized even by the adviser himself, they serve as a starting point for conducting a more detailed calculation.

TABLE 3.8: Expenses allocated to "Pole Hepato-Digestif"'s hospital ward

Category		Expense
Direct	Medical Staff	999 181.59
	Nursing Staff	4 304 773.73
	Other Staff	1 539 062.73
	Pharmacy	3 530 310.81
	Catering and accommodation	83 648.77
	Maintenance and amortization	377 962.89
	Total	10 834 940.52
Logistics and Structure	Medical Logistics	252 372.5
	Logistics et Administrative	2 377 106.67
	Structure	342 822.48
	Total	2 972 301.65
Medico-technical	MT Pathology	182 334.80
	MT Biology	691 869.70
	MT Imaging	1 197 246.93
	MT Other	77.93
	Total	2 071 529.36
TOTAL		15 878 771.53

Table 3.8 summarizes the findings for each expenditure category. We have deliberately excluded the OR, dialysis, anesthesia and functional exploration medico-technical expenses as they should already be taken into account in our OR micro-costing methodology.

According to this table, the highest source of expenses are direct representing 68% of the total spending allocated to the "Pole Hepato-Digestif"'s hospital ward units, largely due to the Nursing Staff's salaries. The portion of the Logistics and Structure category, which includes expenses shared between all the hospital's departments and activities, allocated to the hospital ward units amounts to 2.9 million representing 19% of the total expenditure.

The Medico-technical section of Table 3.8 presents the portion of all medico-technical

centers' expenditures allocated to the "Pole Hepato-Digestif"'s hospital ward units. After excluding the bloc, dialysis, anesthesia and exploration centers, the allocated medico-technical expense represents 13% of the total.

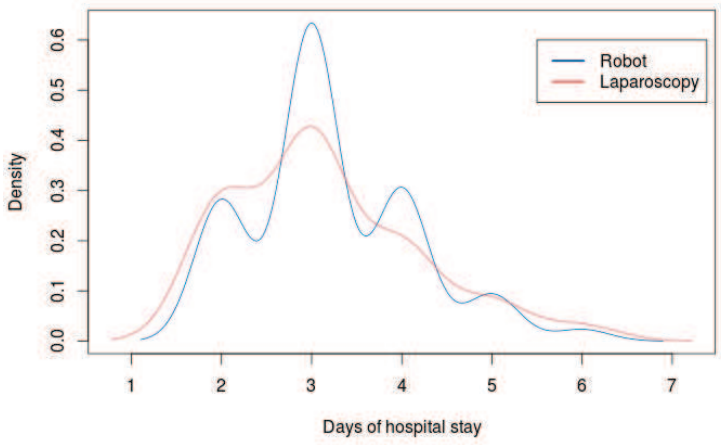
In 2013, A total of 25 327 PMSI hospital days were recorded compared to 32 295 administrative days. Taking the PMSI value as reference, the cost per day in the "Pole Hepato-Digestif"'s hospital ward amounts to 626.95 Euro. Based on the administrative approach, the cost per day sums up to 491.68 Euro which better reflects the reality of resource consumption.

5.1.2 Application to 2013 protocol

Initially, 134 patients were included in the protocol among which 13 were excluded for various reasons during the cost analysis performed in Chapter 2. For the remaining 122, the length of hospital stay was reported for 120 patients with 57 in the computer-assisted group and 63 in the laparoscopic one.

The average length of stay in the computer-assisted and laparoscopy groups are demonstrated to be respectively 3.21 (standard deviation 0.92) and 3.16 (sd 1.03). A Welsh Two Sample t-test indicates that the difference in the means is not statistically significant with a $p - value = 0.7722 > 0.05$.

FIGURE 3.5: Kernel Density of Length of stay



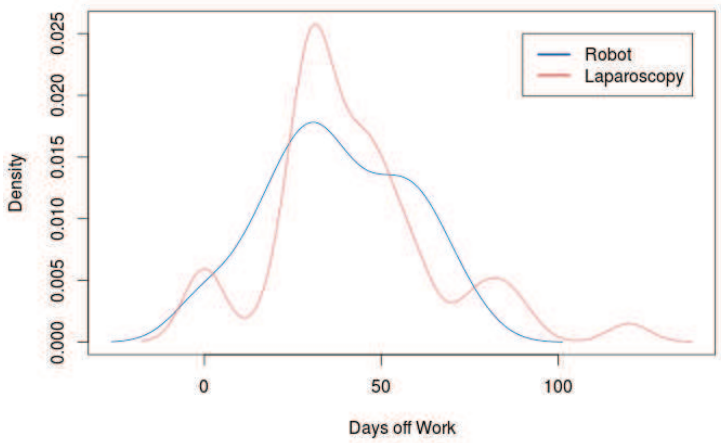
According to Figure 3.5, most patients were admitted at the hospital ward for 3 days; particularly in the computer-assisted group. The laparoscopic group's LoS presents a slightly higher variability with more patients being admitted for either less than 3 days or more than 4 days.

In monetary terms, the average LoS cost for the computer assisted and laparoscopy groups are respectively 1 578.55 (sd 452.7) and 1 553.08 (sd 508.88) Euro based on the administrative approach. When the PMSI logic is adopted, the cost amounts to 2 012.84 (sd 577.25) and 1 980.37 (sd 648.88) Euro respectively. Naturally, a Welsh Two Sample t-test yields the same results as when comparing average length of stay.

5.2 Absenteeism

Data on workplace absenteeism was collected from a total of 83 patients, 38 of which were randomized to the computer-assisted group and 45 to the laparoscopic one. The average days off work in the first and second groups are respectively 37.5 (sd 20.14) and 41.93 (sd 24.25). A Welsh Two Sample t-test indicates that the difference in the means is not statistically significant with a $p - value = 0.3656 > 0.05$.

FIGURE 3.6: Kernel Density of Days off Work



According to Figure 3.6, the laparoscopy group presents a higher number of outliers indicating a higher occurrence rate for absenteeism of more than 80 days. The computer assisted group shows lower variability with most patients taking between 30 and 60 days off work.

In monetary terms, the average absenteeism cost for the computer assisted and laparoscopy groups are respectively 10 329 (sd 5 547.75) and 11 550.12 (sd 6 679.49) Euro assuming the previously discussed cost per day of 275.44 Euro. A Welsh Two Sample t-test yields the same results as when comparing average days off work of the two groups.

Based on these results, it seems that the computer assisted technique does not provide any significant added value over its laparoscopic alternative in terms of workplace absenteeism.

5.3 Quality of life

The QoL analysis focuses on the 2013 protocol's data comparing the clinical and medico-economic impact of computer-assisted versus laparoscopic gastric bypass. The study spans a 1 year period (2013), eliminating the need for discounting, and includes 134 patients with a BMI of over 35 randomized to either a laparoscopic or robotic procedure with the surgeon and patient being blinded to the randomization and the actual grouping.

As with the cost calculation in Chapter 2, a total of thirteen patients were excluded from the Quality of life analysis as they did not undergo their operation in the context of the protocol. Of the remaining 122 patients, 58 were randomized to the robotic group and 64 to the laparoscopic one.

The first step in analyzing multilevel, or hierarchical, longitudinal models with **R** [R Development Core Team, 2011] is to format the database in what is described as "person-level data", which constitutes a requirement for applying these models. Instead of assigning one row for each individual and one column for each variable, or measurement on the same individual, longitudinal structures assign one row for each time that each subject is measured.

Patient		**Period**		**Longitudinal Observation**
Patient1	+	Time1	=	Patient1 Time1
Patient1	+	Time2	=	Patient1 Time2
Patient1	+	Time3	=	Patient1 Time3
Patient2	+	Time1	=	Patient2 Time1
Patient2	+	Time2	=	Patient2 Time2

Using **R** software, the hierarchical linear model (Equation 3.7) can be written as follows:

$$model < -lme(score\ groupe * period, random = \ 1 + period|sujet, na.action = na.omit)$$

The score variable is defined as either the BAROS or GIQLI final survey results, according to which score we are analyzing, in a person-level format. The groupe variable is defined as the patient's surgical procedure as in either computer assisted (= 1) or laparoscopy (= 0). The period variable indicates the time of measurement and, finally, the "sujet" variable indicates the subject's code number.

5.3.1 BAROS

A total of 570 observations of the final BAROS score at different time periods were processed in our hierarchical linear model's compilation. The results, as presented in the **R** software[7], are as follow:

```
Linear mixed-effects model fit by REML
 Data: NULL
      AIC      BIC    logLik
  1254.73 1289.439 -619.3652

Random effects:
 Formula: ~1 + period | sujet
 Structure: General positive-definite, Log-Cholesky parametrization
            StdDev    Corr
```

[7]We deliberately present the results in the software's format as one obstacle to applying the hierarchical linear models is the underlying difficulty in reading its results. This subsection should allow the reader to easily identify relevant information in a statistical software's output and interpret it correctly

```
(Intercept) 0.9432601 (Intr)
period      0.1021730 -0.697
Residual    0.5063096

Fixed effects: score ~ groupe * period
                   Value  Std.Error  DF   t-value p-value
(Intercept)    0.5259871 0.13846692 446  3.798648  0.0002
groupe        -0.0406072 0.19823632 120 -0.204842  0.8380
period         0.1330346 0.01700940 446  7.821236  0.0000
groupe:period  0.0017559 0.02428529 446  0.072305  0.9424
 Correlation:
              (Intr) groupe period
groupe        -0.698
period        -0.756  0.528
groupe:period  0.530 -0.753 -0.700

Standardized Within-Group Residuals:
       Min          Q1         Med          Q3         Max
-3.0878913 -0.4768444  0.0790465  0.5528633  2.2856489
```

From this output, we see that "period" is positively related to BAROS scores with a $p - value = 0.0000 < 0.05$ and a positive slope of 0.13. We can therefore safely say that the BAROS final score increases over time. In other words, both the computer assisted and laparoscopic procedures increase patients' BAROS measured QoL over time.

The "groupe" variable appears to be non-statistically significant with a $p - value = 0.8380 > 0.05$. Therefore, whether patients underwent a laparoscopic or robotic operation does not seem to have a different impact on the patients' final BAROS score.

The interaction between the "groupe" and "period" variables is non-statistically significant with a $p - value = 0.9424$. The effect of "groupe", i.e. undergoing either a laparoscopic or robotic surgery, on BAROS score therefore does not appear to change over time.

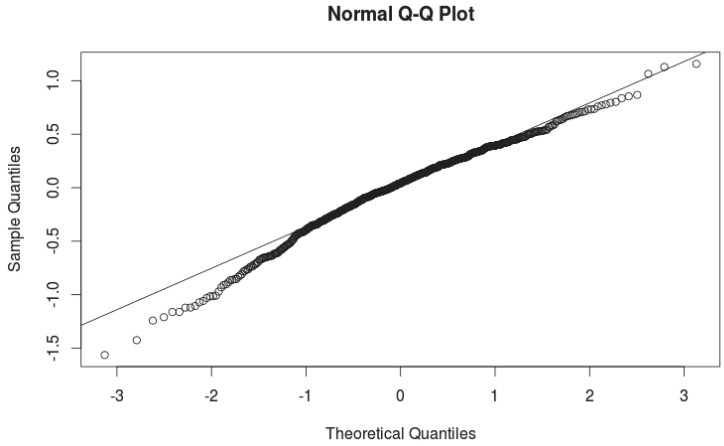
Our results also indicate a positive random effect for the period variable valued at 0.10. To analyze whether this effect is statistically significant, i.e. different from 0, we can calculate the 95% confidence intervals:

```
Approximate 95% confidence intervals

 Fixed effects:
                    lower          est.      upper
(Intercept)    0.25385840  0.525987053 0.79811571
groupe        -0.43310131 -0.040607181 0.35188694
period         0.09960602  0.133034554 0.16646308
groupe:period -0.04597187  0.001755937 0.04948374
attr(,"label")
[1] "Fixed effects:"

 Random Effects:
  Level: sujet
                                lower       est.      upper
sd((Intercept))           0.78613323  0.9432601  1.1317924
sd(period)                0.08095952  0.1021730  0.1289450
cor((Intercept),period) -0.80887544 -0.6972368 -0.5370767

 Within-group standard error:
    lower      est.     upper
0.4685952 0.5063096 0.5470593
```

Our model shows that the period's random effect is statistically significant as the confidence interval $[0.08; 0.13]$ does not include 0. We are 95% confident that the actual variance component for the "period"'s slope was between these two values. We can say that the change rate over time in the final BAROS score differs across patients in the sample.

A quantiles plot allows us to verify the normality assumption of residuals necessary to validate our Hierarchical linear model's results.

FIGURE 3.7: Q-Q plot BAROS



Essentially, the graph displays the data as it actually is on the axis and as it would be if normally distributed on the y axis. The solid line represents the data conforming perfectly to the normal distribution [Finch et al., 2014]. As Figure 3.7 demonstrates, our errors are normally distributed.

5.3.2 GIQLI

A total of 555 observations of the final GIQLI score for different time periods were processed by our hierarchical linear model's compilation. The results, as presented in the **R** software, are as follow:

```
Linear mixed-effects model fit by REML
 Data: NULL
       AIC      BIC    logLik
  4300.321 4334.815 -2142.161

Random effects:
 Formula: ~1 + period | sujet
 Structure: General positive-definite, Log-Cholesky parametrization
            StdDev     Corr
(Intercept) 11.0290497 (Intr)
period      0.9908128 -0.03
```

```
Residual     8.6775418


Fixed effects: score ~ groupe * period
                   Value Std.Error  DF   t-value p-value
(Intercept)     98.02311  4.155291 432 23.589947  0.0000
groupe           0.00670  2.609399 119  0.002569  0.9980
period           1.83039  0.507864 432  3.604092  0.0003
groupe:period -0.00317  0.319353 432 -0.009915  0.9921
 Correlation:
                (Intr) group period
groupe         -0.949
period         -0.483  0.459
groupe:period  0.458 -0.483 -0.949


Standardized Within-Group Residuals:
        Min          Q1         Med          Q3         Max
-3.21390586 -0.48486761  0.02770164  0.54989417  2.88127501
```

From these results, we see that "period" is positively related to GIQLI scores with a $p - value = 0.0003 < 0.05$ and a positive slope of 1.83. We can safely say that the GIQLI final score increases over time. In other words, both the computer assisted and laparoscopic procedures increase patients' GIQLI measured QoL over time.

The "groupe" variable appears to be non-statistically significant with a $p - value = 0.9980 > 0.05$. Therefore, whether patients underwent a laparoscopic or robotic operation, this does not seem to impact the patients' final GIQLI score.

The interaction between the "groupe" and "period" variables is non-statistically significant with a $p - value = 0.9921$. The effect of "groupe", i.e. undergoing either a laparoscopic or robotic surgery, on GIQLI score does not appear to change over time.

Our results also indicate a positive random effect of the period variable valued at 0.99. To analyze whether the effect is statistically significant, we can calculate the 95% confidence intervals[8]:

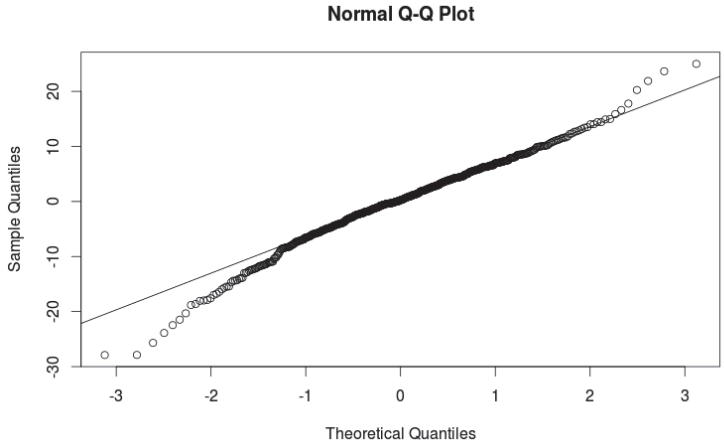
[8]To simplify: The confidence intervals indicates that if we the study is to be repeated an infinite number of times, there is a 95% chance that the "true" value of our estimated parameter would lie in the interval.

```
Approximate 95% confidence intervals


 Fixed effects:
                     lower         est.       upper
(Intercept)     89.8560030 98.023105731 106.1902084
groupe          -5.1601666  0.006704171   5.1735750
period           0.8321974  1.830390046   2.8285827
groupe:period -0.6308459 -0.003166493   0.6245129
attr(,"label")
[1] "Fixed effects:"


 Random Effects:
  Level: sujet
                                lower        est.      upper
sd((Intercept))            7.4253911 11.02904968 16.3816201
sd(period)                 0.2600518  0.99081283  3.7750565
cor((Intercept),period) -0.8941184 -0.03024277  0.8813068


 Within-group standard error:
   lower     est.    upper
7.695763 8.677542 9.784570 .
```

Indeed, our model shows that the period's random effect is statistically significant as the confidence interval $[0.26; 2.83]$ does not include 0. We can therefore say that the change rate over time in the final GIQLI score differs across patients in the sample.

A quantiles plot allows us to verify the normality assumption of residuals necessary to validate our Hierarchical linear model's results.

FIGURE 3.8: Q-Q plot GIQLI



As Figure 3.8 demonstrates, our errors are normally distributed.

5.4 Medical tourism

From a healthcare economic standpoint, the role of medical tourism with regards to innovative minimally invasive surgery is particularly interesting as they allow patients to recover significantly faster. Patients can therefore combine their surgical care travel plan with a vacation one.

Each foreign patient drawn by the IHU injects in the hospital the value of its medico-technical activity, i.e. consultations, blood test, treatment and hospital LoS. For each patient received by the IHU, the local economy also increases its revenue with respect to the value of tourism related activities, i.e. travel, hotel and interpreters. Using a cost-benefit analysis we can clearly identify the impact of each dollar spent by the IHU on both the hospital and the region.

	Charge TTC	
	IHU	Hospital
Consultations	0.00	130.00
Blood test	0.00	44.28
Treatment	0.00	0.00
Hospital LoS	0.00	4 500.00
Organisation	1 416.06	0.00
Travel	672.00	0.00
Hotel LoS	1 188.00	0.00
Interpreters	720.00	0.00
Total	3 996.06	4 674.28

TABLE 3.9: LGB charges convention based

	Charge TTC	
	IHU	Hospital
Consultations	0.00	130.00
Blood test	0.00	44.28
Treatment	0.00	0.00
Hospital LoS	0.00	1 500.00
Organisation	1 416.06	0.00
Travel	672.00	0.00
Hotel LoS	1 188.00	0.00
Interpreters	720.00	0.00
Total	3 996.06	1674.28

TABLE 3.10: POEM charges convention based

In the first clinical care scenario, based on hospital billing records (see section 4.4), the total medico-technical activity value amounts to 4 674.28 Euro for LGB (Table 3.9) and 1 674.28 Euro for POEM (Table 3.10). For the local economy, each foreign patient treated by the IHU generates a total revenue for tourism related activities (hotel, travel and interpreters) of 2 580.00 Euro.

From the IHU point of view, the cost of receiving foreign patients equates the value of organizing the patient's stay and any activity covered by the institute itself. In our case, the total value of these activities amounts to 1 416.06 Euro corresponding to the cost of organization.

Based on these results, each 1 Euro spent by the IHU for LGB generates 1.82 Euro for the local economy and 3.30 Euro for the hospital. In terms of aggregate costs, considering 200 foreign patients per year as projected by the institute, the IHU revenue increases by a total of 283 212 Euro, plus an additional 516 000 for the local economy and 934 856 for the hospital.

In the POEM case, each 1 Euro spent by the IHU generates 1.82 Euro for the local economy and 1.18 Euro for the hospital. In terms of aggregate costs, considering 200 foreign patients per year, the IHU revenue increases by a total of 283 212 Euro, plus an additional 516 000 for the local economy and 334 856 for the hospital.

	Charge TTC	
	IHU	Hospital
Consultations	0.00	130.00
Blood test	0.00	44.28
Treatment	0.00	2 790.64
Hospital LoS	0.00	1 500.00
Organisation	1 416.06	0.00
Travel	672.00	0.00
Hotel LoS	1 188.00	0.00
Interpret	720.00	0.00
Total	3 996.06	4 979.02

TABLE 3.11: LGB charges cost calculation based

	Charge TCC	
	IHU	Hospital
Consultations	0.00	130.00
Blood test	0.00	44.28
Treatment	0.00	1 902.36
Hospital LoS	0.00	500.00
Organisation	1 416.06	0.00
Travel	672.00	0.00
Hotel LoS	1 188.00	0.00
Interpret	720.00	0.00
Total	3 996.06	2576.64

TABLE 3.12: POEM charges cost calculation based

In the second scenario of clinical care, based on the traditional hospital billing system and cost of operations, the total medico-technical activity's value amounts to 4 979.02 Euro for LGB (Table 3.11) and 2 576.64 Euro for POEM (Table 3.12). For the local economy part, each patient received by the IHU generates a total value of 2 580.00 Euro. Finally, from the IHU point of view, the cost of receiving foreign patients amounts to 1 416.06 Euro.

Based on these results, each 1 Euro spent by the IHU for LGB generates 1.82 Euro for the local economy and 3.52 Euro for the hospital. In terms of aggregate costs, considering 200 foreign patients per year, the IHU revenue increases by a total of 283 212 Euro, plus an additional 516 000 for the local economy and 995 804 for the hospital.

In the POEM case, each 1 Euro spent by the IHU generates 1.82 Euro for the local economy and 1.82 Euro for the hospital. In terms of aggregate costs, considering 200 foreign patients per year, the IHU revenue increases by a total of 283 212 Euro, plus an additional 516 000 for the local economy and 515 328 for the hospital.

5.5 Survey results

In an attempt to identify some of the main reasons that could motivate the adoption of surgical innovations, we distributed a 1 page survey to users of the widely successful (in terms of adoption and marketing) da Vinci surgical system.

A total of 29 answers were collected with 24 originating from IRCAD's urology training courses and 5 from French surgeons currently in practice in different specialties. Our participants mostly originated from European/East-European countries (58.62%) while some traveled from the Middle East (20.69%), North America (13.79%), Turkey (3.45%) and India (3.45%).

In terms of practice, 75.86% of our participants work in a hospital while 24.14% work either in private clinics or in both. Surgical experience, in general, ranges from 0 to 30 years with an average of 10 years (sd 7) whereas only 14 participants reported their experience in robotic surgery (57.14% have less than one year experience and 0% over 10). Note that only 5 participants reported to be currently still practicing robot assisted surgery.

Compared to laparoscopy, 10.71% considered that there is no benefit to patients while 50% and 78.57% reported a positive effect on patients and surgeons respectively. Out of 28 answers for both questions, 11 and 6 participants did not know whether robotic surgery had any impact on patients and surgeons respectively.

The effect of the robotic system on the surgical operation and surgical field, compared to laparoscopy, was unknown to 37-38% of our participants. When focusing on room occupation time, 29.63% reported a decrease, 14.81% no effect and 18.52% an increase. The complication rate was estimated to be reduced in 37.04% of answers, 18.52% reported no effect and 7.41% an increase. In terms of work safety, 7.69% reported a decline, 19.23% no change and 34.62% an improvement.

The advantages put forward by the robot's manufacturer, Intuitive Surgical, have also been put forward by our participants with over 70% reporting a high advantage in all categories except the robotic arms (57.14%). A medium advantage was signaled by 6-14% of the answers with only 4-6 participants choosing the "Don't know" option.

The high cost of the robotic system is considered an important disadvantage (10.71% Don't know, 21.43% medium and 67.86% high). To a lesser extent, the lack of direct access to patients has also been reported as a disadvantage (7.69% Don't know, 7.69% Null, 7.69% Low, 50% Medium and 26.92% High).

There does not appear to be a consensus on whether the restriction in the number of uses for da Vinci instruments is an advantage or disadvantage. Answers varied between Don't know (32.14%), Disadvantage (14.29%), Indifferent (32.14%) and Advantage (21.43%).

From a teaching and research perspective, the majority of participants reported a positive effect for all dimensions (67.86% to 85.71%) especially if the double console is used. Only one respondent noted that the robotic system has a negative effect on his laparoscopic skills.

Overall, the overwhelming majority of respondents (93.10%) consider the robotic system to be promising while the rest are indifferent.

6 Discussion

In general, improvements in patient outcomes in 2015 involve the addition of new technologies which also introduce added costs to the healthcare system. Today, it is necessary to justify an investment in such technologies by weighting the cost against the impacts.

The introduction of technology leveraged surgery into the healthcare system raises a number of questions and challenges as to the methods used for their evaluation and decision making in general. Institutes focused on developing these new medical devices and procedures, such as the IHU, do not currently possess the tools to guide their activity or to provide a credible and transparent reporting, justifying their investment decisions.

Such an evaluation exercise is even more difficult for these companies as medical devices share characteristics that render their assessment heavily dependent on large quantities of information. It is no longer a matter of selling products to consumers as is the case with pharmaceuticals, but a question of affecting an entire production process in which the consumer (patient) takes full part in.

Published guidelines for the economic evaluation of health technologies have been repeatedly criticized for focusing on pharmaceutical products rendering them inappropriate for medical devices, particularly surgical technologies. Nevertheless, a number of general principles can still be applied in both cases such as the use of cost-effectiveness, cost-utility or cost-benefit analysis. The most notable differences reside in the choice, and measurement methods, of both cost and outcome variables.

The first observable impact when a new surgical technology is introduced in the operating room, for an economist or a decision maker, is cost. A new technology can either decrease, increase or not alter surgery cost, a variation that will continue during the entire period of use. At adoption for example, most technologies will prove to be expensive due to their investment cost and as their use is limited to a subset of the targeted patient population. The diffusion of the technology, however, will gradually decrease the cost per-operation as it is more demanded by patients or as it substitutes for the existing treatments.

The overhead cost is particularly sensitive to these changes as it is heavily dependent on the number of patients being treated and the effectiveness with which their needs are

processed. While tools for measuring the impact of innovation on direct surgical care cost are well known by hospital administrators and have been explicitly presented in the literature, the inclusion of overhead cost remain situation and hospital specific.

Independently from the volume of use, factors such as patient's age, Body Mass Index (BMI) or surgeon's experience might directly or indirectly influence the cost per-operation. Experienced surgeons, for example, have fewer complications and are able to operate faster thus reducing operative times [Cahill et al., 2014; Eltabbakh, 2000]. Patients with a lower BMI are usually easier to operate on, thus also reducing operative time [McIlwaine et al., 2014]. In various situations, controlling for these effects through econometric methods plays a significant role in determining the impact specifically due to the introduction of new technologies [Ergina et al., 2009].

In comparative studies based on randomization or matching, and for a large enough sample group, the effect of confounding variables (age, sex, surgeon experience etc.) can be ignored as their distributions are similar in both study groups at the beginning of the trial [Ergina et al., 2009]. In such situations, the difference in the cost per operation can be measured by applying our previously suggested methodology [Ismail et al., 2014] without using additional regression models.

Length of Stay and Complications

The literature also suggests that hospital length of stay does not only depend on the type of procedure or technology used but is also affected by economic supply and demand theories [Clarke, 1996]. Supply factors, for example, include individual practice style of clinicians, supply of beds and the method of payment (prepayment or fee for service). Demand factors combine issues related to patients' socio-economic status, medical needs or direct and indirect costs of a longer stay.

Variations in LoS could therefore not be entirely due to the introduction of a new innovative technology but influenced by external variables. As with surgery cost, the impact of these confounding variables can be ignored in randomized or matching based experiments.

As with length of stay and surgery cost, a variation in complication rates can also be due to numerous factors: procedure type, patient health [Kunisaki et al., 2009], surgeon's

experience [Sosa et al., 1998], etc.. Controlling for these variables, when appropriate, plays a major role in correctly assessing the impact of a surgical innovation on the complications induced cost.

In our analysis, we have found that the average length of stay cost per patient amounts to either 1 578.55 or 2 012.84 Euro for robotic surgery and 1 553.08 or 1 980.37 for laparoscopy, with respect to the methodology used. When adding the cost per operation which includes intra-operative complications, the total cost of computer-assisted Gastric Bypass sums up to 7 904.17 (or 8 338.46) Euro while the cost of laparoscopic Gastric Bypass becomes 4 357.82 (or 4 785.11) Euro.

Our results show that even when LoS and intra-operative complications are taken into account, computer-assisted surgery almost doubles the cost per patient for the hospital. At first glance, one would think that hospital managers would immediately refuse investing in the da Vinci System. However, one must also weigh the outcome or benefit of introducing such new technology, for example, on the society and the economy more generally.

Another factor to consider when analyzing the cost of innovations is the impact that the learning curve and adoption rates have on surgical operation. In time, surgeons acquire experience and patients gain confidence in the surgical innovation which directly and repeatedly impacts complication rates, operation duration and number of operations per year. These impacts signal the need for an iterative approach since a cost, at least in minimally invasive surgery, should not be regarded as a static value.

Absenteeism and Presenteeism

Stepping outside of the surgical care pathway, the debate about which method to use for the estimation of labor productivity changes relates to their consideration as a consequence of health care interventions and the extent to which they are affected [Drummond et al., 2005]. As Krol *et al.* [2011] point out, the inclusion of productivity costs could possibly encourage decision makers to adopt innovations that favor the working population over the elderly. Excluding this variable, however, leads to ignoring social costs which is contradictory to welfare based decision making.

The monetary valuation of productivity loss, be it due to absenteeism or presenteeism, is still subject to controversy. For absenteeism, several methods were suggested with varying precision and implementation difficulty. For presenteeism, while many measurement attempts were made, the literature has yet to reach an agreement on the appropriate method of calculation [Schultz et al., 2009].

According to our measurement, loss of productivity due to absenteeism amounts to an average of 10 329 and 11 550.12 Euro per patient for, respectively, computer assisted and laparoscopic Gastric Bypass. Although we are tempted to conclude that the computer assisted system saves 1 221.12 Euro per patient for the government, we must approach these results with care. First because the difference is not statistically significant and, second, because our data on absenteeism is highly unreliable.

Instead of directly asking patients "how much time off work did you take?", the IHU should have based their protocol on social security data. The French "Institut des Donnees de Sante", or IDS, possess an incredible array of healthcare related data including absenteeism which could be used in the future for a more detailed study.

When contacted, the IDS informed us of the possibility to access a sample of French patients which, as they suggest, we could use to build a regression model explaining their time off work through different characteristics. We could then use the same model to estimated a time off work for our patients by integrating their characteristics as explanatory variables[9].

Quality of life

When assessing the benefits of a surgical technology from the patient's perspective, QoL measures emerged as the current best option for economic evaluations. The use of QALYs, although subject to controversy [Kirkdale et al., 2010; Round, 2012; Whitehead and Ali, 2010], has been widely recommended as it is considered to be the expression of the full impact of medical interventions on patients. While the ethical and economic viability of monetizing this measure is also questionable, since life is priceless, health economists continue to use it as it is the only metric currently available that could reflect the monetary gain of healthcare interventions for the patients [Adam and Stevens, 2011].

[9]Permission to access the sample requires a minimum of 6 months waiting time.

Our protocol for the comparison of computer-assisted and laparoscopic Gastric Bypass was built on the principle that patients' QoL would be measured through non-preference based questionnaires. Results of both the BAROS and GIQLI analysis have demonstrated that there is no difference in QoL due to the surgical technique used.

Not only is it impossible to translate the impact of measured QoL into monetary terms or utilities, but the use of the GIQLI questionnaire altogether is completely unsuitable for the study. GIQLI has been created to measure the impact of gastrointestinal diseases on patients' QoL but obesity is not considered a disease! At first glance, and based on an evaluation using such a questionnaire's outcomes, the patient would not understand a decision that favors the introduction of the Da Vinci surgical system in the operating rooms.

Medical tourism

Institutes that aim at acquiring or developing the most cutting edge technologies are often regarded as centers of excellence and innovation. Such centers may be an attraction for more favorable clientele; which may translate into a focus on medical tourism.

With a medical tourism industry in constant growth [Horowitz et al., 2007] and increasingly competitive, such a representation is essential to any healthcare provider's attractiveness on an international scale. Decision makers, especially the government, should not ignore the implications of attracting foreign patients as they can provide benefits varying from an increase in efficiency to the generation of additional economic activity.

From an efficiency standpoint, attracting foreign patients serves as a leverage to decrease the fixed cost per operation for all patients receiving treatment with a specific technology. In publicly financed healthcare system based on activity payment, the benefit extends to the government that derives a higher flexibility in determining the reimbursement amount for the insured.

To further illustrate, according to our calculations, if the government decides to reimburse computer assisted surgery at the current 150 patients per year activity level they would spend at least 1 185 625.5 Euro ($150 * 7\,904.17$) assuming a 100% rate of reimbursement. However, consider that, due to medical tourism, the government can use the

robotic technology to its full capacity with 150 French patients per year and 250 foreign non-reimbursed patients who pay directly out of pocket. According to our sensitivity analysis in Chapter 2 and the cost of LoS and complications in this chapter's subsection 5.1, the reimbursement per French patient decreases to 5 990.73 (4 412.18 + 1 578.55) and the total reimbursement amount decreases to at least 898 609.50 Euro (150 ∗ 5 990.73).

The economic impact, other than on care provision, of foreign patients and even on surgeons in search of training can also be valued through the spending they do during their stay in the receiving country. Hotels, restaurants and various tourist attractions benefit from medical tourism stimulating activity developments, job creation and more generally contributing to the national GDP. However, considering that neither the hospital nor the IHU keeps separate or identifiable records of foreign patients treated using the robotic system in their facilities, we were unable to conduct a medical tourism economic impact for this specific technology.

While it is theoretically possible to conduct an economic impact analysis for foreign surgeons who train on the robotic surgical systems at the IRCAD, it would not be representative of the surgical system that is dedicated to performing surgical operations. From our point of view, the evaluation of the training activity should be done separately from that of the hospital's surgical operations unless a clear correlation is proven to exist.

Applying the studied concepts to laparoscopic Gastric Bypass and POEM surgery allowed us to better understand the data requirements and capabilities of medical tourism's economic evaluations. Our findings, based on hypothetical scenarios, are expressed in the form of cost benefit ratios with every Euro spent on an activity generating a proportional value in economic gain for the region.

One of the patients who underwent POEM surgery for Achalasia in Strasbourg, in 2013, published his story in a blog "mypoemsurgery.blogspot" detailing his experience and activities during his surgical stay. From reading his blog, we better realize the regional economic impact that minimally invasive surgery could have since patients can rapidly recover form surgery and spend the rest of their stay vacationing. Analysts should not hesitate to invest the resources necessary to collect detailed data on patients' expenditures outside of the care pathway.

Intangible benefits

While the Da Vinci surgical system appears to not present any advantage that could explain the higher investment cost neither from the hospital nor the patient's perspective, it still experienced a remarkable commercial success. Our attempt to measure the less obvious advantages were first faced with a clear barrier as Intuitive Surgical refused to share any contact information of surgeons who use their robotic system or even to distribute our survey themselves.

When we attempted to contact the society for robotic surgery, they expressed a high interest in this type of study and agreed to distribute the survey. After sending them the questionnaire, we never heard back from them and our mails remained unanswered, which led to us abandoning the study.

It is only at the end of the thesis that one of the ISIP fellows at the IHU was able to distribute the survey to surgeons training on the Da Vinci System at the IRCAD through his position as a teaching fellow. The results of the analysis are therefore very strongly biased towards the surgical system as we can expect surgeon who travel this far for training to be very optimistic and favorable towards the technology.

Our results show that although surgeons are aware of the high investment cost of the robotic system, they still view it as a promising technology. Indeed, the technology's advantages have been repeatedly been put forward by Intuitive Surgical and taken as facts by their customers who also report the same advantages. When asked about the disadvantages, however, fewer respondents reported knowing the answer.

The biggest advantage of the robotic system appears to reside in its teaching capacity. This, however, is highly conditional on the use of a double-console or a specific simulation software and hardware. All of which further increase the initial investment cost.

Fiscal effect

To take the analysis even farther, we could investigate the "Fiscal effect" that innovative surgical technologies could have on a specific country. Remember that governments play a crucial role in healthcare as a regulating agent and the main source of funding. In that

respect, economic evaluations can and should take into account their budget perspective by, for example, estimating the impact of surgical procedures on reimbursement or sickness and disability benefit payments.

On a macroeconomic scale, improvements in a nation's population's health can also positively affect economic growth [Bloom et al., 2004]. In healthcare, job creation is often overlooked as an impact of introducing innovative surgical technologies even though employment is one of the pillars of a healthy economy. To be more precise, different types of benefits can be derived from innovation-related employment.

Hybrid surgery, for example, requires a specific set of skills and it is this unique combination that attracts specialized surgeons. Following its introduction, we would either observe a reallocation of talents with experienced surgeons choosing to follow the innovative route and their old activity being open for application; or the appearance of a new generation of professionals dedicated to the use of said technologies. Regardless, it would augment the national pool of high level workers.

Aside from the acquisition of valuable skills and expertise, these created jobs can be translated into an increase in revenue for the state as well as a decrease in unemployment benefit payments if the hired individual is a resident.

Another impact that could be interesting from the government's perspective relates to the preference for domestic over foreign investments. To be more precise, Balance of Trade is a common notion in macroeconomic that measures the difference between the monetary value of exports and imports of a country. A trade surplus is mentioned when the value of exports exceeds that of imports, an indication of a good economic situation. In that respect, when faced with a choice between two surgical technologies with the same cost-effectiveness ratio, the one produced domestically should theoretically be favored as it limits currency outflow.

Job creation, increase in tax revenue and possibly an increase in exports translate the social and economic advantages of domestic technology production. To our knowledge, the health economic literature has not addressed the need for a weighting factor that favors the use of domestically produced technologies compared to imports.

6.1 Limits

Both our review of the literature and our application were limited by information access and exchange barriers between the IHU and the hospital as well as Intuitive Surgical. We were not successful in completely breaking the information exchange barrier with the hospital for the purpose of conducting economic evaluation since such discussions were also dependent on the global relationship that exists between the two institutions' director boards.

We therefore had to base our analysis of the surgical care pathway on a combination of two methodologies knowing very well that the hospital's data collection and reporting procedures are questionable from a pure economic standpoint. As an example, the management adviser provided us with a cost per day of hospitalization based on a calculation methodology using data that has been repeatedly proven to be imprecise even by himself.

A major weakness of the hospital's calculation methodology is the distribution of the post-operative complications' cost (excluding re-operations) among all patients in the same hospital ward. The effect of innovative surgical technologies that aim at reducing post-operative complications run the risk of being underestimated as the hospital ward admits other patients with higher complication rates.

By combining both methods, we had to exclude the expenses of several Medico-technical centers which include a part of the hospital's overhead cost. As our micro-costing methodology does not take the overhead into account, we run the risk of underestimating the cost of patient care.

Our ability to analyze the impact of complications in any significant detail was limited for two reasons. First, the hospital's data collection system does not allow the tracing of complications, whether intra-operative or post operative. Second, complications related data from our own protocols were riddled with double counting which cannot be filtered out reliably.

Our survey for the evaluation of the da Vinci System present many weaknesses due to abandoning its development and the sudden opening up of a one time opportunity to distribute it. Nevertheless, it can serve as a pilot study for a more comprehensive analysis.

7 Conclusion

The introduction of technology leveraged innovations in minimally invasive surgery will, more often than not, be associated with an increase in the cost of care. The future of such innovations is therefore highly dependent on the quality of medico-economic evaluations and their considerations of pertinent impact measures.

In this chapter, we sought to identify the mean of measuring the impact of innovations in minimally invasive surgery by shifting the focus from the impact on surgical operations to the entire patient surgical care pathway and beyond. We started out by demonstrating that the economic evaluation of medical devices is a particular subject that the literature has yet to address in a comprehensive manner and that greater attention should be given to the global impact of minimally invasive surgical technologies.

After providing a review of a selection of economic evaluation guidelines, we presented a list of both cost and outcome variable that we consider of significance for medical devices, and minimally invasive surgery in particular. For each variable, we presented the measurement methodologies to be used and also those to avoid such as with the QoL analysis. We hope that these presentations will help analysts gain time for their applications or research.

We have also noted the importance of QALYs and presented a series of possible outcome measures that decision makers should look into more carefully. The current practice of focusing on direct economic measures (cost and reimbursement) is neglecting what should be the center of healthcare, and that is the patient.

To prevent such a mistake, health economists need to decide on a rational way of including patients in the economic evaluation process. The patient's willingness to pay has been admittedly a positive step forward but the controversy over its ethical use keeps pulling it back.

We also presented the difficulties in analyzing some outcomes such as absenteeism with the current information collection and exchange system. The evaluation of presenteeism, on the other hand, was limited not only by data collection but also by the lack of methodological guidelines altogether.

The true added value of this chapter, from our point of view, is the introduction of medical tourism and the measurement of intangible benefits as part of an economic evaluation. Although we could not perform a full evaluation for the da Vinci System, we were still able to gather enough data to provide applications, or at least an overview, for each variable.

Our recommendation for an institute that is genuinely serious about their economic evaluation program, such as the IHU, is to focus their priority on creating an adapted data collection system. As without quality data, any analysis would be of low reliability if even feasible.

The second step would be to create an econometrics based algorithm that automatically and continuously exploits the collected data as to ensure an iterative evaluation of the most innovative surgical technologies. We have already created a large part of this algorithm through our thesis but further refinement will depend on obtaining the necessary information on which data collection software is going to be used.

Hybrid surgical technologies are currently very few in numbers as the concept has only just recently began development. Therefore, before being able to analyze the socio-economic impacts of these innovation we first need to create them!

We cannot help but wonder what would be the impact of the research and development process that leads to the use of these technologies. Is it possible to combine the creation and the use's impacts? The next chapter in this thesis will attempt to provide some elements to help answer this question.

Chapter 4

Impact of Research and Development in Healthcare

1 Introduction

Innovation has been, for a long time, a key concept in macro and micro economic growth as it entails considerable investments in research activities and technological development. Back in 1988, Dosi [1988] stated that a significant part of industrial countries' GDP is dedicated to research and development (R&D) be it in nonprofit institutions or business enterprises. Today, according to the Organisation for Economic Co-operation and Development (OECD)'s 2013 data, OECD countries dedicate an average of 2.4% of their GDP to R&D with France occupying the 14th position at 2.2%.

The culmination in interest for research evaluations has only been reached in the mid 1990's [DSTI, 2009] with the emergence of economic and social impact assessment. In the context of economic instability since 2008, the development of these evaluation methodologies stems from healthcare managers' and governments' need to know whether research is "worth it" as they look to maximize its return on investment. Questions such as "was it done right? Can it be focused? How can the developed knowledge be exploited? What are the benefits of research results to the consumer?" [Ruegg and Jordan, 2007] are currently exerting strong influence on the R&D process while researchers struggle to obtain funds for their projects.

Modern Healthcare systems are suffering from the current economic contraction but also increasingly by the escalating costs of complications and chronic conditions relatively to the lifestyle issues and an aging population. The research community is constantly challenged to avert these health threats but is also expected to generate social and economic impacts by improving the general population's quality of life and longevity as well as generating economic activity and productivity gains [Roback et al., 2011].

The progress and success of healthcare R&D has been historically measured through a fixed number of criteria, such as the number of publications, that form the basis for obtaining grants and expanding teams. However, neither patients nor healthare managers share the same interest as public decision makers or researchers and would prefer to be informed of the impact such activities have on their lives or their institute's activity [Charlton, 2006].

Hospitals, for example, would be more interested in conducting cost-benefit evaluations from a purely business standpoint. Depending on the importance of their research and educational activity, they would also be interested in the innovation and intangible factors aspect. Governments, on the other hand, would prefer a more macro-economic approach and thus adopting a societal perspective would be more logical from their point of view.

As an institute aimed at developing innovative hybrid surgical technologies, the IHU's activities represent a major source of investment and impact for both the society and the economy. Despite recent developments in the field of research evaluations, however, the institute has yet to adopt a comprehensive and adapted approach to assess its R&D activities.

In the previous chapters, we focused on creating and discussing methodologies for evaluating the **use** of innovative surgical technologies with a focus on hybrid surgery. In this chapter, we turn our focus towards the **development process** of hybrid technologies and attempt to establish a solid method for evaluating its impact. Furthermore, conducting such an evaluation should stimulate dialogue between the administration and researchers as it points out both the strengths and weaknesses of the R&D process.

After this introduction section, the second will be dedicated to defining "innovation" as to better understand the objectives of R&D and how the literature approaches the

subject. This second section will also attempt to describe the R&D process with an emphasize on identifying the actors behind technological developments.

Before undertaking an evaluation, it is necessary to understand "what" exactly we are evaluating. Moreover, by pointing out the sources of innovation, analysts will hopefully be able to focus their evaluations as they would already know "where" to look for impacts.

The third section of this chapter will provide the reader with an overview of research evaluation methodologies as presented in the literature. An emphasis will be made on describing the general structure and detailed elements that form such evaluations as to better prepare for either the creation or use of a comprehensive surgical innovation adapted method.

The fourth, fifth and sixth sections of this chapter will focus on describing a BETA[1] developed R&D evaluation methodology (EvaRIO) and will present an IHU based case study of this methodology. Expanding on this established method, we will also attempt to construct a more project oriented surgery specific evaluation method for future pragmatic application in the IHU Strasbourg.

The discussion section will concentrate on interpreting our application's results as well as providing an overview of the difficulties that analysts will encounter using the methods used and developed in this chapter. We conclude by summarizing our main findings and discussing the utility of our results.

[1] Bureau d'Economie Théorique et Appliquée.

2 Overview of innovation definitions and process

Before conducting an evaluation of any type, the analyst must first become familiar with the subject he is studying in order to pose a solid foundation for his work. This understanding is essential to correctly define the study's "perimeter", as in what to analyze and where to look for the information.

The word "innovation" in itself, for a non-specialist, means nothing more than a new technological product or method aimed at enhancing patient care. Similarly, a "hybrid surgical innovation" can have a variety of definitions, impacts and origins.

In this section, we try to show the complexity of innovation by going through its multiple definitions as well as the processes that stimulates its emergence. By understanding what the concept of hybrid innovation entitles, the identification of impacts and sources should become easier.

2.1 Nature of innovation

When discussing innovation, it is easy to misinterpret the term as a new, potentially revolutionary, product or service that emerge from a research process. In reality, innovation is a mutli-stage process [Baregheh et al., 2009] which manifests itself in different forms and appears at different stages of a product or service's life cycle [Tidd et al., 2005].

The first question to answer when conducting an evaluation is therefore a traditional "What to measure?" Far from being straightforward, the answer requires a detailed understanding of the definitions that current experts in innovation have given to the term.

In this sub-section, we attempt to provide the reader with a literature review of these definitions in order to better highlight the challenges in evaluating R&D, particularly for hybrid surgical innovations.

2.1.1 The four "P" of innovation: Product, Process, Position and Paradigm

Firms have historically resorted to innovation to gain a competitive advantage by either improving quality, reducing cost, developing innovative products or devising new methods of sales and financing. To achieve each objective, they sought to perform changes not only to their final product but also to the way they produce and do business more generally [Francis and Bessant, 2005].

The literature on innovation management attempted to understand and explain these changes by creating four "targeting" categories defining each innovation's objective. One way to view these targets, which we consider to constitute the first dimension of innovation, is through the four "P": Product, Process, Position and Paradigm [Francis and Bessant, 2005; Tidd et al., 2005].

"Product innovation" is a term that describes the traditional view we have of innovation corresponding to a change in the products or services offered by a certain organization. **"Process innovation"**, on the other hand, does not concern itself with the product itself but the sequences of activities through which it is produced and delivered [Tidd et al., 2005].

The fiber-optic endoscope, for example, can be viewed as a typical product innovation at the time of its invention in the 1960s. Consequently, the introduction of this innovation in the operating room enabled new therapeutic procedures, considered as process innovations, where flexibility is essential such as in Polypectomy [Rosenberg et al., 1995].

A **"Position innovation"** does not affect the composition or functionality of a product but focus instead on changing the context in which it is introduced and how it is viewed by the customer. Marketing and advertising play a major role in stimulating this type of innovation as communication with the customer, and the ability to persuade him, are essential.

Historically, for example, the endoscope was created and used as a diagnostic tool. The continuous advancements in the late 1960s, however, saw the introduction of channels for biopsy and therapeutic maneuvers which allowed to re-position the endoscopic as a tool for performing surgical operations [Rosenberg et al., 1995].

A **"Paradigm innovation"** reflects changes in the model of an organization's activity. These changes can either be expressed through organization values and staff management (exp: payment for skills, operator-led problem solving, etc.), or in terms of business (exp: change from mandatory subscription to publicity driven service access) [Francis and Bessant, 2005].

The introduction of minimally invasive surgery, whether laparoscopy or endoscopy, is one straightforward and modern example of paradigm innovation considering how it completely changed the relationship between patients and their healthcare institutes. In particular, it marked the increased interest in patients' well-being and post-operative quality of life compared to the previously mortality and morbidity oriented focus.

2.1.2 Traditional Incremental vs Radical

The economic literature has historically separated innovation into two categories, incremental and radical, reflecting a second dimension to be taken into account when distinguishing between the types of innovation. What differentiates these two categories, according to Tidd *et al.* [2005], mainly appears to be the degree of novelty; which remains a highly subjective assessment.

Incremental innovation makes reference to small changes, mostly improvements in the sense of "doing what we do better" [Tidd et al., 2005], that are made to an existing technology in an existing market [Garcia and Calantone, 2002]. A new surgical clip with better holding strength and placement characteristics, for example, would represent an incremental change[Riskin et al., 2006] as it *only* improves current practice from a surgeon's point of view.

Another example of an incremental technology change, more often regarded as a process innovation from the surgeon's point of view, is the invention of the coronary stent. The tube shaped device is used to keep arteries open in the treatment of coronary heart disease, thus changing the way through which care is delivered by replacing the need for open heart surgery and improving outcomes within an existing market without toppling industry leaders [Riskin et al., 2006].

Radical innovation are "new to the world" [Tidd et al., 2005] technologies that stimulate the emergence of a new market [Garcia and Calantone, 2002]. Garcia *et al.* [2002]

argues that such innovations often do not address a recognized demand but create it, thus stimulating the emergence of new markets.

Defining the degree of technological "radicalness" has been a matter of debate due to its reliance on subjective point of views. A difficulty that Dahlin *et al.* [2005] has proposed to answer by defining 3 main criteria of success: novelty, uniqueness and impact on future technologies.

In that sense, a radical innovation is one that can be dissociated from previous (novelty) and current (uniqueness) inventions. To be a successful change agent, it also has to cause a radical change in current practice thus influencing the emergence or change in future technologies [Dahlin and Behrens, 2005].

The introduction of laparoscopy, for example, can be viewed as a radical innovation since it changed surgical practice from traditionally open invasive approaches to ones that are more patient friendly. Over the years following its introduction, it continued to influence innovations as improvements emerged in the form of new instruments, machines (robotics), practice (cholecystectomy, prostatectomy, etc.) or even in terms of care organization and management that made laparoscopy today's golden standard.

2.1.3 Incremental, Radical and Disruptive?

A third term, **disruptive innovation**, has integrated the innovation discussions following Clayton M. Christensen's, a Harvard business administration professor, influential book "The innovator's dilemma" which he first published in 1997 [Christensen, 1997]. The concept relies on his observation of industries' behavior, particularly the hard disk drive sector, when faced with changes in the way existing knowledge is used [Tidd et al., 2005].

From Christensen's perspective, both incremental and radical innovations are considered to be **sustaining** in that they both improve upon existing technologies. Radical innovations, however, drive improvements many order of magnitudes higher than incremental innovations which, from our point of view, does not represent a solid criteria of differentiation.

In his theory, Christensen also highlights the much more important role of markets and their influence on innovation emergence and diffusion. Disruptive innovations, as he

describes, offer less of what customers in established markets wanted and are therefore rarely deployed there. Instead, they offer a different "package of attributes" that define their own market separately from the mainstream [Christensen, 1997].

We can summarize the characteristics of disruptive innovation in two main points. The first characteristic reflects their inferior performance, at the time of their introduction, to existing alternative products as measured by the traditional industry specific metrics. They are therefore considered to be of low interest to users, customers and established firms who's main objective would be to maximize expected profit thus driving resource allocation towards sustaining innovations [Riskin et al., 2006].

The second characteristic relates to the market which the innovation serves. The market of disruptive innovations is one that has either been under-served in the past (i.e. extending service to more users) or did not exist at all (i.e. new users emerge). The emergence of these new markets often drives existing previously successful firms into bankruptcy as they fail to cope with the change and their sustained innovation becomes irrelevant to users needs. The market leaders become the new entrants.

The use of endoscopes, for example, created a whole new market centered around minimally invasive surgery thus filling the second characteristic described by Christensen [Christensen, 1997]. However, the rapid rate of diffusion and inadequate level of training/experience of clinicians in these new procedures increased complications and demonstrated their overall inferior performance to the well established open surgery [Rosenberg et al., 1995]. A conclusion that is not entirely surprising as the performance of minimally invasive surgery is measured through different attributes than those for open (thus the first characteristic is also filled).

The emergence of endoscopes in minimally invasive therapy can therefore either be considered as an example of disruptive innovation in healthcare, following Christensen's definition, or a radical innovation using the traditional definition. Regretfully, further investigations reveal the controversy over the classification of innovative terminologies with no common ground being reached [Markides, 2006].

Percutaneous transluminal balloon angioplasty is one other example, provided by Riskin *et al.* [2006], of a disruptive innovation which was considered dangerous and generally

inferior to the traditional open coronary artery bypass. Over the course of its development, however, it finally proved to be disruptive within the field of cardiothoracic surgery by causing a shift in market share towards interventional cardiology.

By studying the history of endoscopic innovations, we can get a better idea of how different types of innovations can influence markets and current practices. Rosenberg *et al.* [1995], for example, discusses how the introduction of endoscopic techniques offered advantages that open surgery could not meet such as the absence of sequelae, minute scars, hospital stay or outpatient treatment. These advantages were even previously thought impossible to achieve.

2.2 Innovation creation and diffusion

The multitude of innovation definitions presented in the previous subsection reflects the complexity of performing research evaluations. Knowing what to measure seem insufficient as each innovation type generates different impacts but also emerges from different sources.

A second question to answer when conducting an evaluation is a more evasive "Where to look?". To try and provide an answer, we must first understand the underlying mechanisms of the innovation process and identify key players in both the emergence and diffusion of innovative technologies.

2.2.1 The innovator

In his analysis of the "Sources, Procedures, and Microeconomic Effects of Innovation", Dosi [1988] discusses two main sources of innovation: R&D expenditures and "learning by doing"/"learning by using". While both are complementary, measuring the amount of resources dedicated to innovation through R&D activities is often considered to be simpler than for "learning by doing"/"learning by using", the costs of which are hard to trace.

To be more precise, technological innovation can be described as the process of solving problems with solutions that meet both cost and marketability requirements. However, as the problems are often poor in information, i.e. they do not provide an answer by

themselves, this process involves "discovery" and "creation" often accompanied by trial and error mechanisms [Dosi, 1988].

As Dosi [1988] highlights, *the "solution" of technological problems involves the use of information drawn from previous experience and formal knowledge (e.g., from the natural sciences); it also involves specific and uncodified capabilities on the part of the inventors.*

The funding of strategic research programs and centers [Technopolis group & MIOIR, 2012], for example, is based on this exact mindset. Through such investments, nations hope to expand and improve the supply of trained people (who possess such uncodified capabilities), intellectual property and know-how through which they can create innovation platforms or niche markets for business developments.

An important part of what induces innovation is therefore "within" the innovator himself described through his **knowledge base** and creative capacity. It is also through innovation that the innovator can increase his capacity to use in future works [Georghiou et al., 2002].

The creation of semiflexible gastroscopes, for example, takes root in Rudolf Schindler's accumulated experience through hundreds of examinations using rigid gastroscopes. Through 30 years of persistent development, he succeeded in creating an acceptably safe and workable instrument only limited by the tools and materials available before 1960s [Rosenberg et al., 1995].

The knowledge that George Wolf, a Berlin instrument maker, possessed in conveying light rays along a flexible arc also proved central to the continuous improvement of Schindler's initial idea. Building on the knowledge of both specialists, a second semiflexible gastroscope was introduced named after them [Rosenberg et al., 1995].

As leading innovators, institutes may also benefit from first mover advantages arising from technological leadership, preemption of assets and buyers' switching costs [Lieberman and Montgomery, 1988]. Technological leadership can be acquired either through success in patents and R&D races, or decrease in costs due to the economics of scale. Preemption of assets relates to the institute's ability to acquire or control scarce assets rendering them unusable by the potential competition. And finally, late entrants will be burdened by the customer's reluctance to move away from the first mover's product.

By introducing the first computerized surgical system (da Vinci), Intuitive Surgical currently benefit from these first mover advantages after successfully penetrating the surgical market. Maintaining its monopoly in the market, or being "locked-in", will however depend on the users and their relationship with the company.

2.2.2 The user

The definition of innovator is vague in nature as it can designate different individuals, professions or even institutes. An innovator is not only someone who creates innovations destined to be used but is also someone who uses, or tests, developed innovations to further enhance them or provide feedback. In the case of minimally invasive surgery, the surgeon is bound to innovate while simply practicing his profession as the treatment for each patient is unique and the solution for each encountered obstacle is different [Barkun et al., 2009].

In the surgical field, technology adoption and use is characterized by the user's (surgeon) relatively heavy weight in deciding which technology to choose. Surgeons can insist on the acquisition of an innovative instrument expected to improve patient care at a potentially increased cost, even if it constitutes a financial barrier for the employer, hospital or private clinic.

Innovative surgical technologies may also require additional expenses in the form of training, inexperience-induced complications or regulatory paperwork. In each situation, both the surgeon and their employer would be hesitant to adopt a new technology unless it is proven to provide a significant cost-benefit advantage.

Brian Arthur [1989] provides a detailed discussion on the role of users as innovators in one of his articles from Dosi *et al.* [1988]'s influential book "Technical Change and Economic Theory". Throughout his analysis of technology adoption and its role in innovation diffusion, he highlights five particularly important sources of attractiveness caused by adoption:

1. *Learning by using*: the more a technology is adopted, the more it is used and the more is learned about it which facilitates its development and improvement;

2. *Network externalities* [Katz and Shapiro, 1985]: some technologies, such as the telephone, offer a higher advantage the more users there are. Therefore, it is in the adopter's interest to belong to a network of users with whom he "goes along";

3. *Scale economies in production*: as adoption increases, more units of an innovation's product are sold which decreases its cost. The innovation thus becomes increasingly attractive;

4. *Informational increasing returns*: the more a technology is adopted, the more it is known and understood. Risk-averse users become more comfortable acquiring it when compared with less known alternatives;

5. *Technological interrelatedness*: as a technology becomes more adopted, a number of other sub-technologies and products become part of its infrastructure. Emerging technologies face a disadvantage as their adoption could incur a high cost for users of established technologies.

The increasing returns to adoption, with respect to the five cited principles, can possibly lead to a "lock-in" phenomena [Arthur, 1989] in which a technology dominates the market even if its performance is inferior compared to its alternatives. The role users and their perception have of an innovation is therefore essential to technological success.

In that respect, marketing and **reputation** can be considered as some of the most powerful tools of market penetration and dominance. One modern example is the da Vinci Surgical system which the literature has, on various occasions, discussed the lack of evidence of its superiority to laparoscopic surgery. And yet, every hospital wishes to possess one as the reputation gain that it incurs is considered to be worth the cost.

Users have a second role in the emergence of innovation through what the literature describes as "lead users", a term developed Eric Von Hippel in 1986 [1976; 1986]. As he discusses, a lead user is someone who presents strong needs that are expected to become general in the future and are currently not fulfilled by the market. By attempting to fill the needs they experience, lead users either create new product concepts or serve as a need-forecasting laboratory for marketing research.

When taking a closer look at the medical equipment technology field, Lettl *et al.* [2006; 2008] observed that surgeons play a major role in the emergence of, especially radical (in

the traditional sense), innovations. Beside their role as inventors, innovative surgeons are also entrepreneurs and co-developers who rely on network creation to secure sufficient financial resources, experts' talents, institutes' technological know-how and the help of manufacturers to realize the implementation of their concepts. Additionally, surgeons are an inestimable asset for instrument development companies by testing their innovations and providing constructive feedback.

An important part of innovation therefore lies "around" the innovator, or more specifically the surgeon, described through his **network** and practice environment. As with capacity, it is also through his innovative work that the innovator can increase his network and influence his practice environment, which he could then use in future projects [Georghiou et al., 2002].

2.2.3 Cooperation, Communication and Interaction

Innovation in minimally invasive surgery, hybrid surgery in particular, neither comes from a single innovator nor a single user. It is actually the fruit of combining the skill and knowledge of surgeons, radiologists, endoscopists, instrument makers and software engineers among others.

When individuals with different knowledge, backgrounds and perspectives interact, they tend to mutually assist and encourage one another to stretch their capacity for the purpose of bridging and connecting their diverse knowledge. This "cognitive distance", as Nooteboom describes [Nooteboom et al., 2007], yields opportunities for novel combinations of complementary resources strongly stimulating the emergence of innovations.

As the European Commission reports [Technopolis group & MIOIR, 2012], innovation is increasingly dependent on the complementary knowledge and skill of different actors. In a competitive environment, this means that cooperation and knowledge transfer are crucial to maintaining an advantage over the competition; whether through incremental or radical innovation [Ritala and Hurmelinna-Laukkanen, 2013].

The importance of cooperation and communication is well understood by developed nations that continue to promote the creation of innovation brokers (such as science parks, incubators and technology transfer offices) and adoption of cluster policies. Investments that are expected to increase innovation output by providing flexible infrastructures

that suit different needs, stronger knowledge base as well as motivating a greater flow of knowledge and technology between innovators [Technopolis group & MIOIR, 2012].

While cooperation and communication play a major role in stimulating innovations, the latter may interact in unexpected ways pushing the boundaries of what is possible even farther. In a description of endoscopic innovations' history, Gelijns and Rosenberg [1995] highlight the particular impact that some innovations' improvements can have on other complementary innovations.

The development and adoption of the endoscope and gynecological laparoscopy, for example, were greatly influenced by the creation of fiber-optics for light transmission, the development of televisions for image viewing and videorecorders for the permanent storage of images. As Rosenberg [1996] discuss in one of his many insightful articles:

> *"An additional and historically very important reason why it has been so difficult to foresee the uses of a new technology is that many major inventions had their origins in the attempt to solve very specific and often very narrowly defined problems. However, it is common that once a solution has been found, it turns out to have significant applications in totally unanticipated contexts. That is to say, much of the impact of new technologies is realized through inter-sectoral flows. Inventions have very serendipitous life histories."*

The endoscope's improvements, for example, have led to parallel developments in both practice, through the use of expandable wire-loop snares with the endoscope for polypectomy, and new clinical applications. The development of these technologies was therefore not made by a single individual in a single institute, but constituted a series of simultaneous developments that took place in several countries with different specialists and firms interacting to different degrees.

Once more, an important part of innovation seems to lie "between" innovators described through their interaction and collaborations. By combining knowledge from distinct specialties, cooperation significantly increases the chances of creating disruptive and radical innovations.

3 Research impact evaluation methods: the literature

The RAND corporation[2] offers several reports reviewing the health research evaluation literature which we attempt to summarize in this section. The reliance on their reports is due to the fact that very few publications exist in the literature detailing the characteristics of each methodology [Banzi et al., 2011].

In this section, we provide the reader with an overview of R&D activities' evaluation methodologies published in the literature. Taking example on the payback framework, we present a more detailed overview to further clarify the structure and possible uses of a research evaluation method. We try to summarize the most important characteristics to be taken into consideration in this type of analysis as a stepping ground for introducing our own methodology later on in this chapter.

3.1 Overview of evaluation methods and general structure

A first investigation of the methods for evaluating the economic impact of healthcare research revealed one systematic review, by Yazdizadeh *et al.*[2010], which was used as the stepping stone for this subsection. In their article, the authors mainly differentiate between two methodology types:

- Macroeconomic methods examine the relationship between the cost of conducting research and the macro-economic benefits. End results come in the form of "return" such as a national decrease in mortality rate, morbidity, an increase in life expectancy or economic benefits
- Case studies focus on analysing the impact of specific healthcare research by taking into account several dimensions of benefits including economic ones. Methods used in such studies are commonly identified as "Frameworks" that define the categories of impact.

In their systematic review, Yazdizadeh *et al.* [2010] mainly consider four frameworks for comparison: Payback, Canadian Institutes of Health Research, Canadian Academy

[2]RAND Europe is an independent, not-for-profit public research institute whose mission is to improve policy and decision making through research and analysis.

of Health Sciences and Research impact. In a more expansive report by the RAND corporation, Brutscher *et al.* [2008] provide a more detailed comparison of a selection of 8 frameworks from different countries described as follows:

- Leiden University Medical Center (LUMC), from the Netherlands
  Ex-post evaluation framework focusing on the societal impact of research, at the research group's level, to inform policy-makers on the societal value of research. A scoring system is used to translate each research group's performance in terms of communication through "knowledge products", "knowledge exchange & esteem" and "knowledge use" with the surrounding public sector, private sector and the general public;

- Measure of Research Impact and Achievement (MORIA), from Australia
  Ex-ante evaluation framework focusing on outputs ("activity"), outcomes ("recognition") and impacts of research across the "knowledge", "health gain" and "economic benefits" domains using a numerical scoring system;

- Program Assessment Rating Tool (PART), from the USA
  Ex-post evaluation framework focusing on output, outcome and efficiency measures through a questionnaire to evaluate programs based on performance goals. Most weight is given to outcome measures;

- Vinnova (Swedish Governmental Agency for innovation systems), from Sweden
  A three parts evaluation framework consisting of an impact logic assessment, monitoring, and a project evaluation. The ex ante "impact logic assessment"'s purpose is to ensure the evaluation's feasibility and pertinence. "Monitoring" provides early indicators of impact and ensures a continuous assessment of a program. "Evaluation" focus on analyzing whether a program's objectives are being or were achieved;

- Payback, from Canada
  An input-process-output-outcome framework comprised of two components: a definition of evaluation categories for the research's outputs and outcomes, and a logic model of the research process. A more detailed overview is provided in subsection 3.3;

- UK Department for Innovation/Universities and Skills (DIUS), from the UK
  This framework is used to monitor economic impacts at the aggregate economy

level through three phases: innovation outcomes and outputs, knowledge generation, and investment in the research base. Three influence factors are also taken into account: framework conditions, knowledge exchange efficiency, and demand for innovation. The objective being the assessment of the science and innovation system's health and how it generates economic impacts;

- European Union Framework Programme (EU), from the EU
  The EU framework is used to monitor research programs by tracking their results and contribution to policy goals. Additionally, it allows decision makers to identify what needs to be improved to better achieve said goals;

- Congressionally Directed Medical Research Programs (CDMRP), from the USA (specific to the military)
  This framework consists of three parts: a grants management system, a product database and a concept award survey. The first is used to monitor the technical progress of each grant, the second catalogs and tracks research advances while the third assesses the extent of impacts.

As our interest lies in the evaluation of R&D focusing on hybrid surgical technologies, the use of framework type studies appears to be most relevant. Through further research, we were able to identify over 10 different frameworks [Banzi et al., 2011; Brutscher et al., 2008; Guthrie et al., 2013; Panel on Return on Investment in Health Research, 2009] with remarkable variability in their main elements: perspective, objective and temporal dimension.

3.1.1 Perspective

An evaluation can be done from two different perspectives, depending on who performs it (i.e. Internal or External), and using different aggregation levels (i.e. individual researcher, projects, research groups, department/program, institution, field or research system). Each choice presents some advantages but influences both the evaluation's objective and the relevance of impact/outcome measures.

Internal evaluations are performed by someone from within the organization conducting the R&D project whereas external evaluations, as the name implies, are performed by

external contractors (for example). Internal evaluations are mostly useful when the formative dimension is of relevance, that is, the interest lies in examining possibilities of improving the R&D process.

As the European Commission argues [European Commission, 2004], the need for independent evaluators mostly arises when evaluations need to have a strong summative dimension either for accountability purposes or benchmarking. Note that the European Commission considers independence to be influenced by *"the evaluator's competence and integrity, his access to data and dialogue with relevant stakeholders, and also the ability to conclude freely on the basis of analysis made"*.

The choice of an internal vs external evaluation is strongly influenced by the decision maker's objective and, therefore, the level of aggregation. In turn, the choice of aggregation level depends both on the audience and data since confidential information, for example, are not meant to be shared with the public and their use therefore restrict reporting to an institution level and by internal examiners. Additionally, a low level of aggregation is relatively time consuming in terms of both data collection and analysis.

3.1.2 Objective

The evaluation objective depends on the evaluator's perspective whose focus could either be on advocacy, accountability, analysis or allocation [Guthrie et al., 2013]. As shown in several reviews [Brutscher et al., 2008; Panel on Return on Investment in Health Research, 2009], each framework can accomplish several objectives but a comprehensive methodology filling them all has yet to emerge.

Methods promoting advocacy concentrate on demonstrating, to policy makers and the general public, the benefits of investing in R&D and enhance the understanding of its processes. Main implications include an increase in the decision makers' and public's confidence in policies and practice changes that follow on R&D findings.

Frameworks filling the accountability criteria allow analysts to hold researchers, policy makers and funding bodies accountable for their work, decisions and investment. The objective being an increase in efficiency as analysts show that the investments have been used efficiently and effectively.

If analysis is the main objective, evaluations will attempt to provide a better understanding of the factors that render R&D more effective. Results are only meant as an input in the management process providing a stronger evidence base for future decisions and stimulating dialogue between the different actors.

Finally, an allocation purpose reflects the framework's ability to determine where to best allocate R&D funds to maximize their impact. Results would allow decision makers to form more efficient strategies by providing a stronger evidence base for steering R&D.

3.1.3 Temporal dimension

A R&D activity's evaluation can be done at 3 different stages: *ex ante* (before implementation), interim (during the activity) and *ex post* (after completion). Each temporal variant fills a different need and has its own requirements.

Ex ante evaluations take place before the acceptance and start of a R&D activity as a support for new proposals. Its purpose, as described by the European Commission [European Commission, 2004], is to *"gather information and carry out analysis which helps to ensure that the delivery of policy (research) objectives will be successful, that the instruments used are cost-effective and that reliable evaluation will be subsequently possible"*.

Such evaluations should therefore be seen as an integral part of a R&D process's design. Their inclusion allows both the researcher(s) and the decision maker(s) to assess whether the demanded level of funding and resources are in accordance with the described results and impacts [European Commission, 2004]. Another advantage of *ex ant* evaluations, is their ability to prepare for reliable *ex post* evaluations and even insure that the latter provide positive results as objectives are correctly described and met.

Interim evaluations take place either once (mid-term) or several times (quarterly for example) during an ongoing R&D activity. They can be seen as a continuation of ex ante evaluations by assessing whether the initially determined objective and funds are still of relevance. They can also be seen as a starting point of ex post evaluations by measuring the first output elements.

Interim evaluations can be seen as way of introducing direct feedback into the R&D process to help improve quality and efficiency. They also serve as a great source of information to prepare for future projects or spin-offs of the current ones.

Ex post evaluations occur either after the R&D project's objectives have been met or after it is brought to a halt. Their purpose is to assess the impact, efficiency and effectiveness of the R&D process taking into account the entire activity's period.

As some impacts take several years to emerge, this type of evaluation should generally be carried out some time after the project's completion. Yazdizadeh *et al.* [2010] note that the literature suggest a time frame needed to assess the economic benefits of healthcare R&D, for example, which can range from 3 to 25 years depending on the type of study, expected impact and choice of outcome measures to include.

The use of *ex post* evaluations, as described by the European Commission [European Commission, 2004], is meant to provide decision makers with arguments for accountability (i.e what has been achieved and at what cost). As with interim evaluations, they can also be used as a starting point for follow-on projects.

3.2 R&D evaluation elements

Once the perspective, objective and temporal dimension have been defined, the analyst may choose to either use an existing methodology, adapt it, or create a new one more fitting to his needs. In any case, a clear understanding of what constitutes an evaluation methodology, that is, its elements and measurement methods, is necessary.

3.2.1 Type of measures

To conduct any R&D evaluation, outcome measures and categories should be defined early on as to collect relevant and consistent data. Depending on the framework and defined objective, analysts will need to gather information either on inputs, outputs, outcomes, impact or all measures simultaneously [Brutscher et al., 2008].

FIGURE 4.1: Research Evaluation

Enabling R&D first requires human, physical and financial resources that conglomerate into what can be qualified as "input" (See Figure 4.1). Examples of measures include researchers' salaries, cost of materials (machines, instruments), and cost of services such as subcontractors' or access to high technology facilities, the combination of which represents a certain monetary volume.

The utilization and consumption of inputs, feeding the R&D process, translate into the direct production of goods or services considered as "outputs". Measurement examples would include published articles, developed prototypes or created patents which can all be considered as direct short-term consequences of the R&D project.

An outcome is described as the initial impact of a R&D project directly related to its objective(s). In medical R&D, one example would be the improvement in patients' quality of life or even an increase in surgical care efficiency.

Impact measures, as the literature suggests, focus on the long term implications and broader economic benefits of a R&D project. For healthcare, this impact could be reflected through an increase in societal well-being, job creation and decrease in national healthcare spending for example [Banzi et al., 2011].

3.2.2 Measurement methods

A large number of methods exist in the literature to measure inputs/outputs/outcomes/impacts, each with its own degree of relevance depending on the evaluation's objective, purpose and timing. In general, we can distinguish between three broad method categories: quantitative, qualitative and a mix of both [FTEVAL, 2013].

Quantitative methods rely on quantitative data collection, such as surveys or bibliometrics, and analysis techniques be it descriptive or analytical. Descriptive analysis focuses on representing the data's distribution over time while analytical statistical techniques, known as econometrics, exploit sample data to form conclusions on relevant populations.

The exclusive use of quantitative methods relies on high statistical requirements made on the data's quality and knowledge of cause & effect relationships. They are also considered to be time consuming, and therefore costly, which could potentially restrict the analysis' scope.

Qualitative methods rely on qualitative data collection, such as interviews or experts' feedback, and evaluation techniques such as conversational or qualitative interaction analysis. These approaches can either be used along with quantitative techniques or independently, in which case the results' interpretation is not straightforward necessitating a high degree of experience from the analyst.

Mixing both methods, through surveys for example, has seen increased success as the formative presentation of quantitative information is considered to be of particular utility for innovations. These approaches allow decision makers to correctly interpret and assess results in their research context otherwise unachievable using summative data on its own.

Ruegg *et al.* [2007] provide a detailed description and discussion of 14 research evaluation methods whose main objective is improving and justifying the interest in a certain program of research project. Table 4.1 summarizes their report by highlighting the purpose, providing a description and citing the limits of each method all the while distinguishing between the three previously mentioned broad categories.

Fahrenkrog *et al.* [2002] provide further details by specifying which outputs, outcomes and impacts can be measured using each method. However, as choosing the evaluation measures is subject to high variability, information presented in their report should be considered as non exhaustive and only used as an example.

In health R&D, each framework relies on one or several tools for evaluating its elements be it inputs, outputs, outcomes or impacts. According to Brutscher *et al.* [2008], the currently preferred tools of data collection appear to be questionnaires and interviews. Intuitively, both tools are equivalent in the type of data they collect but are convenient in different situations.

On one hand, questionnaires are most useful when all interesting measures can be covered through pre-determined questions that make sense to all recipients. One very important advantage is that they enable the analyst to survey a large number of individuals in a very short time-frame.

On the other hand, interviews are essential when the topic is new and the exploration need is high or when not all interesting measures are relevant to all surveyed individuals, in which case the analyst must adopt an exploratory approach adapting his questions

Table 4.1: Measurement Methods

Category	Method	info provided	Description	Limits
Quantitative	Monitoring	planning, interim progress	Continuous assessment of key program functions through internal data collection and analysis	Data collection quality depends on evaluation measures.
	Bibliometric counts and citation	Interim progress, knowledge output measurement (advocacy)	Include counting publication and patent outputs, analysis of citations of publication and patent outputs, and data mining of textual materials to show that knowledge has been created and disseminated, and to show emergence of new ideas and development of relationships and pattern	Counts do not differentiate between quality and quantity. Bias due to self citation. Limited comparison across fields (high variability in counts).
	Bibliometric data mining	planning, interim progress, Collaboration analysis, knowledge output	Extraction of key concepts or relationships from large quantities of digitized natural language text	Need for skilled "miners" to analyze data.
	Bibliometrics Hotspot Patent Analysis	Planning, interim progress, knowledge output, spillover effect	identifies patents that are highly cited by recently issued patents to uncover technologies with a large impact on innovation.	Incomplete and inaccurate patent data. Limited experience in use.controversy over their interpretation.
	Survey	Planning, interim progress, economic and cost-benefit measuring	Set of questions the answers to which form a database about the respondents' ideas, opinions, attitudes, beliefs, preferences, concerns, plans, experiences, observations, and virtually any other issue	Potential weakness in survey design unless extensively tested. Limited reliability with low response rates. Confidentiality of individual responses unless specified otherwise.
	Benchmarking	Planning, comparison	Systematic comparison of practice, status, quality or other characteristics of programs, institutions, regions, countries, or other entities using a selected set of performance measures	High dependency on quantitative data.
	Technology Commercialization Tracking	Interim progress, economic and cost-benefit measuring, justification	Monitoring of technologies considered to be commercially successful and their associated savings, economic and social benefits	Difficulty to identify commercial applications. Lack of consideration for downstream benefits.

Cathegory	Method	info provided	Description	Limits
	Benefit cost case study	Interim progress, economic and cost-benefit measuring, justification	Quantify positive and negative effects of a project, a cluster of projects, or a program, and compare benefits against the costs using any of several measure	Costly time-consuming analysis.
	Econometrics	Planning, Interim progress, economic and cost-benefit measuring, justification	Uses a variety of statistical and mathematical tools and theoretical models to analyze and measure the strength of functional relationships that underpin a program and to analyze and measure a program 's effects on firms, industries, innovation, and the economy	Need for specialists to perform the analysis. Costly time-consuming analysis due to reliance on large quantities of data.
	Network analysis	Planning, interim progress, Collaboration analysis, knowledge output	Visual mapping, measuring relationships and linkages among researchers, groups of researchers, laboratories, or other organizations	Lack of quantitative measure of collaborations' value. Costly time-consuming analysis
Qualitative	Peer review/Expert judgment	Planning, interim progress, justification (steer, accountability and advocacy)	Qualitative review based on feedback on a specific subject being evaluated from experts in the field	Variable quality due to dependence on experts knowledge and conflict of interest. Difficulty in defining evaluation criteria for innovative work. Inappropriate to evaluate impacts of a program due to unavailability of needed data.
Mix	Case Study	planning, economic and cost-benefit measuring	Information in a narrative form supported by data to describe, explain, and explore R&D programs	Considered less persuasive due to reliance on anecdotal evidence.
	Spillover using a combination of methods	knowledge output, spillover, justification	Measurement of positive and negative effects that result when an undertaken activity affects external parties.	Complex and challenging due to interactions between outputs and project. Difficulty of attributing outcomes to a certain knowledge. Lack of experience in spillover measurement.
	Historical tracing	Knowledge outputs, justification	traces chronologically a series of interrelated events either going forward from the research of interest to downstream outcomes or working backward from an outcome along a path that is expected to lead to precursor research	Events highly time dependent. Costly time-consuming analysis.

Source: Ruegg *et al.* [2007]

to the answers. One major advantage is the minimization of information loss, provided one of the interviewers is experienced in the method's application.

To measure scientific output, most frameworks rely on bibiometrics be it for publications, patents or research funding. Broad socio-economic impacts of policy intervention are estimated through macroeconomic modeling while microeconomic models measure outputs, outcomes and impacts at an individual level.

Cost benefit analysis is preferred for establishing whether a project or program is economically efficient. Network analysis can be used to assess cooperation relationships and their consequences on an individual's decisions. Only one of the presented frameworks in Brutscher *et al.* [2008] appears to take interest in cost-benefit while none perform a network analysis.

3.3 Health research evaluation example: Payback Framework

The Payback method has been described as the most used [Yazdizadeh et al., 2010] and most cited [Banzi et al., 2011] health research evaluation framework with several versions/adaptations/extensions being created in the UK, Canada and Sweden. In this subsection, we provide the reader with a detailed description of this method as an illustrative example.

The framework was first developed by Martin Buxton and Stephen Hanney, at the Health Economics Research Group (HERG) at Brunel University (UK) in 1994, to examine the impact of health research. Over the years, it has seen a number of improvements by the National Health Service (NHS) in 1998 and in collaboration with RAND Europe in 2004/2005 [Donovan and Hanney, 2011]. In its basic form, the framework is made up of two main elements with some variations taking into account different perspectives such as research funders.

Most data collected for this method are based on documents, literature, interviews, and bibliometric databases. The preferred implementation canal has been argued to be case studies [Brutscher et al., 2008] with a main objective of measuring return on investment in health research [Guthrie et al., 2013].

3.3.1 Logic model

The first element of the payback framework is a "logic model" representation of the research activity to highlight the relationship between resources, activities, outputs and outcomes of a program. Modeling this relationships and the resulting interactions significantly facilitates the analysis of a research idea's evolution from concept to product development and adoption, as well as the assessment of its economic benefits and impact on society.

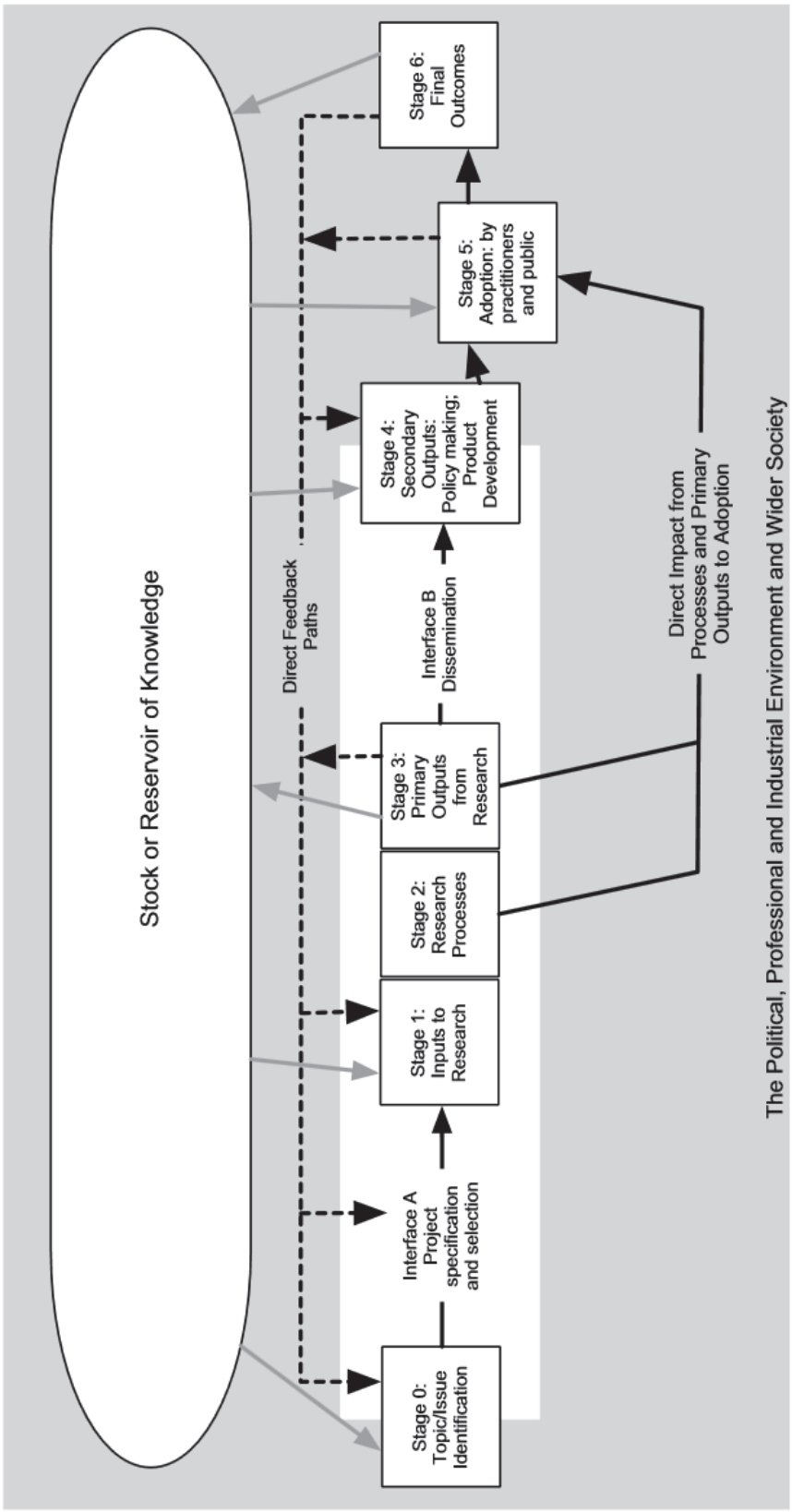


FIGURE 4.2: Payback Logic Model

Source: [Hanney et al., 2004]

A schematic representation of a research process such as Figure 4.2, as proposed by Hanney *et al.* [2004], allows us to distinguish between at least seven stages and two interfaces. Note that the model contains several feedback loops demonstrating the non-linearity of the process.

The first stage (Stage 0) covers the identification of the topic or issue that will determine the research's subject. Most topics will either be based on examination of the existing reservoir of knowledge, to identify gaps and opportunities, or the assessment of needs with a certain activity/community. Typically, the research project's documentation and proposal follows up in Interface A.

Stages 1 to 3 form the core of research during which financial inputs, the research team's experience and knowledge base generate different categories of output. Stage 2 mainly serves as a filter to analyze whether the proposed methods are appropriate and to discuss encountered difficulties, possibly opening up new research opportunities.

Findings that emerge from previous steps then go through dissemination (Interface B), extending their utility from their source to other activities in the form of secondary outputs. Examples of the latter include informing local guidelines and care pathways or possibly contributing to improving products as well as their development process (Step 4).

To observe the final outcomes (Step 6), secondary outputs first need to be adopted implying a change in behavior whether of clinicians or the public (Step 5). The ultimate goal of medical research being to drive improvements in health, mainly, and on a more macro-economic level.

3.3.2 Payback categories

The second element of the payback framework is a multi-dimensional list of benefits [Hanney et al., 2004] that extends the "traditional academic" impacts of knowledge production and capacity building by including the wider benefits to society. In total, the payback framework distinguishes between five categories of benefits:

- Knowledge production;
- Research targeting, capacity building and absorption;

- Informing policy and product development;
- Health benefits;
- Broader economic benefits.

The knowledge produced by research is signaled by a number of measures among which the quantity, quality and impact of peer-reviewed papers in international journals [Hanney et al., 2004]. Other potential measures, as mentioned by Donavan *et al.* [2011], include the number of conference presentations, books, book chapters and research reports.

Through research, institutes and research teams are able to identify key points and difficulties that might favor one subject (idea) over another; possibly attracting more funds as they try to solve existing problems or go farther in their objective. At the same time, research funds can be used to increase a team's capacity by either hiring new skills or funding training programs and career developments.

The completion of research projects can manifest itself either through the development of an innovative product or recommendations for a new policy[3]. In both cases, the health and socio-economic benefits can only be observed after adoption.

As is natural in health economics, the benefits for patients in terms of improved health or QoL as well as the economic impact in terms of cost savings play a major role in evaluating medical innovations. The payback framework extends this consideration to include the impact of medical research in the same way as it is done for their products.

Commercially exploiting the research's products can have significant macro-economic benefits be it in the form of job creation, increase in profits, export and even reduction/substitution of imports. As often mentioned in health economics, another macro-economic benefit reside in the value of a healthy workforce reflected through an increase in production levels and reductions in days off work.

[3]Note that Hanney *et al.* [2004] interpret policy as "not just the national policies of the government, but also includes: policies made by managers at many levels within a health service; policies agreed at national or local level by groups of health-care practitioners in the form of clinical or local guidelines; policies developed by those responsible for training education/ inspection in various forms including training packages, curricula and audit and evaluative criteria; and policies about media campaigns run by health-care providers"

4 EvaRIO Method

Through our literature review, we have pointed out the existence of various methodologies for the evaluation of R&D activities and analyzed their respective characteristics. The studied evaluation frameworks appear to be mostly designed for the assessment of research and development activities in the healthcare sector. As such, they do not go into much detail in their exploration of the R&D process. More precisely they do not provide an in-depth analysis of micro-mechanisms such as how the use of newly created knowledge generates economic value. As a consequence they neglect the possible occurrence of important side effects of R&D projects, which we will call indirect effects in the rest of this chapter.

Moreover, the presented frameworks rely on performance measures (such as the number of publications) that cannot be translated into a monetary value, thus limiting the possibility of their inclusion as an impact in a cost-benefit analysis. EvaRIO, however, bypasses this difficulty by considering such outputs as inputs from which economic impacts can emerge.

Furthermore, our literature analysis is not sufficient if we are to apply any of the cited methods for two main reasons: lack of detailed documentation over the methods' implementation processes and severe lack of experience in the application of any previously cited method.

Strasbourg University's BETA enjoys over 25 years of experience in the evaluation of projects' impact using the BETA method [Bach et al., 2008]. Building on its success, a recent European funded project allowed the creation of the Evaluation of Research Infrastructures in Open innovation and Research Systems (EvaRIO) methodology developed by the same laboratory.

The EvaRIO method is designed to provide policy makers with guidelines for the optimization of resources dedicated to Research Infrastructures (RIs). The main objective being the development of an evaluation framework as well as valuation methods and tools well suited to RIs in a context of open innovation and research environment. The second objective consists in motivating discussions between the actors involved in the R&D process as problems and expectations are identified.

We opted for the application of EvaRIO, using the IHU as a case study, considering the availability of documentation for the correct implementation of this method as well as the existence of experienced users. In this section, we attempt to describe the method with sufficient detail as to facilitate the application's understanding.

4.1 RI definition

The term "research infrastructures", as defined by the European Commission, refers to facilities, resources or services of a unique nature that are used by the scientific and technological communities for conducting either basic or applied research. Examples of what this definition covers include:

- Major equipment or group(s) of related instruments used for research purposes;
- Knowledge based resources such as collections, archives, structured information or systems related to data management, used in scientific research;
- Information and communication technology-based infrastructures such as grid computing, networks and communications.

The emergence of RIs has been historically motivated by the cost-saving possibilities of avoiding resource duplication as well as stimulating resource sharing, standardization and access coordination. The observable impact have been scientifically expressed in terms of scale economies, scope economies and reduced transaction costs considered at the level of building, upgrading as well as managing resources.

RIs are also a way to assemble, even generate, an increasing variety of either highly specialized or complementary resources, the use of which generates knowledge and expertise. In that sense, RIs can be seen as a trigger, hub and reservoir of knowledge creation, sharing, diffusion and accumulation which can be considered a resource in themselves [Avadikyan et al., 2013].

The EvaRIO method seeks to evaluate these interconnected and often mutually reinforcing impacts by mainly interviewing the different actors benefiting from the RI in some way or another. Depending on the type of actor, however, the evaluation must

be adapted as the impact for the operator, for example, is essentially different than for suppliers or users.

An operator can be defined as a combination of researchers and supporting staff who provide the necessary means, whether physical or intangible, for hosting research projects. An operator of RI is often given some money in order to build, maintain, enhance the resources and to simply operate.

A supplier is given a number of contracts in order to supply goods or services to the RI. Contributions include building, maintaining and even enhancing the set of resources acquired by the infrastructure.

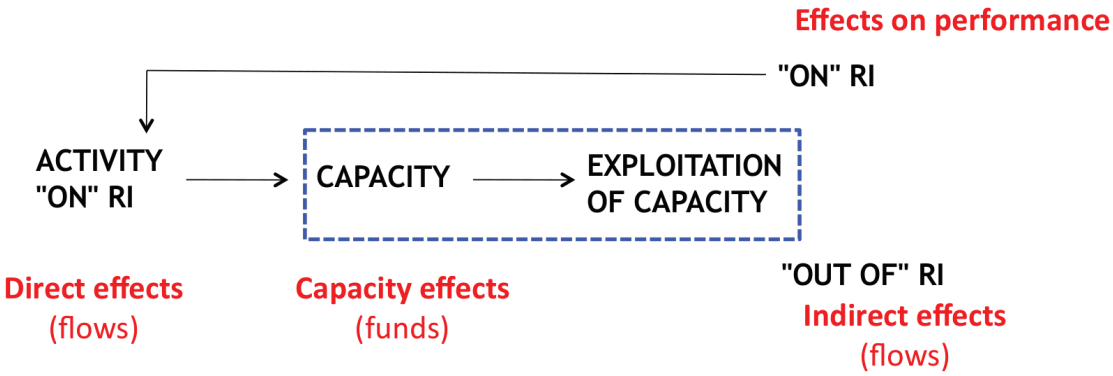
Users are mostly researchers who are "attached" to the RI by using its services for achieving some research activity which is part of a larger set of R&D activities, typically a R&D project or program. This definition also include researchers who only temporarily visit the RI site in order to use it as well as those who only possess remote access.

4.2 Evaluation approach

As a mean to justify the interest in R&D, EvaRIO is traditionally performed by an external examiner seeking to fill an advocacy objective. To fully exploit the method's potential, *ex post* application should be performed as to allow the emergence of measurable impacts. Nevertheless, it is possible to perform an interim application to identify "impact departure points", or future impacts, to be re-measured or to stimulate talks between the interviewed actors and the management.

The idea behind the EvaRIO evaluation approach can be schematically summarized in three phases as shown in Figure 4.3. Each phase corresponds to the measurement of one type of effect: Direct, Capacity, Performance and Indirect.

FIGURE 4.3: EvaRIO Measures



Direct effects are mainly expressed in monetary terms as they represent the value of building, upgrading, operating or using the RI each representing a certain economic activity. For some actors, benefiting from the RI resources (in terms of equipment, data, services, etc.) to conduct scientific experiments also has a value of its own, especially when compared to existing alternatives.

By carrying out activities in the RI, participants proceed to consume its resources, previously measured as direct effects, to acquire and generate a wide range of "capacity". The increase in scientific knowledge and competence (Science&Technology), creation/reinforcement of ties with other actors (Network), gain in reputation (Reputation), organizational changes (Organization&Management) and recruitment of new staff (Human Capital) are all dimensions considered to be part of measurable capacity effects.

The **"Science and Technological" (S&T) effect** relates to the discovery of new knowledge, developed during activities, or its transfer from the RI to the actor. Interesting evaluation measures range from scientific expertise to worker's know-how, including technology laid down as a blueprint, new theories or 'tricks of the trade'.

An RI, by its construction, is considered as an open complex system in interaction with its environment and the components of which interact with one another. We can therefore expect that each actor taking part in the RI activity would expand his personnel network, noted as **"Network" effect**, to include other actors with whom he cooperated.

The **"Reputation" effect** results from the reputation acquired by actors working on the RI-based activities and is highly dependent on the reputation of the RI itself. The **"Organization & Method" (O&M) effect** focuses on the tools and methods that

are put at the actor's disposal to facilitate his research or that he develops during his activities with the RI.

Some projects require specific skills that neither the RI operator, supplier nor the user possess or have convenient access to. In such situations, the operator may choose to increase the human capital at his disposal to further diversify the RI's skill set in consistency with the user's needs.

Part of the capacity effect generated when carrying out an activity in an RI is specific to the environment in which the project was brought to fruition and cannot be exploited in other situations. Another part, however, is embedded in the people and organizations that were involved in the project and can be used to generate additional economic value.

A first impact qualified as **"effect on performance"**, of the previously mentioned increase in capacity, can be potentially observed as a change in the conduct of suppliers/operators/users with the RI and its activities. This change often translates an increase in the level of scientific, technical, managerial or economic performance of the actors on those activities. In other words, actors are more effective at filling their role, be it supplying, operating or using the RI.

A second impact, qualified as **"indirect effect"**, corresponds to the economic flows generated by the exploitation of increased capacity outside of the RI. This is the most interesting particularity of the EvaRIO methodology and a strong added value compared to existing R&D evaluation methodologies.

The transfer of S&T capacity, for example, could potentially lead to the design of new or improved products, processes or services, allowing actors to carry out further activities in the same field, or contribute to research activities in other related domains.

The O&M indirect effect occurs when experience gained through the RI-based activities allows an actor to modify his internal organization and/or apply new methods in project management, quality management, industrial accounting, etc.. We can then expect some gain in performance for the actor potentially translatable into economic savings.

Enlarging one's network has several advantages, when exploited correctly, including the emergence of new business opportunities and scientific collaborations. Similarly, the increase in reputation through the RI activity could serve as a future marketing tool.

4.3 Evaluation Metrics

For every type of effect, the EvaRIO method has established a list of metrics for their quantitative and qualitative measurement. To complement the method's overview in the previous subsection, we present the reader with a summary of proposed measures.

As explained previously, the direct effect is a measure of the economic activity undergone with or within the institute. For operators, this is represented by the organization's budget including all costs incurred for its operation. For suppliers, this is represented by the value of awarded contracts for the supply of goods and services necessary to build up, maintain, or develop the institutes' resources.

TABLE 4.2: Direct effect metrics

Standard	**R&D projects linked to RI use:** amount of budget of the projects and or research contracts related to RI use, or equivalent in jobs **Training:** budget for training on RI, equivalent in number of trainees and training time **Collaborative agreements with RI:** amount of budget of collaborative agreements, equivalent in jobs NB: including follow-up projects on RI
Comparative Advantage	**Direct advantage from using the RI compared to alternative means (opportunity cost):** No alternative means for doing research, Time/cost sparing, better results, other qualitative advantage,etc.

Source: Evario Final report

In the users' case, see Table 4.2, the direct effect can be divided into two types. The first refers to the volume of research activities carried out in the RI, mostly in the form of projects, measured through their associated expenditures. The second corresponds to the direct advantage of conducting research in the evaluated institute, compared to other institutes, in the form of gained resources (cost savings, time saved).

Measuring capacity effects is usually the most challenging part as it can hardly be done directly, therefore requiring the combination of both qualitative (through interviews) and

quantitative (external data, objective observations) evidence. The EvaRIO method attempts to measure the increase in capacity, or pool of learning related assets (knowledge, connections, competences etc.), and ability to exploit it following the work undertaken within a RI.

TABLE 4.3: Capacity effect metrics

S&T	**Increase in knowledge signaled by**: publications as (co-)author, patents, thesis; new or improved prototype, product, demonstrators, pilot, process, equipment, databases, etc.
Network	**Collaborations:** Number of projects, of different partners and new partners; idem for pre-competitive, academic or industrial projects; Signals of collaborations such as co-publications and co-invention of patents; **Other network enrichment (qualitative description)**: new contacts, higher visibility in the network, relational ability:, know-who-is-doing-what, know-how to work with others, strengthening quality of links.
Reputation	Prizes, awards; invitations to conference as keynote, round table, position in ranking; Citations in specialized or general press; Other reputation enhancement: qualitative description of events or factors signaling reputation increase, for instance TV or press broadcasts including those for general audience.
O&M	Existence of dedicated service/ dedicated FTE-full time equivalent (how much) for: managing RI activities; quality, technology transfers; Formal tools in: project management; accounting / cost procedures; Quality management, evaluation and strategic planning, etc. linked to RI; Significant organizational changes.
Human Capital	Number and origin (univ, industry...cf inward-mobility) of staff (scientific/engineers/technicians) recruited or maintained for operating/using/designing and building the RI ; qualification and turnover

Source: Evario Final report

Table 4.3, provides some examples of measures that would potentially reflect an increase in capacity. Each indicator can be considered as reflecting a link between the user/supplier/operator and the institute.

The EvaRIO report indicates that the performance effect appears to be mostly relevant for operators as the effect on users and suppliers is implicitly measured through direct effects. By performing their RI-based activity, both actors become more efficient whether in supplying goods and products or increase direct gains from projects with the RI, for example.

Indirect effects, as explained in subsection 4.2, measure the economic impact of the previously measured increase in capacity effects. In that sense, it follows the same decomposition presented in Table 4.3.

TABLE 4.4: Indirect effect metrics

S&T	**Valuation of gains in S&T capacity** in a new research projects or in new products/services/process, measured in revenue (sales, royalties, new contracts, scientific prizes, etc.) or cost/time savings.
Network	Idem.
Reputation	Idem.
O&M	Idem.

Source: Evario Final report

Table 4.4, provides some examples of measures that would potentially reflect indirect effects expressed in monetary terms. For example, the increase in S&T capacity could lead to the design of new or improved products, processes or services, which allow the actors to increase sales, protect market shares, reduce costs or win new research contracts. Similarly, the increase in network and reputation may lead to new sales or research contracts while better organization and management could lead to cost reductions.

It is not uncommon that an increase in capacity effect, due to undertaking an activity with the RI, only partially influences its associated indirect effect. In such situations, a "fatherhood coefficient" is used to correctly associate a percentage, equivalent to the influence, of the indirect effect's monetary value to the activity with the RI.

The estimation of indirect effects is usually done *ex post* to their emergence. However, depending on the context, the EvaRIO method suggests following a two years forecasting period. In both situations, it is recommended that all estimations of figures provided by interviewed actors should be minimized as to avoid over-estimations.

5 Application: IHU case study

Strasbourg's institute of image guided surgery (IHU) can be viewed as a small research infrastructure, especially with the existence of its animal experimentation platform, used by researchers to develop innovative surgical technologies. In that sense, the use of EvaRIO should be well suited for the evaluation of its R&D activity and to feed the discussions between researchers and the management.

In the previous chapters, we only focused on providing IHU related details that are pertinent to the study being conducted (cost and benefit). In this section, we extend our description of the institute to include its partners' role in the R&D activity. We also go over the application guidelines as presented in the EvaRIO methodology to provide the reader with some elements of reproducibility.

5.1 IHU partners and relationship

The first step in applying EvaRIO consists in identifying the different actors (users, suppliers and operation) involved in the institute's R&D activity. However, a more detailed exploration of the interaction that exists between the IHU, researchers and the industry pointed out the absence of this differentiation. To be more precise, to the institute, all actors are identified as research and development **partners** and will therefore be viewed as such throughout our analysis.

We base our review of IHU partners on the institute's submission form to 2010's "investissement d'avenir" call for proposals which describe the institute's most important collaborations. Although we describe a total of 6 industrial and scientific partners, the list should be regarded as non-exhaustive and will certainly require updating depending on how and if the collaborations with various partners evolve.

5.1.1 IRCAD

Founded in 1994 by Professor Jacques Marescaux, the "Institut de Recherche contre les Cancers de l'Appareil Digestif" (IRCAD) is a non-profit training and research center dedicated to the minimally invasive surgical treatment of abdominal diseases. As a

financially independent institute, IRCAD's activity attracts more than 4300 surgeons per year from 106 countries.

Today, the institute's training activity covers minimally invasive surgery techniques in a total of 13 disciplines with lectures being given by over 800 international experts. Websurg, a web-based surgical university provides free access to videos, medical procedures' descriptions and experts' comments for more than 300 000 members.

In terms of research and development, the multidisciplinary team of surgeons, engineers and scientists holds 36 medical device and 10 software patents. Established relationships with private partners facilitate the transfer of technologies to the market with the most notable examples including operating ports, retraction tools, and advanced platforms for endoscopic surgery.

As a founder and big brother of the IHU Strasbourg, IRCAD is bound to share its expertise and reputation to accelerate the development and success of the institute be it either in education or research. The most notable impacts are expected in the IHU's medical devices' development, surgical simulation and image processing.

Current projects in augmented reality include "AR-FLEX", a model for the development of 4 dimensional (3D+Time) vision of the position, form and orientation of flexible catheters or endoscopic instruments. This is achieved through the 3D reconstruction of patient specific anatomy, including organs and blood vessels, based on CT/IRM preoperative images.

In endoscopic surgery, the "FLER" project attempts to create a software for the calculation of digestive anastomoses' vascularization as to reduce complications' risk. The "EMBARGO" project tests the effectiveness of a stomach blood flow deviation in the reduction of hunger inducing hormone. At the same time, this deviation is expected to increase vascularization in the concerned area during bariatric surgery.

5.1.2 SIEMENS

Siemens is a German multinational conglomerate company subdivided into nine divisions covering Industry, Energy, Healthcare, and Infrastructure related activities. The Siemens healthcare division alone employs over 49 000 individuals worldwide and is

present in more than 130 countries. In France, Siemens has a large presence with over 8 000 employees.

Siemens healthcare is one of the world's largest suppliers to the healthcare industry and a leader in medical imaging, laboratory diagnostics, medical information technology and hearing aids. Their activity is centered around patient care with products and solutions enhancing prevention, early detection, diagnosis, treatment and even after-care.

As a confirmed leader in interventional radiology, Siemens healthcare defined hybrid surgery as one of its ten major strategic objectives. Their partnership with the IHU Strasbourg falls in naturally as their contributions to medical imaging, augmented reality, new devices' development and robotics are invaluable for the development of hybrid surgery.

5.1.3 STORZ

Karl STORZ Endoskope is a family owned German company that employs more than 3 800 specialists worldwide and with a history that stretches back over 60 years. The company's contribution to patient care culminates with the fusion of their products in what they call integrated operating rooms "OR1TM" and the introduction of flexible endoscopy into various specialties.

As an internationally renowned expert in the field of endoscopic devices for minimally invasive surgery, STORZ plays a major role in developing hybrid medical devices with the IHU. A collaboration that is all the more interesting as the company also possess considerable expertise in haptic force-feedback concepts as well as devices/surgical simulators that prove valuable for the development of surgical simulators and surgical robotics. Finally, another interest lies in the development of several integrated navigation devices that are prone to further improvements with the IHU's attention to tracking and augmented reality.

5.1.4 INRIA

The National Institute for Research in Computer Science and Control (INRIA) is a French public, scientific and technical research establishment focused on computer science. Since its creation in 1967, it expanded to include 1300 researchers, 1000 Ph.D.

students and 500 postdoctoral researchers. As a founding member of the IHU Strasbourg, INRIA created a Strasbourg antenna of its teams focusing on medical image analysis and medical simulation.

The medical image analysis team includes 6 Researchers, 1 postdoctoral researcher and 1 PhD student who also focus on simulating physiological systems and the application of their tools to assist prevention, diagnosis and therapy. The team's "Bilikimo" project consists in developing real time biomecanical patient specific models of soft organ deformations such as the liver or kidneys.

The medical simulation team employs 4 researchers, 2 engineers, and 2 PhD students who work on real time simulation computing and the integration of user movements through the use of dedicated hardware devices, haptic feedback and robust algorithms. The research goal is to improve the realism of interactive medical procedure simulations through the development of accurate models coupled with fast and robust computational strategies.

Their "Haystack" project consists in developing a software for planning percutaneous needle insertion procedures by modeling the interaction between flexible needles and soft tissues (liver principally). The combination of simulation and planification provides the user with predictions of needle movements as well as suggestions of optimal ways for reaching a tumor.

5.1.5 Surgical Perspective

Surgical Perspective is a young start-up company founded in Strasbourg in 2009, from Protomed SA Marseille, that conceives, develops and sells retractors for minimally invasive surgery. Their surgical retractors are essentially designed with surgeons in mind, providing them the means to clear the operating field and use direct approaches for treating organs.

As an IHU partner, Surgical Perspective develops new devices for Natural Orifice Translumenal Endoscopic Surgery (NOTES) and Single Incision Laparoscopic Surgery (SILS) minimally invasive procedures and investigate the automation of such devices. They also bring their expertise into the development of medical devices improving the IHU's understanding of the transformation process from design to markets.

5.1.6 ICUBE - AVR Team

Created in 2013, ICUBE is the conglomeration of four laboratories[4] with over 500 members working in the fields of engineering science, computer science and medical science with imaging as their unifying theme. Four departments currently regroup a total of 14 teams, four of which directly collaborate with the IHU.

The Automatic, Vision and Robotics (AVR) research team specializes in the field of automation of surgical gestures and design of new robotic systems. Most of the team will participate in IHU projects including 4 professors, 7 associate professors, 7 engineers and 10 PhD students all of whom will have their offices relocated at the new IHU building.

Current collaborations between the IHU and AVR team include MRE-Cas, ProteCT and iMRI-Surg projects. MRE-CAS consists in developing a quantitative ERM protocol for precise measurements of the liver's viscoelasticity and information on spatial variation (ie. heterogeneity, anisotopy). ProteCT develops a robotic system for performing X-ray image guided percutaneus procedures (ie. needle placement, insertion) and protecting the user in non-vascular interventional radiology (ie. hepatic biopsy, liver tumor ablation). The third project, iMRI-Surg, focus on a software/hardware solution for performing guided percutaneus procedures using the IRM which allow the user to track, reposition and monitor used needles and instruments.

The Model, Image and Vision (MIV) research team addresses the problems of image registration, image segmentation, atlas based modeling and change detection in sets of images, whether for longitudinal follow-up or comparison with or between populations. The part of the team who participates in IHU projects includes 3 professors, 2 associate professors and 2 PhD students.

The Informatics, Geometry and Graphics (IGG) research team activity focus on developing a virtual reality software platform with a direct application in medical simulation. The part of their team who participates in the IHU project includes 2 professors, 5 associate professors, and 1 engineer.

Finally, the Networks and Protocols (RP) research group investigates, designs and evaluates computer network architecture and protocols mainly contributing their expertise

[4]From "Centre National de la Recherche Scientifique" (CNRS), "Universitée de Strasbourg" (UdS), "Ecole nationale du génie de l'eau et de l'environnement de Strasbourg" (ENGEES) and "Institut national des sciences appliquées Strasbourg" (INSA Strasbourg)

to telemedicine related projects. The part of their team participating in IHU projects includes 2 professors, 3 associate professors, 1 postdoctoral researcher, and 1 PhD student.

5.2 Evario's evaluation guidelines

Following EvaRIO's recommendations, we first proceeded to identify the different users and suppliers involved in the IHU's activity through interviews of the institutes' employees. We namely interviewed the director of operation, platform manager, project managers and the clinical trial manager followed by several informal discussions with other employees to supplement the investigation. All framing interviews were done in the last semester of 2014.

FIGURE 4.4: Framing Interview guideline

Interview guidelines: Framing interview (IHU officials)

1. Presentation of EvaRIO evaluation approach

2. Topics of interview

History of the IHU: initial context, main dates and steps (creation, first operation, significant change,...), strategic background,...

Mission and current operation: mission, type of resources, instruments and service provided,...

Access rules: access rules and criteria for IHU access: open, very selective, market mechanisms, importance of remote access, specific rules for specific users...

Characterising the partner: existence of different profiles/communities, place and number of partners, experience learned back from partners, existence of sources of information on partners, impacts of visitors upon the region

Relationships with partners: co-development of instruments with industry, TTO (technology transfer office), patents and licences (MTA), spin-offs, ...

3. Discussion about the possibility to explore the case of IHU further: relevance in the context of EvaRIO, selection of additional contacts for further interviews, at IHU, among IHU partners.

Source: Evario Final report

Each framing interview follows a typical format, presented in Figure 4.4, established by the EvaRIO project. We started off by asking the employee to present his activity, or role, at the IHU as to better understand the origin, current operation of the RI and which actors he is potentially in contact with.

For each identified partner, we started by gathering information on his role, interest in the IHU, projects being conducted and general activity. The idea being that in order to interview these actors in the most efficient way, we need to know as much as possible about them which allows us to focus on the direct, capacity and indirect effects' measurement.

We identified a total of 20 individuals that we could interview, most of whom are affiliated to industrial partners or researchers/research laboratories. This exercise is crucial for helping elaborate the specific indicators, identify the most relevant "external" sources of information for indicators and ultimately interpret the results or identify the limits of the evaluations exercise.

FIGURE 4.5: Partners' Interview guideline

Interview guideline: Effects on partners
Analysis of benefits and knowledge creation for a given partner due to the collaboration with the IHU

Interview topics

1. Presentation of the partner, history of relations with the IHU and rapid introduction of the project(s) carried at/with the IHU, scientific & tech issues, social and economic issues.

2. Existence of alternative resources (other instrument) to perform the experiment and comparative advantage of IHU (time saving, IHU as a necessary condition,...)

3. Reminder of the different ways of access to IHU with comparative advantages

4. **Experience gains/new skills/contacts** generated during the collaboration with the IHU, in different areas: Science and Technology (including publications, patents,...), Networks (new partners, quality of links,...), Organization and Management (project management, certification,...), Reputation (price, rankings,...), Human Capital (PhD students, post-doc,...).

5. **Valuation** of gains in experience/new skills/contacts acquired in a first collaboration with IHU, when they are reused **in the IHU** or another institute of the same type: gain in time / cost when making experiments, or raising (project) funding for a new project

6. **Valuation** of gains in experience/knowledge/contacts **outside IHU** (or outside insitutes of the same type), in particular the development of new research projects, or products/services/process by the user, measured in revenue (sales, royalties, new contracts, scientific prize, ...) and cost savings/time/quality.

Partners' interview were carried out during 2015 by one experienced member (in the application of the EvaRIO method) and one novice, using the guideline presented in Figure 4.5. For both types of actors, the approach for the interview is basically identical with only very few exceptions.

The first phase of the interview is dedicated to the interviewee's presentation, introduction to the EvaRIO method and explanation of the interview's progress plan. A large focus is given to the identification of the interviewee's projects that are financed by and/or conducted in collaboration with the IHU, their associated budget and the possibility of conducting them elsewhere (comparative advantage).

Capacity effects can be highly variable from one individual to another making their measurement through specific surveys or a series of questions practically impossible. During the first phase, the interviewers need to adopt an exploratory approach by paying attention to signals of potential capacity effects; in which case they interrupt the interviewee to increase his awareness over their existence.

The second phase attempts to complete the capacity effects' measurement by going through each dimension (Science&Technology, Network, Reputation, Organization& Management and Human Capital) individually. Naturally, the analysis is not limited to positive impacts but also include negative ones expressed by the actors.

The third phase consists in evaluating the impact of increased capacity, be it in terms of performance or indirect, by asking the interviewee to explore the possible effect of each dimension. The only obstacle being the need for a significant time lapse before the emergence of most indirect effects.

Each interview is digitally recorded, leading to a confidential report and a series of internal debriefing meetings to present, share and discuss the empirical material obtained. Data is extracted with the most possible detail and organized in tables, see Tables 4.2-4.3-4.4, for each interviewed individual. Contact with interviewees is maintained in case further clarifications or information are needed (especially quantitative on specific points not fully covered during the interviews).

6 Results

A total of 15 interviews were recorded with an average duration of 81 minutes (range: 30 to 128). For each interview, we extracted relevant information to fill out the table in Appendix G. A synthesis of the results is provided in the following subsection with respect to the direct, capacity and indirect effects differentiation and the three previously stated types of partners: Industrials, research laboratories and IHU/IRCAD fellows/researchers.

During the EvaRIO application, we also identified some weaknesses in the methodology, or more precisely its inability to measure some interesting elements. In the particular IHU case, conducting these interviews allowed us to establish a theoretical base for a reworked version of EvaRIO that we consider to be more pertinent with respect to the IHU's R&D activity.

6.1 Evario results

Based on IHU data and as provided by the institute's accounting manager, the administration estimated a total R&D and clinical projects budget of 7 342 159 Euro since the institute's creation in 2012, all partners included. This value represents the financial investment that was committed to all projects including researchers' salaries, equipment value and administrative fees but does not represent the actual amount spent.

According to the IHU, the institute has also engaged an estimated 3 565 000 Euro in the form of support, whether material or human capital, shared between all projects. Industrial partners, as they report, donated at least 1 277 000 Euro through various forms for the purpose of conducting research. In total, the IHU's Research and Development activity generates a global direct effect of 12 184 159 Euro, all partners included.

The gain in capacity effect, all partners included, has been particularly significant for Science&Technology, Network and Human Capital. All partners have expressed a mostly positive to very strong positive feedback while the gain in the other capacity effects (Reputation, Organization&Management) was more variable.

6.1.1 Industry partners

During our interviews, we identified a total of at least 28 projects that the IHU conducts with industrial partners, a majority of which are being led by SIEMENS healthcare. The direct effect reflected through the amount invested in these projects could not be precisely determined as most industrial partners consider such data to be confidential or unavailable.

Furthermore, all IHU projects are based on the principles of encouraging collaborations between the industry and the academic world which naturally limits our ability to separate between industry specific and academic projects. Nevertheless, each industrial has taken part in filling some of the financial or material requirements with a total of at least 1 177 000 Euro in donations (already included in the previously calculated 12 184 159 Euro) which represents a direct effect of the industry specific projects .

Conducting these projects at, and along with, the IHU have reportedly participated in increasing each industrial partner's capacity in one way or another. All industrial partners have reported a generally positive feedback reflecting their satisfaction with the collaboration highlighted through their gain in capacity.

Science and Technology capacity: positive effect

Most industrial partners have started by indicating that, by working with the IHU, their competence domain was extended to new specialties in which they did not work before. Each partner became more comfortable working with surgeon, endoscopists or radiologists which could be expected to provide them the means necessary to extend their focus beyond their initial activity.

Even though the activity extension is not expressed through expected products and sales at this early stage, a good consideration would be in terms of publications, prototypes and patents that increase a company's competences. During the interviews, it was reported that there are currently at least 2 patents and three published (+ 1 expected) articles that signal collaborations between the IHU and the industry.

The IHU's experimental platform contains some of the most state-of-the-art imaging machinery allowing users to conduct experiments on big animals, specifically pigs, or

large phantom models. Industrial partners unanimously consider this platform to be a major asset for their collaboration.

Network capacity: strong positive effect

The IHU's role as a pioneer in hybrid surgery has particularly been considered as a mean to combine industrial partners' distinct activities. In that sense, several partners have increased their collaboration for the creation of intelligent operating rooms combining their complementary expertise.

The institute is also considered to be an opportunity for the industry to widen and diversify their network by meeting new specialists, surgeons for some and radiologists for others with whom they did not work before. In that sense, most industrial partners reported greatly benefiting from practitioners' feedback to improve projects and enhance machines on site.

One partner has reported communicating with the ISIP fellows on a regular basis since they present an important advantage over other surgeons by providing more easily accessible feedback. To remind the reader, the ISIP are four experienced surgeons who spend 1 or 2 years at the IHU conducting research projects preferably focused on hybrid surgery.

Reputation capacity: no effect

In terms of reputation, small industrial partners could benefit from the IRCAD's reputation through a spillover effect on the IHU. At this early stage of the IHU's existence, it is not uncommon to confound both institutes to some degree.

Large industrial partners, on the other hand, do not report any increase in reputation. At this stage, it is actually the other way around with the IHU benefiting from, particularly, SIEMENS and Storz's renown.

Organization and Management capacity: strong positive effect

In terms of organization and management, the IHU's platform presents interesting advantages with the industry's ability to test their prototypes at the early stages of development. By assessing the prototypes' potential success or failure early on, the industrial can expect to decrease costs incurred by failed projects.

Another effect concerns industrial partners with a heavy hierarchy and protocol driven approval for conducting innovative projects. It was reported that some partners are able to facilitate acceptance and quicken kickoffs by submitting projects as other partners'. By submitting an IHU project through a more flexible partners, it is possible to bypass complex hierarchies and accelerate innovation emergence.

Human Capital capacity : very strong positive effect

In terms of human capital, the IHU's creation has motivated the creation of at least 5 full time jobs at different industrial partners. Most job creations are for representatives of each partner at the IHU paid by their respective companies.

To provide machine maintenance and develop the collaborations with practitioners, each partner occasionally sends engineers to the IHU. In total, we count at least 100 days per year spent by engineers and account managers at the IHU.

Performance effects

As explained in subsection 4.2, performance effects reflect the impact of gains in capacity on the conduct of an industrial partner with the IHU and its activities. To be more precise, the increase in capacity could allow partners to become more effective at undertaking R&D projects with the institutes.

Indeed, the creation of hybrid surgical technologies requires the combination of skills and competences that were previously considered to be distinct. The traditional organization of complex companies reflects this differentiation with a large number of departments being created, each with its own focus and research subjects.

Working on IHU projects has reportedly stimulated communication between departments and the creation of contract templates that fill the expectations of all departments. In the future, concerned industrial partners may expect an increase in efficiency during the project validation and creation processes when working on hybrid projects.

Indirect effects

As explained in subsection 4.2, indirect effects correspond to the economic flows generated by the exploitation of increased capacity outside of the IHU. The institute currently does not measure or follow up on this kind of effect for industrial partners, which the EvaRIO method particularly focus on.

Interviewed representatives from various industrial partners have yet to signal the emergence of any significant indirect effect considering that it is still too early to commercially exploit the capacity increase in activities outside of the IHU. Nevertheless, we managed to identify several examples of potential impact departure points that could serve as a stepping ground for a second analysis.

With the extension of activity to new domains, the IHU should take interest in observing how it will influence each industrial partner's strategy. An industrial group specialized in endoscopy, for example, may use the skills and experience acquired by working with radiologists to create a new hybrid market or simply as a leverage for creating further collaborations with institutes other than the IHU. Naturally, as the skills were gained by working with the IHU, a fatherhood coefficient should be applied to any economic value generate as to highlight the institute's role as an indirect effect.

Similarly, considering that fellows are surgeons who come from all over the world for a 1 or 2 years fellowship, industrial partners who choose to collaborate with them potentially create a gateway to new markets. Fellows who choose to return to their home country present the ideal candidate for future international projects and a good mean to extend sales internationally.

One of the most important events that are currently underway is the completion of the IHU's new building, with a construction budget of 23 million Euro, which should allow the institute to greatly expand its activity. This expansion is also expected to be accompanied by an increase in influence and reputation which is ought to benefit every

industrial partner, fellow and researcher working with or at the institute. To correctly observe the associated indirect impact, an analysis of how industrial partners benefit from this increase in reputation should be estimated in the future.

The previously reported increase in project management's efficiency should, theoretically, allow concerned industrial partners to increase the number of projects they can undertake and decrease their processing cost. Other impacts may include a complete or partial reorganization to either expand an activity or reduce expenses.

6.1.2 University and other research laboratories

Based on IHU data for research laboratories, the accounting manager estimated a total R&D activity volume of at least 4 658 379 Euro since the institute's creation in 2012. This value, already included in the global direct effect (12 184 159 Euro) calculated previously, represents the direct effect of R&D projects specific to academic partners.

Conducting these projects at the IHU has reportedly participated in increasing each research laboratory's capacity to some extent. The provided feedback, however, appears to be mixed with only a limited number of positive impacts being emphasized.

In general, the IHU is viewed as a potential knowledge hub that stimulates the creation of ideas by introducing researchers to new surgical fields such as endoscopy, for example. It is also perceived that the institute is a great opportunity for translating research into concrete applications, especially using the imaging platform on big animals.

In some cases, such as for the MRI (Magnetic resonance imaging), it is not possible to conduct experiments on big animals in Strasbourg, other than at the IHU, without going through some extensive paperwork. Estimation of the time necessary to gain permission and fill the regulatory requirements for such experiments revealed that it would require the equivalent of 6 months of work and training.

Science and Technology capacity: strong positive effect

The increase in scientific capacity of Research laboratories is estimated to, at least, 16 published articles that are highly dependent on the use of the institute's services. Additionally, interviewees reported at least 4 conference presentations and 4 thesis defenses

that were financed by the institute.

Through the interviews, two patents were reported to be dependent on the IHU in one way or another. Note, however, that patent submission, acceptance and validation take time which explains our current relatively low reported number. In the future, it would be essential to also follow the effect from such scientific outputs, such as in the creation of new international collaborations or royalties, as it has yet to be reported or even observed.

Through its partnership with the industry, the IHU is expected to facilitate access to the industries' products' research tools transforming the usual commercial industry-research laboratories' relationship into collaborations. Several labs have reported being able to access data from machines for free as they get to be considered as testers. Industrial partners should also benefit from this situations as it means having access to highly skilled testers not only for healthcare products but also for simulation, health economics, clinical research and software development.

Courses provided by the IHU in animal experimentation have allowed the training of 2 PhD students, 3 full time researchers and 2 engineers at a cost of 4 900 Euro instead of 16 000 Euro asked by the University. The ensuing certificate allows them to personally conduct animal experiments and write associated protocols which they otherwise would be unable to do.

Network capacity: strong positive effect

The relationship research laboratories have with surgeons and medical practitioners in general has been highlighted as essential to the success of any project. Besides their role as feedback providers through sheer experience and clinical testing, practitioners are also considered as lead users who provide ideas for innovative projects.

It is in that respect that some labs view the ISIP fellowship program in high regard since it provides researchers with easily accessible surgical skills, especially when a project is proposed by an expert not practicing in Strasbourg. Indeed, when international experts teaching at IRCAD's courses propose new projects, they are unable to continuously work with the researchers and test their prototypes. The ISIP fellows, however, are able to

easily access the platform and animal models while also being present on-site for any necessary communication exchange.

The IHU is clearly a hub in which researchers, clinicians and other specialists interact to create innovative technologies in the surgical field. Unexpectedly, interviewees repeatedly emphasized that a lack of communication on IHU projects exists due, in large part, to its stance over confidentiality. A lack of means and stimulus for researchers to exchange ideas and collaborate with one another has been signaled as one obstacle to the idea of creating innovation mixing different specialties.

Reputation capacity: no effect

In terms of reputation gain, interviewed research laboratories consider the IHU to have no positive effect on their renown. Considering that the institute has not been fully established, its reputations is clearly overshadowed by its parent company, the IRCAD.

Several researchers have even highlighted the existence of a gain in reputation but which was translated into a decrease in the probability of obtaining funds from the national research agency as well as a decrease in the number of collaborations with research laboratories of other cities. The former is due to the high financial investment that the IHU represents, which is unduly considered as a sufficient source of research funding. The latter resides in other laboratories' jealousy particularly those whose city does not possess an IHU.

Organization and Management capacity: no effect

Based on our interviews' results, most partners reported no increase in Organization and Management's capacity. However, some complaints were expressed when analyzing whether the management and organization capacity of users have been improved in some way.

Most researchers have appreciated the freedom that is given to them in their research with a low number of follow-up reports thus allowing them to focus on their projects. Others, however, view the low number of follow up as problematic since there is no continuous control of expenses, intellectual property, etc., to make sure no mistakes are being made.

Researchers were also disappointed by, what they consider, their lack of visibility on the imaging platform. Considering that the IHU hosts important events and occasionally receives VIPs on its platform, researchers have reported having no real time visibility of the latter's schedule and often having their access slot taken away, sometimes at the last minute.

Human Capital capacity: positive effect

In terms of human capital, interviews' synthesis reveal that the IHU has provided research laboratories with funds for 2 post-doc fellowships, 1.5 PhD , one fellow during 6 months and 2.5 engineers. Unexpectedly however, some interviewed researchers have expressed their disappointment over the IHU's decision to no longer fund PhDs as well as their use of feasibility studies. We highlight this feedback as to stimulate further discussions between the IHU and researchers.

To elaborate on the problem, the IHU imposes on each project submitted for funds to be preceded by a 6 months feasibility study to determine whether it has a high or low, positive or negative potential. While this is advantageous from an economic perspective as it decreases poor investments, some interviewed researchers signaled that the chances of finding anyone willing to be recruited for a 6 month period with an uncertainty over the project's future are very dim.

Performance effects

As explained in subsection 4.2, performance effects reflect the impact of gains in capacity on the conduct of an academic partner with the IHU and its activities. To be more precise, the increase in capacity could allow partners to become more effective at undertaking R&D projects with the institutes.

Currently, no significant performance effect has been signaled neither by the university nor by other research laboratories' researchers working with the IHU. At this stage, it is too early to observe such an effect since the first projects have yet to be completed.

Indirect effects

As explained previously in subsection 4.2, indirect effects correspond to the economic flows generated by the exploitation of increased capacity outside of the IHU. The institute currently does not measure or follow up on this kind of effect, which the EvaRIO method particularly focus on.

As with industrial partners, interviewed researchers from various laboratories have yet to signal the emergence of any significant indirect effect considering that it is still too early to exploit the increase in capacity in activities outside the IHU. Nevertheless, we managed to identify two examples of potential impact points that could serve as a stepping ground for a subsequent analysis.

A first indirect effect to monitor relates to the acquisition of animal experimentation certificates by a number of IHU collaborators. In the long term, the use of these certificates to conduct further experiments other than at the IHU is destined to produce some economic value reflecting, at least partially, one indirect effect.

Using future animal experimentation, outside of the IHU, to create products with a high market penetration rate, for example, should generate a considerable economic impact in terms of sales. A part of this economic impact can be viewed as being due to the acquisition of the animal experimentation certificates and thus, the IHU.

Currently, the IRCAD, and in the future the IHU, attracts international experts who represent a potential source of knowledge hardly accessible otherwise by research laboratories. While projects that emerge from their presence are mostly punctual, it is essential for the IHU to follow up on the labs-experts relationship to observe whether any future economic value is generated through other projects reflecting, at least partially, another indirect effect.

This labs-experts relationship, when maintained outside of the IHU, can for example lead to the creation of new research projects, products or even start-ups. Each scenario generates economic impacts be it in terms of funding, sales or job creation which can be considered to be partially due to the IHU's activity.

6.1.3 Fellows and IHU/IRCAD researchers

Based on IHU data for fellows and IHU/IRCAD researchers, we can estimate a total R&D activity volume of at least 2 683 780 Euro since the institute's creation in 2012, to which at least 100 000 Euro can be added as contribution from research and industrial partners. The sum of these values, already included in the global direct effect (12 184 159 Euro) calculated previously, represents the direct effect of R&D projects specific to the fellows and IHU/IRCAD researchers.

Conducting these projects at the IHU have reportedly participated in increasing each of the IHU/IRCAD researchers and fellow's capacity to some extent. The provided feedback appears to be mostly positive.

Science and Technology capacity: very strong positive effect

Working for the IHU/IRCAD has allowed researchers and fellows to gain easy access to the imaging platform considered as the IHU's major technological asset. ISIP fellows have reported spending more than 25 hours per week conducting experiments either on pigs (5h per week on average) or phantom models.

Researchers and fellows even sought to create their own phantom models, of pig organs' tumors, to be used for their experiments as some have been reported to be inexistent. In the future, these models are expected to have significant impact on research projects through possible cost reductions due to replacing live animals.

The scientific output in terms of publications has been estimated at more than 50 published articles, over 8 presentations and one provisional patent. These results, however, should be treated very cautiously as some researchers did not distinguish between IHU-induced publications and those in which the institute plays no role.

Network capacity: positive effect

For some researchers and fellows, the IHU provides an easier mean of approaching international experts who are part of its scientific committee, including the very cautious

Intuitive Surgical (creators of the da Vinci robotic system). While this network capacity effect can be considered to be of importance, the interviewees have yet to signal any significant impact be it direct or indirect.

The lack of communication from the IHU over which projects are currently being undertaken has again been signaled as one major obstacle to collaborations. Interviewed actors consider their skill to not be used to their maximum effect due to the low amount of collaborations that exist between researchers.

Reputation capacity: positive effect

As with research laboratories, the IHU appears to have very limited impact on the reputation of its researchers as it is strongly overshadowed by the IRCAD's. Even when discussing individual projects, differentiating between those that are related to the IRCAD from those that are IHU appears to be difficult.

In the ISIP fellowship program's case, fellows that have returned to their country have signaled a potentially positive reputation effect in the form of conference presentations and new career opportunities. In the future, follow-up on each fellow should be maintained if the IHU's indirect effect is to be measured.

Organization and Management capacity: strong positive effect

By conducting projects at the IHU, researchers have been faced with a number of obstacles that resulted in the discovery of new efficiency increasing management methods. In one case, a new method for stocking pigs under experiments have allowed saving the equivalent of 44 500 Euro per pig per month.

Other methods are expected to increase the chance of having projects correctly reflect the expectations of different specialists, thus increasing research efficiency in hybrid technologies. A method called CAUTIC, for example, has been adopted as it seems to focus on studying the nature of an innovation with respect to the characteristics of it destined users, knowledge created and new practices required compared to what is existent.

Human Capital capacity: positive effect

In terms of human capital, some researchers consider the IHU to be providing the teams necessary to work on project the IRCAD receives and for which it does not necessary have the resources or skills required. In that respect, three full time research jobs were recorded as being created for IHU related projects.

Performance effects

As explained in subsection 4.2, performance effects reflect the impact of gains in capacity on the conduct of fellows and IHU/IRCAD researchers with the IHU and its activities. To be more precise, the increase in capacity could allow partners to become more effective at undertaking R&D projects with the institute.

As with academic partner, no significant performance effect has been currently signaled.

Indirect effects

As explained previously in subsection 4.2, indirect effects correspond to the economic flows generated by the exploitation of increased capacity outside of the IHU. The institute currently does not measure or follow up on this kind of effect, which the EvaRIO method particularly focus on.

Interviewed fellows and researchers have yet to signal the emergence of any significant indirect effect considering that it is still too early to exploit the capacity increase in activities outside of the IHU. Nevertheless, we managed to identify at least two examples of potential impact points that could serve as a stepping ground for a second analysis.

Experience gained through animal experimentation and the creation of phantom models should particularly be interesting from the ISIP fellows' perspective. If and when they return to their home country, we would expect them to exploit their gained capacity to either teach or create new projects. In both situations, any generated economic value can be partially considered to be an indirect effect of the work done at the IHU.

The discovery of new management and organization methods could benefit not only the researcher/fellow behind them but also the IRCAD and IHU as a whole. The expected

economic gains, in the case of stocking pigs for example, should be straightforward to estimate in the future.

Capacity effects summary

In general, the capacity gain for industrial partners and IHU/IRCAD fellows and researchers appears to be the most significant. Research laboratories, however, have reported negative impacts as their expectations appear to not have been met by the IHU.

Table 4.5: Capacity effects' results

Capacity effect	Industrial partners	Research labs	IHU/IRCAD Fellows and Researchers
S&T	+	+ +	+ + +
Network	+ +	+ +	+
Reputation	0	0	+
O&M	+ +	0	+ +
Human Capital	+ + +	+	+

0: No effect + : Positive effect

Table 4.5 provides a summary of our findings of the IHU's effect on the capacity of each partner.

6.2 EvaRIO reworked: focus on projects

As we can observe from the results, the EvaRIO method takes a general perspective by aggregating all the activities a partner has with the IHU and analyzing their impacts without distinguishing between the different types of projects to point out the dynamic that exists between them. When analyzing the cost-benefit of a specific hybrid technology developed by the IHU, the EvaRIO method therefore does not allow us to identify the long term succession of different projects conducted by the same organization.

In innovative surgical institutes such as the IHU, the reliance on lead users (surgeons), for example, signifies a strong correlation between their practice and the emergence of subsequent innovation projects. We can therefore expect that each project could give birth to other innovative ones, or at least be responsible for their appearance to a certain degree.

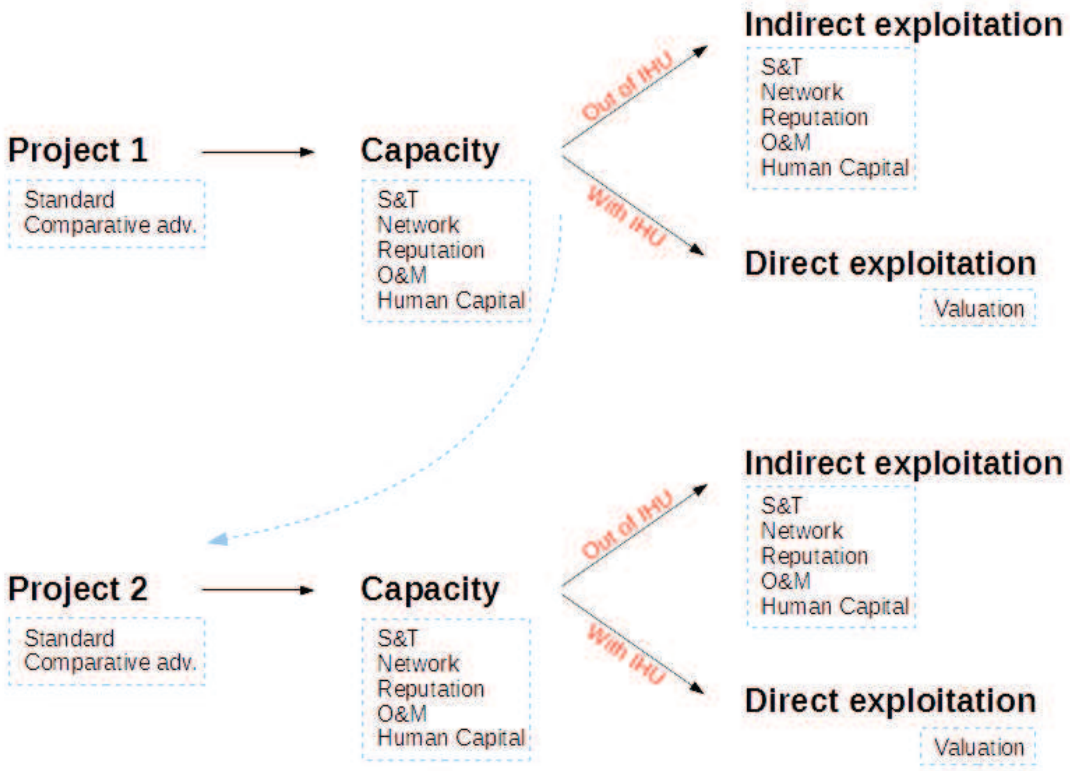
To further clarify, consider the hypothetical example of a new endoscopic instrument development (project 1) for which the innovator realized he needs a shorter endoscope. To remedy this problem, he undertook a second project (project 2) for developing a shorter but extensible endoscope which is expected to have a significant economic impact even without using the instrument developed in project 1. Both projects are clearly intertwined in our example, and it would be unfair to assume that project 1 has no economic impact in case it is proven to be a complete failure. In fact, a part of project 2's economic impact is actually due to project 1 and should therefore be correctly attributed.

It is with these questions in mind that we thought to rework the EvaRIO methodology with a focus on individual projects and their relationship. By construction, it is more aligned with a return on investment logic than with representing the economic activity that is dependent on the IHU. The main objective is to provide advocacy for the IHU's R&D activity and hold researchers accountable for their specific project results.

Furthermore, by allowing us to evaluate specific projects, we are able to determine the impacts of the R&D activity related to one particular innovative surgical technology. Using our methods from the previous chapters to analyze the socio-economic impact of using a surgical innovation and EvaRIO reworked, we are able to cover the impact of the entire life cycle (from conception to abandonment) of a minimally invasive surgical innovation.

Figure 4.6 provides a schematic representation of the reworked EvaRIO evaluation method with a focus on innovative projects' impacts. As with EvaRIO, we differentiate between direct and capacity effects to which we add indirect exploitation out of the IHU, an equivalent to indirect effects out of RI, and direct exploitation with the IHU.

FIGURE 4.6: EvaRIO reworked



For each project, the researcher consumes resources that are put at his disposal by the hosting institute, the IHU in our case, the amount of which represents the IHU's total expenditures, or "direct effect". In this dimension, we also present the comparative advantage value of conducting each R&D project at the IHU compared to the most cost-efficient alternative; which could be not going through with the project at all.

While advancing his R&D project, the innovator increases his capacity with respect to the classification used in the EvaRIO methodology: S&T, Network, Reputation, O&M and Human capital. With the reworked EvaRIO, we only focus on the capacity effect specifically due to the project being evaluated and not to the entire activity being conducted on the RI.

Once the project has been brought to fruition, the researcher can observe two potential impacts. Direct exploitation corresponds to the value created by the evaluated project notably in terms of sales, awards and service delivery.

Indirect exploitation corresponds to the use of acquired capacity, with respect to each category, to create value out of the IHU. Value creation can take the form of new projects with, or employment by, other companies or even creating start-ups.

The capacity acquired during this R&D project may also lead the researcher to new research opportunities. A link can therefore be created between the increase in capacity and the subsequent projects that emerge from its use.

For both types of exploitation (direct and indirect), the link between projects is established mainly by asking the interviewee, for example: To what extent has your first project, or more precisely the capacity developed while proceeding with it, influenced the emergence of your second project?

The researcher is expected to give an answer in the form of a percentage (exp. 30%), equivalent to EvaRIO's fatherhood coefficient, reflecting the causal relationship at a minimum. If a relationship does exist, it would be logical to assume that 30% of the second project's direct and indirect exploitation economic value is attributable, respectively, to the first project's direct and indirect exploitation.

7 Discussion

Hybrid surgical technologies attempt to combine previously distinct, and often opposite, specialties in what is considered to be a revolutionary idea. Naturally, the IHU needs to invest a great amount of resources in research and development to achieve such a goal.

To assess whether each investment is "worth it", the literature extensively analyzed the R&D process as to understand its nature as well as that of innovation as a whole. As we have shown, the word "innovation" in itself can designate different forms of products and ideas the comprehension of which is essential to accurately steer economic evaluations.

The first step for any evaluation is therefore to understand the role of hybrid surgical technologies. From our understanding, hybrid surgery aims to position itself as both a product and process innovation by redrawing the boundaries between medical specialties and inventing products that combine them. Treating patients will no longer need as many specialists as before nor as many distinct facilities.

Beyond their role in treating patients, hybrid surgical technologies are also posed to generate socio-economic impacts on different levels, whether micro or macro. To understand how such impacts are generated, we first must be aware of how innovation is defined, its origins, and the relationship that it shares with society.

Nature of innovation

To date, hybrid surgery has yet to show its full potential due to the extremely limited number of technologies that can currently be qualified as such. At this stage of development, it is not possible to determine whether hybrid technologies are process, position, product or paradigm innovations. Moreover, we cannot confirm whether these technologies will be mainly incremental, radical or disruptive.

Distinguishing between the four P's of innovation plays an important role in identifying the potential and impacts of R&D. Projects that enable increases in reputation capacity, for example, should provide partners with a higher possibility of enabling position innovations since, as we discussed in section 2.1, this type of innovation is heavily dependent on marketing power and the partner's persuasion capacity. Both of which are enhanced with a higher reputation.

Although the economic literature has provided solid definitions for both incremental and radical innovations, recent developments saw the introduction of one additional definition (disruptive) that appear to have changed the way innovation is looked at in the medical field. Considering that the root of disruptive innovation as a concept can be found in management, it mainly serves to highlight the distance that exists between economics and the medical field.

This differentiation will be essential for future evaluations of the R&D process. The emergence of disruptive innovations, for example, will heavily rely on an increase in network and science&technology capacity of different partners as they need to "think outside the box" and mix previously distinct knowledge. The impact in terms of direct or indirect effect of such innovations should be substantial, compared to incremental or radical innovations, as new markets are created generating a "chain effect" leading to new projects and start-ups.

Sources of innovation

Regardless of the definition given to innovation, the process of creation and diffusion follows similar principles with different actors playing different roles and fueling their capacity through various sources. As innovators, for example, surgeons and researchers draw inspiration from within themselves exploiting their capacity and knowledge to create. Similarly, as users, they are able to draw inspiration from around themselves whether by trying to improve their practice environment or using their network. In both cases, the literature has shown that cooperation and collaboration between surgeons and researchers is an essential part of the innovation process.

Hybrid surgery, due to its reliance on three distinct specialties, depends heavily on the innovator's capacity to communicate and cooperate with professionals who have been known to rarely collaborate. In this surgical field, the user (i.e. surgeon, endoscopist, radiologist etc.) is considered as the main source of inspiration with researchers and industrial partners forming the backbone of technical and technological know-how.

Intuitively, the introduction of hybrid surgery as a R&D focus should initiate important changes in the way research is performed. By taking interest in evaluating these changes,

institutes will potentially be able to increase their efficiency and provide advocacy for their R&D activity.

Measuring the impacts

The literature review on the methods for evaluating the impact of health research highlight the numerous tools and methodologies that currently exist. Each method is created with a certain objective in mind, a fixed perspective and a defined temporal horizon making their application in different contexts questionable.

When compared to other methodologies, EvaRIO can be viewed as an *ex post* evaluation providing advocacy for R&D activities which is essential for emerging institutes such as the IHU. In terms of aggregation, however, the method was created to analyze the research activity on an institute's level without differentiating between projects whereas most of the cited methods were created to evaluate specific missions or projects.

One major difference between the EvaRIO methodology and those reviewed in this chapter relates to the consideration of knowledge production as either an output or input. The payback method, for example, considers publications and patents as a primary output of research whereas EvaRIO interprets them as an increase in capacity/input, the exploitation of which generates indirect economic impacts.

To test the pertinence of the EvaRIO method in the surgical field, we proceeded to apply it using the IHU as a research infrastructure case study. We were well aware that it was too early to identify significant indirect effects but were nevertheless confident of our ability to identify key impact departure points that should be monitored for future evaluations.

Unexpectedly, during the interviews, interviewees saw an opportunity to express their ideas and concerns regarding their collaboration with the IHU. Even though it was not our initial intention to evaluate how the institute's activity is organized, it turned out to be an interesting result which should stimulate dialogue and allow the institute to improve its collaboration potential.

The most observable effect of working with the IHU appears to be an increase in S&T capacity with all partners, especially fellows and researchers working at the IHU/IRCAD, reporting some positive effect. In terms of network capacity, it seems that most

partners believe in the IHU's high potential even though we have yet to observe significant increases and some partners encountered difficulties in exploiting this capacity due to the lack of communication.

Such a lack of interaction between researchers should be viewed as a lost opportunity for developing innovations, particularly disruptive ones. For such innovations to emerge, it is essential to gather individuals who "think outside the box", view traditional practice from different angles or simply possess different knowledge.

The literature also discusses the importance of such cross-functional cooperation and more generally open communication as a way to facilitate the emergence of innovation. The flow of information, ideas and knowledge among organization units and between partners appear to have repeatedly produced positive results [Georghiou et al., 2002].

Considering that the IHU is a young institute that has yet to finish building its infrastructure, and thus start its main activity, the reputation effect it has on its partners was expected to be low or even nonexistent.

Working with the IHU has reportedly had beneficial effect on partners' organization and management increasing their efficiency in various ways. Research laboratories, however, emphasized the current weaknesses in the institute's organization and communication which they consider to be not up to their expectations.

For all partners, the institute's creation has encouraged the creation of numerous jobs whether paid by the institute itself (directly or through projects) or its partners. Recent decisions, however, such as the refusal to finance PhD students have been repeatedly criticized by most researchers.

By looking to understand the reasons behind this decision, we began to point out the distance that exists between the IHU's and researchers' objectives. Apparently, the IHU has decided to focus on translational research with short term applications, technology transfer and product development. Researchers, however, are more focused on long term applications.

Creation of a new method

EvaRIO's application as an internal investigation, even if premature, was overall informative and should increase the management board's awareness towards current weaknesses and strengths in the institute's activity. The reworked version of the EvaRIO methodology focuses on providing advocacy either for projects or the R&D activity as a whole, as well as increasing accountability of researchers. Theoretically, EvaRIO reworked should fill in the weaknesses from which the initial method suffers within a context of potentially intertwined projects.

Another major advantage of the EvaRIO reworked method lies in our ability to merge its results with a health economic cost-benefit analysis, as presented in the two previous chapters. To illustrate, consider that the IHU is developing a hybrid surgical system to be used in its own facilities.

We start off by using our previously developed methodologies to assess the surgical system's cost-benefit when compared to the most common alternative. Results will either indicate a positive cost-benefit advantage or disadvantage to using the new technology.

Note that in either case, we only take into account part of the technology-induced cost and benefit by looking at usage and not the development itself. Using the reworked EvaRIO method, it is possible to conduct a complementary cost-benefit evaluation of the R&D process that lead to the technology's emergence. Thus we can combine traditional health economic impacts with the serendipitous results typically generated through R&D, otherwise not evaluated in health economics.

By combining both cost-benefit analysis, we solve one of the biggest shortcomings of both the EvaRIO and its reworked version; that is the lack of Quality of Life and economic/social impact measurement of R&D. Health specific frameworks, such as the payback, often include "outcome" measures to reflect a project's impact on patients' quality of life or even on an increase in surgical care efficiency.

The developed reworked method should be particularly interesting for analyzing the ISIP fellowship program's impact. Based on our findings, IHU partners appear to rely extensively on ISIP fellows who are also considered as lead users by their employer. In the future, the fellows' importance is posed to increase with the development of the institute's activity and collaborations.

7.1 Limits

We were faced with numerous challenges while writing this thesis' chapter and conducting the associated evaluation. Even though we managed to overcome some of them, others remain as limitations of our work.

EvaRIO's application was subject to a few difficulties mainly due to the lack of proper communication at the IHU. Even after interviewing the institute's employees, we were unable to identify (early enough) all partners that are involved in IHU projects or that benefit from its activity. Written documentation is strongly outdated with no direct way of updating the information relevant to our analysis.

Updating the list of partners should form the next step to conducting a second complete EvaRIO application. To fully exploit the potential of this methodology, it would be essential for the IHU to start its activity in the new building and for the analysts to allow a time lapse (2-3 years) for indirect impacts to emerge.

More challenges were encountered relating to the confidentiality of data and existence of bias in its collection. The latter is particularly present in the medical field's published literature where a large number of authors on the same article does not necessarily reflect concrete collaborations or participation in the associated study. Reports on the number of published articles were therefore treated with caution as we do not currently possess the tools to eliminate double counting.

Discussions are currently underway between the IHUs and the French government to create a software to track each institute's scientific output. At the moment, however, the tool put at the IHU Strasbourg's disposal is unusable. Once the development reaches its final stages, it will be essential to use this tool to precisely identify the scientific and technology gains for each partner.

One of our study objectives consisted in analyzing the IHU's R&D economic impact on the region in terms of attracting foreign investment (through industrial partners) or human capital (through research laboratories from other cities). However, most data on investment were viewed as confidential by both the IHU and its partners which limited our presentation to aggregated information of the institute's investments.

Although we present the focus of EvaRIO reworked's evaluation on projects as one major advantage, it also raises a barrier that we have yet to address. As an illustrative example, consider a R&D project that involves the cooperation of several researchers from different institutes/partners. To correctly evaluate its impact, we will need to interview every researcher individually which could prove to be a time consuming task if even feasible.

Admittedly, the biggest limit to our study is the lack of application for the EvaRIO reworked methodology as the IHU was too young at the time of analysis. Nevertheless, we discussed the interest of this method with one IHU partner who follows a large number of projects. His feedback was highly positive particularly in pointing out the importance of highlighting the dynamics that exist between the different projects. In future evaluations of IHU projects, it would be essential to test the practicability of this method and the strength of its theoretical foundations.

8 Conclusion

In this chapter, we shifted the focus from the use of surgical technologies to the R&D activity that enables their development. We started out by describing the process of technology creation with an emphasis on identifying main actors and potential sources of impact.

A literature review of health R&D impact evaluation methodologies allowed us to identify their key elements but also the tools for their measurement. Although none of the presented methodologies could be applied in our evaluation, they did serve as a comparative frame for the chosen EvaRIO method.

By interviewing the IHU's partners and collaborators, we identified a number of positive impacts but also some barriers. Our results' synthesis will hopefully provide the institute's management with enough data to stimulate discussions, and improve its R&D activity or collaborations more generally.

The application of EvaRIO on the IHU's R&D activity was riddled with challenges, whether due to a lack of communication or organization, as the institute is still in an early stage of development. Nevertheless, we were still able to determine key strengths and potential weaknesses in the current collaborations between the institute and its partners.

More importantly, we tested the applicability of EvaRIO in a healthcare institute specialized in surgical instruments' development. Our analysis has allowed us to create a new, more adapted, version of the method that can be concurrently applied with the cost and benefit methodologies presented in previous chapters.

Compared to the traditional methods of evaluation based on outputs (publications etc.), our reworked method should provide the IHU with the means to express its activity's socio-economic impact. From a government's perspective, this constitutes a much more interesting argument for justifying the investments in the institute.

In future work, it is essential to test the practicability of the EvaRIO reworked method by applying it on different completed projects. Ideally, the analyst should select an IHU developed hybrid surgical technology and attempt to conduct a cost-benefit evaluation of both its use and development.

Chapter 5

Thesis' general conclusion

1 Introduction

Innovations in hybrid minimally invasive surgery are directly affected by the need for socio-economic impact assessments since they are, because of their complexity, highly likely to significantly increase the cost of care. Nevertheless, they are also expected to offer considerable advantages to the society and the economy among which the possibility of reducing length of stay, increasing the region's attractiveness, reorganizing care pathways to make them more efficient, stimulating research and facilitating teaching/learning.

This thesis revolved around the IHU's need to assess its highly interdependent activities of **care**, **development** and **education** focused on hybrid surgical innovations. Each activity, according to the institute, is expected to generate impacts on different types of actors. As we pointed out throughout this thesis, however, there are currently few tools for assessing these impacts. To be more precise, we did not identify any methodology that enables us to evaluate all three activities and combine their impacts in a unique cost-benefit ratio.

The main driving question was therefore: **How can we evaluate the efficiency and the socio-economic impacts of surgical innovations?** To answer, we divided our study into three chapters corresponding to the analysis of the impact of introducing surgical innovations on the surgical operation's cost; the benefit to patients, the hospital

and the economy arising from their use; and the impact of the research and development process that lead to their creation.

In our study, we mainly focused on assessing the impacts of the creation process and use of innovative technologies considering that they were the institute's most developed activities. The methods we sought to create are meant to evaluate the impact of these activities on IHU partners and patients as well as on the society and the economy more generally.

Our literature reviews for the cost, benefit and innovation chapters were mainly focused on identifying calculation methodologies for each impact measure (cost, Quality of Life, medical tourism, presenteeism, absenteeism etc.) that permits their combination into a unique cost-benefit ratio. Such a combination would allow the IHU, and any other institute developing innovative surgical technologies, to provide advocacy for its activities by pointing out their impact on patient care, the society and the economy.

Whenever we identified a lack of methodological guidelines or weaknesses in published/used methods to accurately calculate each impact measure, we proposed our own alternative with a focus on evaluating (hybrid) minimally invasive surgery. When the methods proposed by the literature were adequate, we made a synthesis of calculation proposals in order to identify how they can be applied in the context of a global cost-benefit analysis.

For each created or identified calculation methodology, we performed an illustrative application using an IHU (hybrid) minimally invasive surgical technology as an example. Similarly, we focused on analyzing the IHU's R&D activity in order to evaluate the process's impact in terms of innovation development and knowledge creation.

The existence of different, separate, applications is mainly due to the lack of sufficient data to apply all our calculations on one innovative surgical technology - which would have allowed us to derive a unique all inclusive cost-benefit ratio. Nevertheless, through our different applications, we were able to validate each measure's relevance and applicability which constitutes an important step for future studies.

2 Cost evaluation of minimally invasive surgical technologies: the existing methods and our contribution

After an introduction of this thesis' framework, our analysis began with an investigation of the French healthcare system's functioning mechanisms as to identify its strengths/weaknesses and the reasons behind its inability to determine the cost of using innovative technologies. After highlighting the lack of cost evaluation methodologies for surgical innovations, we sought to create the basis for such a method thus covering the first part of assessing the impact that surgical innovations can have on patient care.

2.1 Literature review

The literature on cost evaluation methodologies began with a comparison of relevant national and international recommendations in health economics. We focused primarily on identifying commonalities as to establish a solid basis for comparing scientific publications and for creating our own costing method.

A second literature review, specific to publications in the surgical field, comparing the methods used to analyze the cost of surgical operations revealed a significant lack of rigor in the calculations as well as in their publication. By pointing out this weakness, we were able to justify the need to create and publish a costing methodology to be used by surgeons, hospital managers and the IHU.

2.2 Method

Our cost analysis of minimally invasive image-guided surgical operations was based on the development of four formulas covering both fixed and variable costs. In the fixed costs category, we included the medical equipment and the personnel while the variable costs category covered reusable instruments and disposables.

The application and validation of our formulas were based on a comparison between two types of interchangeable minimally invasive surgical operations, namely: computer assisted gastric bypass and traditional laparoscopic gastric bypass. Two approaches

were followed during the application which allowed us to demonstrate our methodology's utility in two situations, availability as well as unavailability of a comprehensive database.

2.3 Results

The results of our cost calculation method's applications demonstrated that we can accurately determine the impact of introducing a minimally invasive surgical technology on the cost of surgery. We were also able to demonstrate the flexibility of our methodology by following two approaches for our application:

- The first approach uses a minimum amount of information mainly based on surgeons' feedback, average data and estimations;
- The second approach focuses on exploiting a complex database to derive a maximum number of conclusions.

The first version was created to easily perform rapid calculations but the results of which are not meant for publications due to the lack of standard deviations and density plots. The second version is based on extensive data usually collected during clinical protocols and allows for scientifically valid calculations. Typically, such a database would contain, **for each patient**, details on:

- Medical equipment present in the operating room;
- Category and number of each medical personnel;
- Time from start to finish for each step of a surgical operation;
- Number and type of each reusable instrument and disposable used;

A comparison of computer assisted surgery versus traditional laparoscopy was made as an example of application using data from the hospital and from a clinical trial protocol established by the IHU. Our results clearly demonstrate that we can precisely and correctly calculate the cost per operation of any surgical procedure. Indeed, we were able to show that the robotic surgical system's introduction significantly increases the cost per operation up to 225 % of laparoscopy's cost.

The analysis of robotic surgery as a case study revealed a significant disregard for the cost of surgical innovations. Indeed, according to our calculations, it seems inconceivable that a technology which costs more than two times its alternative is adopted without having fully proven its effectiveness.

2.4 Our main contributions and limitations

One of the major contributions of this chapter was the development of two algorithms, with over 500 lines of code, to determine the impact of introducing an innovation on the cost of a surgical operation. Both algorithms, created using the open source statistical software **R** [R Development Core Team, 2011], allows the user to rapidly calculate the cost of any surgical operation without any limitation as to the database's size.

Other variations of these algorithms were also created allowing the IHU to determine the price of technologies they develop or the break-even point for new surgical procedures they adopt. Although calculations using our tools are done in one click, the extension and adaptation of these algorithms require the user to have a solid knowledge in statistics, cost management and programming.

The method developed following this analysis is particularly suitable for the evaluation of innovations in minimally invasive surgery which served as a basis for its construction. Furthermore, the formulas that make up this method can also be applied in a number of other areas such as in imaging, in pharmaceutical or in general medicine.

We pointed out several limitations in our study, some of which are technical. Applying our costing methodology, for example, is limited by a lack of data access which hinders our ability to include overhead costs. Moreover, the lack of direct access to the hospital's database implies the need to rely on some assumptions to render the analysis feasible. Note that any change in the assumptions and any decision to include the overhead cost, generally specific to each institute, may require additional developments or adaptations to the algorithms.

In health economics, cost calculations are an essential part of the four medico-economic assessment practices presented in Chapter 1: cost-minimization, cost-effectiveness (CEA), cost-utility (CUA) and cost-benefit (CBA). However, analyzing the impact of surgical

innovations on the cost per operation risks doing more harm than good as the increase in cost, which is more than likely to occur for technology leveraged innovations, would often dissuade decision makers from adopting the evaluated technology. An important part of health economic evaluations therefore revolves around combining cost and effectiveness impacts to derive efficiency based decisions.

3 Extended health economic evaluation for medical devices

In three of the four health economic evaluation methodologies (CEA, CUA, CBA), cost is only one part of the analysis. In cost-benefit, our interest in this thesis, the second element necessary for conducting such an evaluation is naturally the impact of surgical innovations in terms of "benefit". This thesis's third chapter therefore concentrated on extending our cost analysis to include the benefit side of the cost-benefit equation.

3.1 Literature review

This chapter's literature review began by identifying the particularities of medical devices, minimally invasive surgical technologies included, and of their use. As we demonstrated, the evaluation literature on this type of innovation is highly heterogeneous. We therefore sought to establish a common ground on which we can build our own impact evaluation method.

To do this, we compared international economic evaluation guidelines and identified the measures that are generally regarded as representing a benefit in healthcare. In the case of (hybrid) minimally invasive surgery, we specified which impact measures may reflect a cost or a benefit for the society or the economy from our point of view. In total, we identified six outcome measures that we considered of relevance to our analysis; namely the impact of surgical innovations on complications, length of stay, medical tourism, presenteeism, absenteeism and quality of life.

Each measure was then subject to an individual literature review in order to determine the best calculation methods (how to determine the cost of absenteeism or the economic value of Quality of Life for example). We were also particularly interested in identifying the necessary calculations and adjustments that enable their inclusion in a cost-benefit analysis.

3.2 Method

For each identified impact measure, we performed an illustrative application with respect to available data and access permissions. When possible, we based our calculations on data from the clinical protocol comparing laparoscopy and computer assisted surgery previously used in one of our cost calculation approaches. Alternatively, we either created or utilized existing IHU databases from other minimally invasive surgical operations.

Our medical tourism impact study, for example, required going over the IHU's files on international patients to create a usable database. We then conducted a specific cost-benefit analysis with the primary objective being the determining of this activity's return on investment. In other words, we focused on calculating the impact on the region and in terms of profit of every Euro spent by the IHU.

The analysis of quality of life data was performed using a hierarchical linear model which was shown to be rarely used in the surgical field. To justify our choice and show the ambiguity that exists on the usefulness of some used statistical models, we detailed and commented the methods commonly used in the literature for *ex post* evaluations.

Given the important role of surgeons in the choice of surgical technologies, we were also interested in the reasons (intangible benefits) that motivate them to adopt surgical innovations. The da Vinci robotic system was used as a case study since, although it has experienced a significant commercial success, it is still unclear as to why it gained such momentum. To conduct this analysis, we created and distributed a one page survey for surgeons currently practicing or learning to perform robot-assisted surgery.

3.3 Results

The clinical protocol's data comparing computer assisted gastric bypass and its laparoscopic equivalent allowed us to test the application potential of three benefit measures: hospital length of stay, absenteeism and quality of life. For all three measures, our results showed a non-statistically significant difference suggesting that the robotic surgical system does not offer any advantages in these three dimensions despite its higher cost.

Following the analysis of another minimally invasive procedure ("Peroral Endoscopic myotomy" (POEM)) and of laparoscopic gastric bypass operations, we were able to establish a business model for the IHU's medical tourism activity (at their request). Through this analysis, we were also able to demonstrate the possibility of assessing the economic impact of an innovative procedure, or technology, on the region and its healthcare institutes.

To measure intangible benefits, we analyzed a total of 29 replies to our robotic surgical system's survey. The evaluation results showed that despite the high investment cost necessary for the acquisition of the robotic system, the majority of respondents appeared to be favorable towards it. According to our analysis, one of the main benefits of the surgical system lies in its use as a teaching tool and a simulator.

3.4 Our main contributions and limitations

From our point of view, the literature has so far strongly neglected some impact measures for surgical technologies such as medical tourism, absenteeism or presenteeism. Our reviews and applications enable decision makers to include these measure in a comprehensive benefit assessment to complement our previous chapter's cost analysis, thus contributing to the implementation of a comprehensive cost-benefit evaluation.

Other than for health economists, the concepts of quality of life, quality adjusted life years and willingness to pay remain unfamiliar to healthcare professionals. Through our experience, we noticed that an important confusion exists over the significance of and the difference between these terms. As this thesis is not only intended for health economists, but also for surgeons and hospital managers, we took great care in explaining these concepts in as much an accessible way as possible.

We have described in great detail the kind of quality of life data generated by minimally invasive surgery and the econometric method (Hierarchical linear models) which, from our point of view, is best suited for evaluating this kind of measures. The research we conducted should allow surgeons and statisticians to improve the validity of their quality of life studies and understand how this impact can be included into a cost-benefit analysis.

The biggest obstacle we were faced with during this thesis was the lack of data which neither the IHU nor the hospital collected (such as for presenteeism). When collected, some data was either of questionable quality such as in the case of absenteeism, or succinct such as for medical tourism. Therefore, our applications were scattered over different databases and procedures limiting our ability to perform a comprehensive cost-benefit analysis of a single innovative technology.

Given the low number of responses to the "da Vinci" survey analyzing intangible factors, the results of our application should be handled with caution as they could be considered as non representative. Nevertheless, our approach can serve as a pilot study for a more detailed evaluation of another innovation, the users of which can be preferably contacted more easily.

4 Impact of Research and Development in Healthcare

Hybrid minimally invasive surgery is an entirely original field that the IHU wishes to create and lead. As such, the introduction of such innovations in the surgical operating room can only occur after a R&D process that enables their creation. An assessment of the socio-economic impacts of a hybrid surgical technology should therefore not be limited to the use in the operating room (treatment) but must also include the impact of all the necessary steps that lead to its creation.

The analysis of the research and development activity is therefore an integral part of the evaluation of hybrid care pathways. In addition, this extension of our thesis allowed us to introduce a dynamic dimension in our evaluation method since we were no longer assessing an innovation at a given moment but analyzing its impacts throughout its life cycle from conception to use.

4.1 Literature review

The research and development process's impact assessment began with a synthesis of the various definitions that the literature use to describe an innovation; namely incremental, radical and disruptive. Understanding the differences between these categories and the enablers of each innovation type allowed us to identify key "departures of impact" which we included in our assessment.

By conducting a literature review of R&D evaluation methods, we found a significant lack of systematic documentation and a number of weaknesses (such as the impracticability of deriving a cost-benefit ratio) in their impact measurement. An analysis of their main characteristics allowed us to better position the "EvaRIO" method, developed by BETA [1], which we adapted to the IHU's R&D activity. Our choice for EvaRIO relies on the ability to benefit from the experience of a large number of researchers behind its development, its focus on in-depth analysis of micro-mechanisms (indirect effects) and the ability to include its results in a cost-benefit analysis.

[1] Bureau d'Economie Théorique et Appliquée

4.2 Method

Extending our analysis to the R&D process is based on the application and adaptation of the EvaRIO method for the assessment of research infrastructures. The method and its adaptation, which we named "EvaRIO reworked", focus on measuring capacity gains and their exploitation to generate economic impacts.

In our thesis, and with respect to EvaRIO's definition, the term "capacity gain" designates: the creation of scientific and technical knowledge, the creation/strengthening of links with other actors, the gain in reputation, the development of new organizational and management techniques, and the increase of human capital. As we have shown, IHU partners develop their capacity by collaborating with the institute and conducting research projects using its experimental platform. In addition, as discussed in our thesis, it is possible to **exploit this increase in capacity** either with or without the IHU to generate significant economic impacts.

After identification of the IHU's most important industrial and scientific partners, we conducted a total of 15 interviews the synthesis of which allowed us to identify the strengths and weaknesses of each collaboration. This analysis was also used to evaluate the appropriateness of applying Evario for the measurement of capacity gains in a surgical institute such as the IHU.

4.3 Results

Through our impact analysis of the R&D process for minimally invasive image-guided surgical technologies, we were able to highlight several departures of impact of collaborations between the IHU and its three types of partners: industry, research laboratories, and IHU/IRCAD researchers/surgeons. Although numerous capacity gains (Science & Technology, Network and Human Capital) have been identified, some interviewees reported the existence of some obstacles particularly for gains in terms of reputation and organization. In general, industrial partners and IHU/IRCAD's researchers/surgeons seem to benefit the most from this collaboration.

Following our EvaRIO method's application and the review of health research assessment methodologies, we adapted our initial method to focus more on the impact of individual

projects and to take into account the dynamics that exist between them. Hence, we were able to establish the theoretical framework for EvaRIO reworked which allows the IHU to perform more precise analysis of its R&D activity, the results of which are complementary to our cost-benefit analysis performed in the previous chapters.

4.4 Our main contributions and limitations

Through this chapter, we tested the applicability of the EvaRIO methodology whose high potential was well highlighted. However, to created a method that is complementary to what we established in the previous chapters, we needed to create an adaptation that focuses on a project-by-project analysis. This specificity allows decision makers to trace the impact of the development and the use of a specific surgical innovation.

The impact assessment of the IHU's R&D activity and its partners' gain in capacity was limited by the degree of confidentiality. Consequently, some results can be considered inaccurate.

The lack of indirect effects measurement, associated with the exploitation of capacity, in our application is quite normal. These affects necessitate a certain time before emerging and were, at the time of analysis, still in their early phase. Nevertheless, we were able to devise a list of potential impacts that should be monitored in the future.

The application's quality for EvaRIO, and its adaptation, relies heavily on the experience of the person conducting the evaluation as well as on the time invested in the results' preparation and synthesis. These requirements indicate the need for a dedicated staff to conduct such analysis as surgeons and hospital managers can rarely have the time and experience for such applications.

5 Perspectives

As an institute specialized in the development and the use of hybrid surgical innovations, the Institute of Image Guided Surgery (IHU Strasbourg) will be faced with a constant need for evaluating its activity. Indeed, the premise of IHU Strasbourg is that advances in image guided therapy, with an aim to minimizing the access trauma of surgery, will lead to better patient care and overall cost reduction/positive economic impact. These developments, however, require a robust program to track and measure the impact of IHU funded projects not only in terms of cost but also in terms of benefit for both users and partners.

One considerable danger of current health technology assessment guidelines resides in their regard of medical innovations as static objects. Evaluations are always done at a certain point of time following a clinical trial with a focus on the cost and effectiveness of studied devices. Little attention is given to the learning effects and the impact of subsequent innovations, whether incremental or otherwise, which can significantly change the results of an evaluation throughout the product's life cycle.

The impact evaluation of hybrid surgical innovations should be considered as covering a process in which an idea becomes a project, a product and finally a treatment; which, in turn, can lead to new ideas. The creation and introduction of an innovative technology in the surgical operating room can therefore have impacts on several levels.

The first observable impact translates a change in the cost of patient care which the French system of data collection and processing does not assess precisely enough. Our proposal of a cost calculation method is a step in the right direction to solving this problem by allowing anyone to access fast and simple of use algorithms.

The second impact affects both the society and the economy by improving the population's health and productivity all the while increasing the attractiveness of the health care activity. The surgical literature has, up to this point, greatly neglected some of these impacts with few studies taking all of them into account in the same assessment. Our synthesis and discussions of the various impact measures is meant to contribute in determining the possibility of combining these measures.

A particularly innovative point of this thesis lies in the exploration of how to integrate the research and development process's impact (third impact) into a cost-benefit equation. To meet this objective, we created our own method enabling a project by project evaluation of the IHU's R&D activity.

In that sense, our work has helped establish several complementary impact assessment methodologies to conduct a comprehensive cost-benefit analysis. The ensuing cost-benefit ratio would not only express the impact of an innovation's use on the patient and the economy but would also take into account the creation process's impacts.

The next step for validating our methods would consist in testing their complementarity by applying them to a single surgical technology. To do this, however, the IHU must focus on establishing a data collection system specifically designed to make such analysis possible.

In order to expand our method, it would be essential to further develop the assessment tools for some measures of effectiveness. Medical tourism, for example, was evaluated by following a cost-benefit method while an input-output analysis could prove to be wider. Furthermore, analyzing the impact of surgical innovations on learning abilities and education could represent a real added value. Indeed, one of the particularities of surgical practice is the importance of experience gain, its transmission and impact on treatments. To complete our methodologies, it is essential to explore the possibilities of assessing the impact that a surgical technology could have on these dimensions.

Even though health is a unique and fundamental right, universally regarded as having no price, it has, like any other economic good, a cost that is constantly growing with the development of medical innovations and the aging of populations. The importance of integrating discussions of socio-economic impacts in the use and development processes of innovative minimally invasive surgical technologies have already become essential to their emergence. Luckily, with the right tools, the IHU and any other institute specialized in the development and use of innovative surgical technologies can already prepare for the many challenges that such changes will induce.

Bibliography

Adam, J. and Stevens, A. March 2011. Comment on: The cost of a QALY. *QJM*, 104 (3):272–273.

Apelgren, K. N., Blank, M. L., Slomski, C. A., and Hadjis, N. S. 1994. Reusable instruments are more cost-effective than disposable instruments for laparoscopic cholecystectomy. *Surgical endoscopy*, 8(1):32–34.

Arrow, K. J. 1963. Uncertainty and the welfare economics of medical care. *Bulletin of the World Health Organization*, 82(2):141–149.

Arthur, W. B. 1989. Competing technologies, increasing returns, and lock-in by historical events. *The economic journal*, 99(394):116–131.

ASMBS. Story Of Obesity Surgery. URL https://asmbs.org/resources/story-of-obesity-surgery. [Accessed July 6, 2015].

Avadikyan, A., Bach, L., Guittard, C., Héraud, J.-A., Hussler, C., Kahn, R., Lambert, G., Lerch, C., Muller, E., Müller, M., Pénin, J., and Wolff, S. 2013. Evaluation of research infrastructures in open innovation and research systems. Final Report, Delivrable D5.2, Contract n262281, FP7 (Parts I and III available at http://evario.u-strasbg.fr/final-report) .

Bach, L., Héraud, J.-A., and Matt, M. 2008. L'évaluation des effets économiques des grands programmes publics de R&D. Colloque europèen de la Société Française d'Evaluation.

Banzi, R., Moja, L., Pistotti, V., Facchini, A., and Liberati, A. 2011. Conceptual frameworks and empirical approaches used to assess the impact of health research: an overview of reviews. *Health Research Policy and Systems*, 9(1):26.

Baregheh, A., Rowley, J., and Sambrook, S. 2009. Towards a multidisciplinary definition of innovation. *Management Decision*, 47(8):1323–1339.

Barkun, J. S., Aronson, J. K., Feldman, L. S., Maddern, G. J., and Strasberg, S. M. 2009. Evaluation and stages of surgical innovations. *The Lancet*, 374(9695):1089–1096.

Bloom, D. E., Canning, D., and Sevilla, J. 2004. The Effect of Health on Economic Growth: A Production Function Approach. *World Development*, 32(1):1–13.

Bolenz, C., Gupta, A., Hotze, T., Ho, R., Cadeddu, J. A., Roehrborn, C. G., and Lotan, Y. 2010. Cost Comparison of Robotic, Laparoscopic, and Open Radical Prostatectomy for Prostate Cancer. *European Urology*, 57(3):453–458.

Brazier, J. E., Harper, R., Jones, N. M., O'Cathain, A., Thomas, K. J., Usherwood, T., and Westlake, L. 1992. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ : British Medical Journal*, 305(6846):160–164.

Breitenstein, S., Nocito, A., Puhan, M., Held, U., Weber, M., and Clavien, P.-A. 2008. Robotic-assisted Versus Laparoscopic Cholecystectomy. *Annals of Surgery*, 247(6): 987–993.

Broome, J., Pomeroy, S., and Solorzano, C. C. 2012. Expense of robotic thyroidectomy: A cost analysis at a single institution. *Archives of Surgery*, 147(12):1102–1106.

Brutscher, P.-B., Wooding, S., and Grant, J. 2008. Health research evaluation frameworks. Technical report.

Buchwald, H., Avidor, Y., Braunwald, E., Jensen, M. D., Pories, W., Fahrbach, K., and Schoelles, K. 2004. Bariatric surgery: a systematic review and meta-analysis. *JAMA*, 292(14):1724–1737.

Burfisher, M. E. 2011. *Introduction to Computable General Equilibrium Models*. Cambridge University Press.

Burgan, B. J. and Mules, T. 2000. Event Analysis - Understanding the Divide Between Cost Benefit and Economic Impact Assesssment. Australian Centre for Event Management.

Burton, W. N., Morrison, A., and Wertheimer, A. I. 2003. Pharmaceuticals and Worker Productivity Loss: A Critical Review of the Literature. *Journal of Occupational and Environmental Medicine*, 45(6):610–621.

CADTH. 2006. Guidelines for the economic evaluation of health technologies Canada. Technical report, Canadian Agency for Drugs and Technologies in Health.

Cahill, P. J., Pahys, J. M., Asghar, J., Yaszay, B., Marks, M. C., Bastrom, T. P., Lonner, B. S., Shah, S. A., Shufflebarger, H. L., Newton, P. O., Betz, R. R., and Samdani, A. F. 2014. The Effect of Surgeon Experience on Outcomes of Surgery for Adolescent Idiopathic Scoliosis. *The Journal of Bone & Joint Surgery*, 96(16):1333–1339.

CBO. 2008. Technological change and the growth of health care spending. Technical report.

Charlton, B. G. 2006. Boom or bubble? Is medical research thriving or about to crash? *Medical Hypotheses*, 66(1):1–2.

Chassany, O., Marquis, P., Scherrer, B., Read, N., Finger, T., Bergmann, J., Fraitag, B., Geneve, J., and Caulin, C. 1999. Validation of a specific quality of life questionnaire for functional digestive disorders. *Gut*, 44(4):527–533.

Christensen, C. M. 1997. *The innovator's dilemma: when new technologies cause great firms to fail*. The management of innovation and change series. Harvard Business School Press, Boston, Mass.

Clarke, A. 1996. Why are we trying to reduce length of stay? Evaluation of the costs and benefits of reducing time in hospital must start from the objectives that govern change. *Quality in Health Care*, 5(3):172–179.

Collins, J. J., Baase, C. M., Sharda, C. E., Ozminkowski, R. J., Nicholson, S., Billotti, G. M., Turpin, R. S., Olson, M., and Berger, M. L. 2005. The Assessment of Chronic Health Conditions on Work Performance, Absence, and Total Economic Impact for Employers. *Journal of Occupational and Environmental Medicine*, 47(6):547–557.

Connell, J. 2006. Medical tourism: Sea, sun, sand and ... surgery. *Tourism Management*, 27(6):1093–1100.

Connell, J. 2013. Medical tourism in the Caribbean Islands: a cure for economies in crisis? *Island Studies Journal*, 8(1):115–130.

Costi, R., Himpens, J., Bruyns, J., and Cadière, G. B. 2003. Robotic fundoplication: from theoretic advantages to real problems. *Journal of the American College of Surgeons*, 197(3):500–507.

Dahlin, K. B. and Behrens, D. M. 2005. When is an invention really radical?: Defining and measuring technological radicalness. *Research Policy*, 34(5):717–737.

Darzi, A. and Munz, Y. 2004. The Impact of Minimally Invasive Surgical Techniques. *Annual Review of Medicine*, 55(1):223–237.

Delaney, C. P., Senagore, A. J., and Fazio, V. W. 2003. Comparison of robotically performed and traditional laparoscopic colorectal surgery. *Diseases of the colon & rectum*, 46(12):1633–1639.

Deloitte. 2008. Medical tourism: Consumers in search of value. Technical report, Deloitte Center for Health Solutions.

Dennis, T., de Mendonça, C., Phalippou, J., Collinet, P., Boulanger, L., Weingertner, F., Leblanc, E., and Narducci, F. 2012. Study of surplus cost of robotic assistance for radical hysterectomy, versus laparotomy and standard laparoscopy. *Gynécologie Obstétrique & Fertilité*, 40(2):77–83.

Desborough, J. P. 2000. The stress response to trauma and surgery. *British Journal of Anaesthesia*, 85(1):109–117.

DGOS. Financement des ́tablissements de sant́. URL http://www.sante.gouv.fr/financement-des-etablissements-de-sante,6619.html. [Accessed Mars 31, 2015].

Donaldson, C., Baker, R., Mason, H., Pennington, M., Bell, S., Lancsar, E., Jones-Lee, M., Wildman, J., Robinson, A., Bacon, P., Olsen, J. A., Gyrd-Hansen, D., Kjaer, T., Bech, M., Nielsen, J. S., Persson, U., Bergman, A., Protière, C., Moatti, J. P., Luchini, S., Prades, J. L. P., Mataria, A., Khatiba, R. A., Jarallah, Y., van Exel, J., Brouwer, W., Topór, R.-M., Kozierkiewicz, A., Poznanski, D., Kocot, E., Gulácsi, L., Péntek, M., Manca, A., Kharroubi, S., and Shackley, P. 2010. European value of a quality adjusted life year. Technical report, EuroVaq.

Donovan, C. and Hanney, S. 2011. The 'Payback Framework' explained. *Research Evaluation*, 20(3):181–183.

Dosi, G. 1988. Sources, procedures, and microeconomic effects of innovation. *Journal of economic literature*, pages 1120–1171.

Dosi, G., Freeman, C., Nelson, R., Silverberg, G., and Soete, L. L. 1988. *Technical Change and Economic Theory*.

DRESS. 2014. Les comptes nationaux de la santé en 2013. Technical report.

Drummond, M., Griffin, A., and Tarricone, R. 2009. Economic Evaluation for Devices and Drugs–Same or Different? *Value in Health*, 12(4):402–404.

Drummond, M. F., Sculpher, M. J., Torrance, G. W., O'Brien, B. J., and Stoddart, G. L. 2005. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford University Press, USA, 3 edition.

DSS. 2014. Les chiffres clés de la sécurité sociale 2013. Technical report.

DSTI. 2009. Enhancing public research performance through evaluation, impact assessment and priority setting. Technical report, Directorate for science, technology and industry.

El nakadi, I., Mélot, C., Closset, J., De Moor, V., Bétroune, K., Feron, P., Lingier, P., and Gelin, M. 2006. Evaluation of da Vinci Nissen Fundoplication Clinical Results and Cost Minimization. *World Journal of Surgery*, 30(6):1050–1054.

El Nakadi, I., Mélot, C., Closset, J., De Moor, V., Bétroune, K., Feron, P., Lingier, P., and Gelin, M. 2006. Evaluation of da vinci nissen fundoplication clinical results and cost minimization. *World Journal of Surgery*, 30(6):1050–1054.

Eltabbakh, G. H. 2000. Effect of surgeon's experience on the surgical outcome of laparoscopic surgery for women with endometrial cancer. *Gynecologic Oncology*, 78 (1):58–61.

Ergina, P. L., Cook, J. A., Blazeby, J. M., Boutron, I., Clavien, P.-A., Reeves, B. C., and Seiler, C. M. 2009. Challenges in evaluating surgical innovation. *Lancet*, 374 (9695):1097–1104.

European Commission. 2004. Evaluating EU acrivities: a practical guide for the commission services. Technical report, Luxembourg.

Eypasch, E., Williams, J. I., Wood-Dauphinee, S., Ure, B. M., Schmülling, C., Neugebauer, E., and Troidl, H. 1995. Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. *The British Journal of Surgery*, 82 (2):216–222.

Fahrenkrog, G., Polt, W., Rojo, J., Tübke, A., Zinöcker, K., Arvanitis, S., Boden, M., Bührer, S., Capron, H., Cincera, M., Cowan, R., Eaton, J., Georghiou, L., Keilbach, M., Kinsella, E., Kuhlmann, S., Licht, G., Patel, P., Rigby, J., Sirilli, G., Stern, E., and Woitech, B. 2002. RTD evaluation toolbox. *European Commission, Seville*.

Finances Hospitalières. Finalités et définitions des indices de coût relatif (icr). URL http://finances-hospitalieres.fr/print.asp?67A054883B78B9. [Accessed Mars 5, 2015].

Finch, W. H., Bolin, J. E., and Kelley, K. 2014. *Multilevel Modeling Using R*. CRC Press, Boca Raton, FL, 1 edition edition.

Finkler, S. A. 1982. The distinction between cost and charges. *Annals of internal medicine*, 96(1):102–109.

Fontaine, K. R., Redden, D. T., Wang, C., Westfall, A. O., and Allison, D. B. 2003. Years of life lost due to obesity. *JAMA*, 289(2):187–193.

Francis, D. and Bessant, J. 2005. Targeting innovation and implications for capability development. *Technovation*, 25(3):171–183.

FTEVAL. 2013. Research and technology policy evaluation evaluation standards in research and technology policy. Technical report, Austrian Platform for Research & Technology Policy Evaluation.

Furlong, W. J., Feeny, D. H., Torrance, G. W., and Barr, R. D. 2001. The Health Utilities Index (HUI) system for assessing health-related quality of life in clinical studies. *Annals of Medicine*, 33(5):375–384.

Garcia, R. and Calantone, R. 2002. A critical look at technological innovation typology and innovativeness terminology: a literature review. *Journal of Product Innovation Management*, 19(2):110–132.

Georghiou, L., Rigby, J., Cameron, H., Vonortas, N., Prastacos, G., Spanos, Y., Kuhlmann, S., Henize, T., Bach, L., Cohendet, P., and others. 2002. Assessing the Socio-economic Impacts of the Framework Programme (ASIF).

Goetzel, R. Z., Long, S. R., Ozminkowski, R. J., Hawkins, K., Wang, S., and Lynch, W. 2004. Health, Absence, Disability, and Presenteeism Cost Estimates of Certain Physical and Mental Health Conditions Affecting U.S. Employers. *Journal of Occupational and Environmental Medicine*, 46(4):398–412.

Gold, M. R. 1996. *Cost-Effectiveness in Health and Medicine*. Oxford University Press.

Gordon, T. A. and Cameron, J. L. 2000. *Evidence-based Surgery*. PMPH-USA.

Guthrie, S., Wamae, W., Diepeveen, S., Wooding, S., and Grant, J. 2013. Measuring research: A guide to research evaluation frameworks and tools. Technical report.

Hagen, M. E., Pugin, F., Chassot, G., Huber, O., Buchs, N., Iranmanesh, P., and Morel, P. 2012. Reducing Cost of Surgery by Avoiding Complications: the Model of Robotic Roux-en-Y Gastric Bypass. *Obesity Surgery*, 22(1):52–61.

Hanney, S. R., Grant, J., Wooding, S., and Buxton, M. J. 2004. Proposed methods for reviewing the outcomes of health research: the impact of funding by the UK's' Arthritis Research Campaign'. *Health research policy and systems*, 2(1):4.

Harrell, A. G. and Heniford, B. T. 2005. Minimally invasive abdominal surgery: lux et veritas past, present, and future. *The American Journal of Surgery*, 190(2):239–243.

HAS. 2012. Choices in methods for economic evaluation. Technical report, Haute Autorité de Santé.

HAS N37. L'évaluation médico-économique prend une nouvelle ampleur. URL http://www.has-sante.fr/portail/jcms/c_1649369/fr/l-evaluation-medico-economique-prend-une-nouvelle-ampleur. [Accessed October 6, 2015].

Healey, A. and Chisholm, D. 1999. Willingness to pay as a measure of the benefits of mental health care. *The journal of mental health policy and economics*, 2(2):55–58.

Horowitz, M. D., Rosensweig, J. A., and Jones, C. A. 2007. Medical Tourism: Globalization of the Healthcare Marketplace. *Medscape General Medicine*, 9(4):33.

Hout, W. B. v. d. 2010. The value of productivity: human-capital versus friction-cost method. *Annals of the rheumatic diseases*, 69 Suppl 1:i89–91.

Hubens, G., Balliu, L., Ruppert, M., Gypen, B., Tu, T., and Vaneerdeweg, W. 2007. Roux-en-Y gastric bypass procedure performed with the da Vinci robot system: is it worth it? *Surgical Endoscopy*, 22(7):1690–1696.

INCA. 2015. Les cancers en france. Technical report, Insitut National du Cancer.

INSEE. Les salaires dans l'industrie, le commerce et les services en 2010. URL Lessalairesdansl'industrie,lecommerceetlesservicesen2010. [Accessed October 6, 2015].

Intuitive Surgical. The da vinci® surgical system. URL http://www.intuitivesurgical.com/products/davinci_surgical_system/. [Accessed 31-May-2013].

Ismail, I., Wolff, S., Gronfier, A., Mutter, D., and Swanström, L. L. October 2014. A cost evaluation methodology for surgical technologies. *Surgical Endoscopy*, pages 1–10.

ISPOR. Pharmacoeconomic guidelines around the world. URL http://www.ispor.org/peguidelines/index.asp. [Accessed April 28, 2015].

Jackson, J., Houghton, M., Russell, R., and Triandos, P. 2005. Innovations in Measuring Economic Impacts of Regional Festivals: A Do-It-Yourself Kit. *Journal of Travel Research*, 43(4):360–367.

Johannesson, M. 1996. The willingness to pay for health changes, the human-capital approach and the external costs. *Health Policy*, 36(3):231–244.

Johns, G. 2009. Presenteeism in the workplace: A review and research agenda. *Journal of Organizational Behavior*, 31(4):519–542.

Johnston, R., Crooks, V. A., Snyder, J., and Kingsbury, P. 2010. What is known about the effects of medical tourism in destination and departure countries? A scoping review. *International Journal for Equity in Health*, 9:24.

Katz, M. L. and Shapiro, C. 1985. Network externalities, competition, and compatibility. *The American economic review*, pages 424–440.

Kingkaew, P. and Teerawattananon, Y. 2014. The economic evaluation of medical devices: challenges. *Journal of the Medical Association of Thailand*, 97 Suppl 5: S102–107.

Kirisits, A. and Redekop, W. K. 2013. The Economic Evaluation of Medical Devices: Challenges Ahead. *Applied Health Economics and Health Policy*, 11(1):15–26.

Kirkdale, R., Krell, J., Brown, C. O., Tuthill, M., and Waxman, J. 2010. The cost of a QALY. *QJM: An International Journal of Medicine*, 103(9):715–720.

Koberg, C. S., Detienne, D. R., and Heppard, K. A. 2003. An empirical test of environmental, organizational, and process factors affecting incremental and radical innovation. *The Journal of High Technology Management Research*, 14(1):21–45.

Kristensen, F. B. and Sigmund, H. 2007. *Health Technology Assessment Handbook*. National Board of Health.

Krol, M., Papenburg, J., Koopmanschap, M., and Brouwer, W. 2011. Do productivity costs matter? the impact of including productivity costs on the incremental costs of interventions targeted at depressive disorders. *PharmacoEconomics*, 29(7):601–619.

Kunisaki, C., Makino, H., Takagawa, R., Sato, K., Kawamata, M., Kanazawa, A., Yamamoto, N., Nagano, Y., Fujii, S., Ono, H. A., Akiyama, H., and Shimada, H. 2009. Predictive factors for surgical complications of laparoscopy-assisted distal gastrectomy for gastric cancer. *Surgical Endoscopy*, 23(9):2085–2093.

Kurichi, J. E. and Sonnad, S. S. 2006. Statistical Methods in the Surgical Literature. *Journal of the American College of Surgeons*, 202(3):476–484.

Larsen, R. J., Asmussen, M., Christensen, T., Olsen, J., Bo Poulsen, P., and Sørensen, J. 2003. Economic Evaluations in International Health Technology Assessments - A Study of Methodologies. *Danish Health Technology Assessment*, 5.

Lau, S., Vaknin, Z., Ramana-Kumar, A. V., Halliday, D., Franco, E. L., and Gotlieb, W. H. 2012. Outcomes and Cost Comparisons After Introducing a Robotics Program for Endometrial Cancer Surgery. *Obstetrics & Gynecology*, 119(4):717–724.

Lee, R., Ng, C. K., Shariat, S. F., Borkina, A., Guimento, R., Brumit, K. F., and Scherr, D. S. 2011. The economics of robotic cystectomy: cost comparison of open versus robotic cystectomy. *BJU International*, 108(11):1886–1892.

Lettl, C., Herstatt, C., and Gemuenden, H. G. 2006. Users' contributions to radical innovation: evidence from four cases in the field of medical equipment technology. *R&D Management*, 36(3):251–272.

Lettl, C., Hienerth, C., and Gemuenden, H. G. 2008. Exploring How Lead Users Develop Radical Innovation: Opportunity Recognition and Exploitation in the Field of Medical Equipment Technology. *IEEE Transactions on Engineering Management*, 55(2):219–233.

Liang, K.-Y. and Zeger, S. L. 1986. Longitudinal data analysis using generalized linear models. *Biometrika*, 73(1):13–22.

Lieberman, M. B. and Montgomery, D. B. 1988. First-mover advantages. *Strategic Management Journal*, 9(S1):41–58.

Lotan, Y., Cadeddu, J. A., and Gettman, M. T. 2004. The new economics of radical prostatectomy: cost comparison of open, laparoscopic, and robot-assisted technique. *The Journal of Urology*, 172(4, Part 1):1431–1435.

Lunt, N. and Carrera, P. 2010. Medical tourism: Assessing the evidence on treatment abroad. *Maturitas*, 66(1):27–32.

Mack MJ. 2001. MInimally invasive and robotic surgery. *The Journal of the American Medical Association*, 285(5):568–572.

Markides, C. 2006. Disruptive Innovation: In Need of Better Theory. *Journal of Product Innovation Management*, 23(1):19–25.

Massetti, M., Aballéa, S., Videau, Y., Rḿuzat, C., Roïz, J., and Toumi, M. 2015. A comparison of HAS & NICE guidelines for the economic evaluation of health technologies in the context of their respective national health care systems and cultural environments. *Journal of Market Access & Health Policy*, 3(0).

Mathes, T., Jacobs, E., Morfeld, J.-C., and Pieper, D. 2013. Methods of international health technology assessment agencies for economic evaluations–a comparative analysis. *BMC health services research*, 13:371.

McCulloch, P., Altman, D. G., Campbell, W. B., Flum, D. R., Glasziou, P., Marshall, J. C., and Nicholl, J. 2009. No surgical innovation without evaluation: the IDEAL recommendations. *The Lancet*, 374(9695):1105–1112.

McDonald, J. H. 2009. *Handbook of biological statistics*, volume 2. Sparky House Publishing Baltimore, MD.

McIlwaine, K., Manwaring, J., Ellett, L., Cameron, M., Readman, E., Villegas, R., and Maher, P. 2014. The effect of patient body mass index on surgical difficulty in gynaecological laparoscopy. *The Australian & New Zealand Journal of Obstetrics & Gynaecology*, 54(6):564–569.

Morgan, J., Thornton, B., Peacock, J., Hollingsworth, K., Smith, C., Oz, M., and Argenziano, M. 2005. Does robotic technology make minimally invasive cardiac surgery too expensive? a hospital cost analysis of robotic and conventional techniques. *Journal of cardiac surgery*, 20(3):246–251.

Morino, M., Benincà, G., Giraudo, G., Genio, G. M. D., Rebecchi, F., and Garrone, C. 2004. Robot-assisted vs laparoscopic adrenalectomy: a prospective randomized controlled trial. *Surgical Endoscopy And Other Interventional Techniques*, 18(12): 1742–1746.

Morino, M., Baracchi, F., Miglietta, C., Furlan, N., Ragona, R., and Garbarini, A. 2006. Preoperative endoscopic sphincterotomy versus laparoendoscopic rendezvous in patients with gallbladder and bile duct stones. *Annals of Surgery*, 244(6):889–893; discussion 893–896.

Morris, S., Devlin, N., and Parkin, D. 2007. *Economic Analysis in Health Care*. Wiley, Chichester ; Hoboken, NJ, 2 edition edition.

NaRanong, A. and NaRanong, V. 2011. The effects of medical tourism: Thailand's experience. *Bulletin of the World Health Organization*, 89(5):336–344.

NICE. 2013. Guide to the methods of technology appraisal 2013. Technical report, National Institute for Health and Care Excellence.

Nooteboom, B., Van Haverbeke, W., Duysters, G., Gilsing, V., and van den Oord, A. 2007. Optimal cognitive distance and absorptive capacity. *Research Policy*, 36(7): 1016–1034.

O'Brien, P. E., McPhail, T., Chaston, T. B., and Dixon, J. B. 2006. Systematic review of medium-term weight loss after bariatric operations. *Obesity Surgery*, 16(8):1032–1040.

O'Connell, A. A. and McCoach, D. B. 2004. Applications of Hierarchical Linear Models for Evaluations of Health Interventions Demystifying the Methods and Interpretations of Multilevel Models. *Evaluation & the Health Professions*, 27(2):119–151.

Oria, H. E. and Moorehead, M. K. 1998. Bariatric analysis and reporting outcome system (BAROS). *Obesity Surgery*, 8(5):487–499.

Oria, H. E. and Moorehead, M. K. 2009. Updated Bariatric Analysis and Reporting Outcome System (BAROS). *Surgery for Obesity and Related Diseases*, 5(1):60–66.

Panel on Return on Investment in Health Research. 2009. Making an impact: A preferred framework and indicators to measure returns on investment in health research. Technical report.

Park, C. W., Lam, E. C. F., Walsh, T. M., Karimoto, M., Ma, A. T., Koo, M., Hammill, C., Murayama, K., Lorenzo, C. S. F., and Bueno, R. 2011. Robotic-assisted Roux-en-Y gastric bypass performed in a community hospital setting: the future of bariatric surgery? *Surgical Endoscopy*, 25(10):3312–3321.

Pasic, R. P., Rizzo, J. A., Fang, H., Ross, S., Moore, M., and Gunnarsson, C. 2010. Comparing Robot-Assisted with Conventional Laparoscopic Hysterectomy: Impact on Cost and Clinical Outcomes. *Journal of Minimally Invasive Gynecology*, 17(6): 730–738.

Pauly, M. V., Nicholson, S., Xu, J., Polsky, D., Danzon, P. M., Murray, J. F., and Berger, M. L. 2002. A general model of the impact of absenteeism on employers and employees. *Health Economics*, 11(3):221–231.

Peeters, A., Barendregt, J. J., Willekens, F., Mackenbach, J. P., Al Mamun, A., Bonneux, L., and NEDCOM, the Netherlands Epidemiology and Demography Compression of Morbidity Research Group. 2003. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Annals of Internal Medicine*, 138(1):24–32.

Phillips, C. and Thompson, G. 2009. *What is a QALY?*, volume 1. Hayward Medical Communications.

Preedy, V. R., Watson, R. R., and Martin, C. R. 2011. *Handbook of Behavior, Food and Nutrition*. Springer Science & Business Media.

R Development Core Team. 2011. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/. ISBN 3-900051-07-0.

Riskin, D. J., Longaker, M. T., Gertner, M., and Krummel, T. M. 2006. Innovation in Surgery. *Annals of Surgery*, 244(5):686–693.

Ritala, P. and Hurmelinna-Laukkanen, P. 2013. Incremental and Radical Innovation in Coopetition – The Role of Absorptive Capacity and Appropriability. *Journal of Product Innovation Management*, 30(1):154–169.

Roback, K., Dalal, K., and Carlsson, P. 2011. Evaluation of Health Research: Measuring Costs and Socioeconomic Effects. *International Journal of Preventive Medicine*, 2(4): 203–215.

Rosenberg, L. and Schlich, T. 2012. Twenty-first century surgery: Have we entered uncharted waters? *Bulletin of the American College of Surgeons*, 97(7):6–11.

Rosenberg, N. 1996. Uncertainty and technological change. *Conference Series ; [Proceedings]*, 40(Jun):91–125.

Rosenberg, N., Gelijns, A. C., and Dawkins, H. 1995. *Sources of Medical Technology: Universities and Industry*. National Academies Press.

Round, J. 2012. Is a QALY still a QALY at the end of life? *Journal of Health Economics*, 31(3):521–527.

Ruegg, R. and Jordan, G. 2007. Overview of evaluation methods for R&D programs. Technical report.

Sarlos, D., Kots, L., Stevanovic, N., and Schaer, G. 2010. Robotic hysterectomy versus conventional laparoscopic hysterectomy: Outcome and cost analyses of a matched case-control study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 150(1):92–96.

Schultz, A. B., Chen, C.-Y., and Edington, D. W. 2009. The Cost and Impact of Health Conditions on Presenteeism to Employers. *PharmacoEconomics*, 27(5):365–378.

Schumpeter, J. A. 1934. *The Theory of Economic Development: An Inquiry Into Profits, Capital, Credit, Interest, and the Business Cycle*. Transaction Publishers. ISBN 978-0-87855-698-4.

Sécurité Sociale. Historique du système français de sécurité sociale. URL http://www.securite-sociale.fr/

Historique-du-systeme-francais-de-Securite-sociale. [Accessed October 7, 2015].

Skinner, B. J. 2013. Medical devices and healthcare costs in Canada and 65 other countries, 2006 to 2011. *Canadian Health Policy*, pages 1–15.

Smith, A., Kurpad, R., Lal, A., Nielsen, M., Wallen, E. M., and Pruthi, R. S. 2010. Cost Analysis of Robotic Versus Open Radical Cystectomy for Bladder Cancer. *The Journal of Urology*, 183(2):505–509.

Smith, R., Martinez alvarez, M., and Chanda, R. 2011. Medical tourism: A review of the literature and analysis of a role for bi-lateral trade. *Health Policy*, 103(2-3): 276–282.

Sorenson, C., Drummond, M., and Bhuiyan-Khan, B. 2013. Medical technology as a key driver of rising health expenditure: disentangling the relationship. *ClinicoEconomics and Outcomes Research*, page 223.

Sosa, J. A., Bowman, H. M., Tielsch, J. M., Powe, N. R., Gordon, T. A., and Udelsman, R. 1998. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. *Annals of Surgery*, 228(3):320–330.

Swanstrom, L. L., Rieder, E., and Dunst, C. M. 2011. A stepwise approach and early clinical experience in peroral endoscopic myotomy for the treatment of achalasia and esophageal motility disorders. *Journal of the American College of Surgeons*, 213(6): 751–756.

Taylor, R. S. and Iglesias, C. P. 2009. Assessing the clinical and cost-effectiveness of medical Devices and Drugs: Are They That Different? *Value in Health*, 12(4): 404–406.

Technopolis group & MIOIR. 2012. Evaluation of innovation activities. guidanceon methods and practices. Technical report, Study funded by the European Commission, Directorate for Regional Policy.

Tidd, J., Bessant, J., and Pavitt, K. 2005. *Managing Innovation: Integrating Technological, Market and Organizational Change*. John Wiley & Sons, Hoboken, 3rd edition edition edition.

Torrance, G. W., Feeny, D., and Furlong, W. 2001. Visual Analog Scales Do They Have a Role in the Measurement of Preferences for Health States? *Medical Decision Making*, 21(4):329–334.

van Dam, P., Hauspy, J., Verkinderen, L., Trinh, X., van Dam, P., Van Looy, L., and Dirix, L. 2011. Are costs of robot-assisted surgery warranted for gynecological procedures? *Obstetrics and Gynecology International*, 2011:1–6.

Venkat, P., Chen, L.-M., Young-Lin, N., Kiet, T. K., Young, G., Amatori, D., Dasverma, B., Yu, X., Kapp, D. S., and Chan, J. K. 2012. An economic analysis of robotic versus laparoscopic surgery for endometrial cancer: Costs, charges and reimbursements to hospitals and professionals. *Gynecologic Oncology*, 125(1):237–240.

von Hippel, E. 1976. The dominant role of users in the scientific instrument innovation process. *Research Policy*, 5(3):212–239.

Von Hippel, E. 1986. Lead users: a source of novel product concepts. *Management science*, 32(7):791–805.

Whitehead, S. J. and Ali, S. 2010. Health Outcomes in Economic Evaluation: the QALY and Utilities. *British Medical Bulletin*, 96(1):5–21.

WHO. 2000. The world health report 2000 - health systems: improving performance. Technical report, World Health Organization.

WHO. 2008. WHO guide for standardization of economic evaluations of immunization programmes. Technical report, World Health Organization.

WHO. 2011. Health technology assessment of medical devices. Technical report, World Health Organization.

Wikipedia. Multiple comparisons problem, a. URL https://en.wikipedia.org/wiki/Multiple_comparisons_problem. [Accessed May 22, 2015].

Wikipedia. Joseph schumpeter, b. URL https://fr.wikipedia.org/wiki/Joseph_Schumpeter. [Accessed October 6, 2015].

Wright, J. D., Ananth, C. V., Lewin, S. N., Burke, W. M., Lu, Y.-S., Neugut, A. I., Herzog, T. J., and Hershman, D. L. 2013. Robotically assisted vs laparoscopic hysterectomy among women with benign gynecologic disease. *The American Journal of Surgery*, 309(7):689–698.

Wright, K. N., Jonsdottir, G. M., Jorgensen, S., Shah, N., and Einarsson, J. I. 2012. Costs and Outcomes of Abdominal, Vaginal, Laparoscopic and Robotic Hysterectomies. *Journal of the Society of Laparoendoscopic Surgeons*, 16(4):519–524.

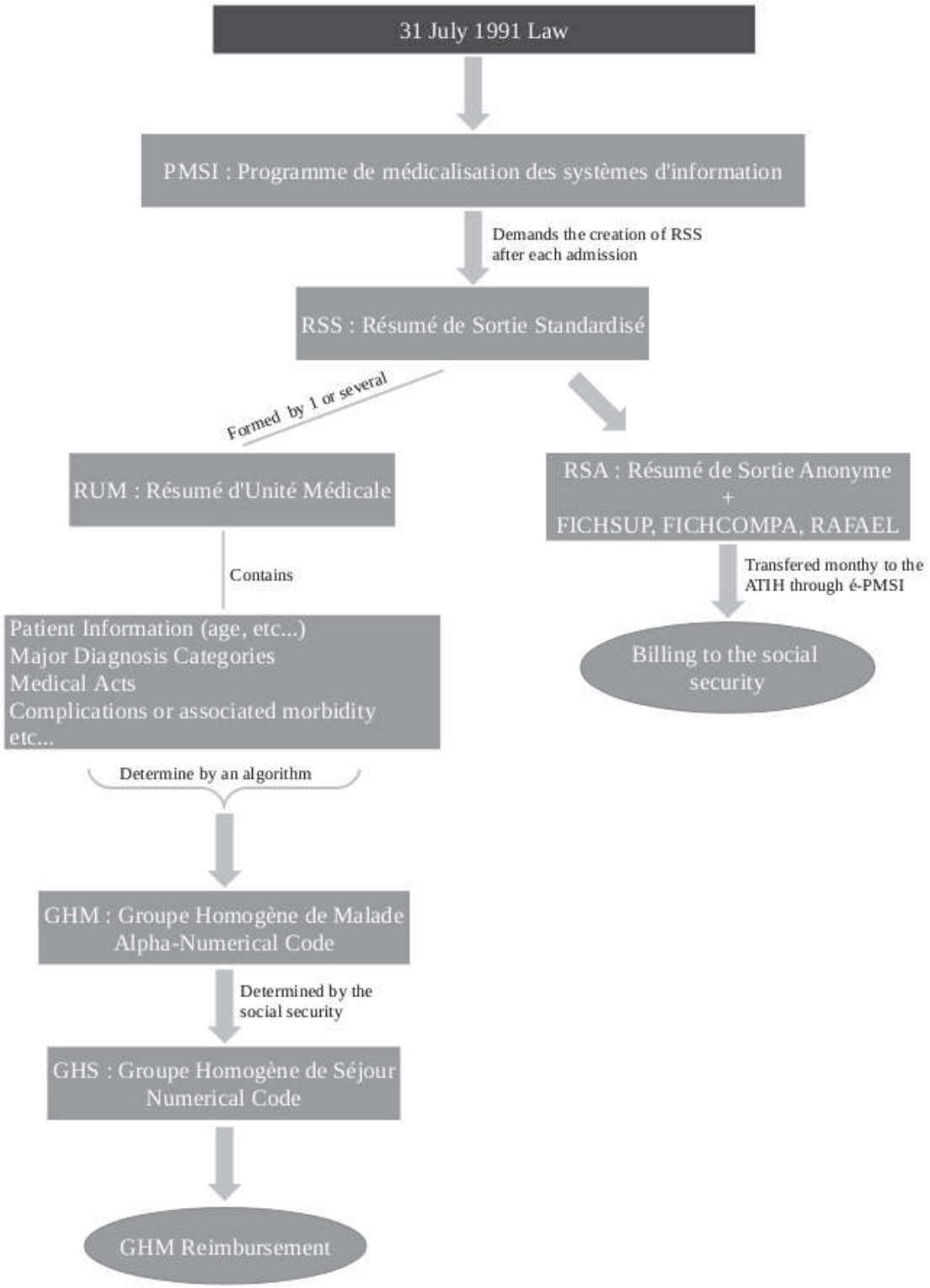
Yazdizadeh, B., Majdzadeh, R., and Salmasian, H. 2010. Systematic review of methods for evaluating healthcare research economic impact. *Health Res Policy Syst*, 8(6).

Yung, E., Gagner, M., Pomp, A., Dakin, G., Milone, L., and Strain, G. 2010. Cost Comparison of Reusable and Single-Use Ultrasonic Shears for Laparoscopic Bariatric Surgery. *Obesity Surgery*, 20(4):512–518.

Appendix

Appendix A

PMSI Description


31 July 1991 Law
PMSI : Programme de médicalisation des systèmes d'information
Demands the creation of RSS after each admission
RSS : Résumé de Sortie Standardisé
Formed by 1 or several
RUM : Résumé d'Unité Médicale
Contains
Patient Information (age, etc...)
Major Diagnosis Categories
Medical Acts
Complications or associated morbidity
etc...
Determine by an algorithm
GHM : Groupe Homogène de Malade
Alpha-Numerical Code
Determined by the social security
GHS : Groupe Homogène de Séjour
Numerical Code
GHM Reimbursement
RSA : Résumé de Sortie Anonyme
+
FICHSUP, FICHCOMPA, RAFAEL
Transfered monthy to the ATIH through é-PMSI
Billing to the social security

Appendix B

Demonstration: Medical Equipment

Objective:

MEC_i= Cost per operation of medical device i's purchase and maintenance costs.

Let:

- P_i = Purchase price
- M_i = Maintenance fee per year
- E_i = life expectancy expressed in years
- N_i = Mean number of operations per year for which medical device has been used
- r = discount rate

$$\text{Purchase cost per operation} = \frac{P_i}{E_i \times N_i}$$

$$\text{Year n's maintenance discounted present value} = M_i \times \frac{1}{(1+r)^n}$$

$$\begin{aligned}
\text{Maintenance cost per operation} &= \frac{1}{E_i \times N_i} \times (M_i + M_i \times \frac{1}{1+r} + \cdots + M_i \times \frac{1}{(1+r)^{E_i}}) \\
&= \frac{1}{E_i \times N_i} \times M_i \times (1 + \frac{1}{1+r} + \cdots + \frac{1}{(1+r)^{E_i}}) \\
&= \frac{1}{E_i \times N_i} \times M_i \times \frac{1 - (\frac{1}{1+r})^{E_i+1}}{1 - \frac{1}{1+r}} \\
&= \frac{1}{E_i \times N_i} \times M_i \times \frac{1 - (1+r)^{-E_i-1}}{1 - (1+r)^{-1}}
\end{aligned}$$

By summing the Purchase cost and Maintenance cost per operation:

$$MEC_i = \frac{1}{E_i \times N_i}(P_i + M_i \times \frac{1 - (1+r)^{-E_i-1}}{1 - (1+r)^{-1}})$$

Appendix C

Demonstration: Personnel

Objective:

PC_i = Personnel i's cost per operation

Let:

- W_i = Annual loaded salary
- L_i = Weekly paid working hours
- t_i = Mean time spent in operations, expressed in minutes

$$\text{Monthly loaded salary} = \frac{W_i}{12}$$

$$\text{Weekly paid working minutes} = L_i \times 60$$

$$\text{Effective working days per month} = \frac{Effective\ working\ days\ per\ year}{12}$$
$$= \frac{(Working\ days\ per\ year - Paid\ leave)}{12}$$

$$\text{Effective working weeks per month} = \frac{Effective\ working\ days\ per\ month}{5}$$
$$= \frac{(Working\ days\ per\ year - Paid\ leave)}{(12 \times 5)}$$

$$\text{Effective working minutes per month} = (L_i \times 60) \times \frac{(Working\ days\ per\ year - Paid\ leave)}{60}$$
$$= L_i \times (Effective\ working\ days\ per\ year)$$

Cost per minute of personnel i × Minutes personnel i spent in operation j:

$$PC_i = \frac{\frac{W_i}{12}}{L_i \times (Effective\ working\ days\ per\ year)} \times t_i$$
$$= \frac{1}{12} \times \frac{W_i \times t_i}{L_i \times Ewd_i}$$

Appendix D

GIQLI Questionnaire

Durant les 5 derniers jours, vous avez :	Toujours	La plupart du temps	Quelques fois	Rarement	Jamais
1. vous avez eu mal au ventre					
2. vous avez eu la sensation d'avoir l'estomac gonflé					
3. vous avez eu la sensation d'avoir beaucoup de gaz dans le ventre					
4. vous avez été gêné(e) par l'émission de «vents»					
5. vous avez été gêné(e) par des éructations ou des renvois					
6. vous avez été gêné(e) par des bruits de «glouglou» dans le ventre					
7. vous avez été gêné(e) par des selles fréquentes					
8. vous avez mangé avec plaisir et appétit					
	De façon très importante	De façon importante	Un peu	Un tout petit peu	Pas du tout
9. A cause de votre maladie, vous êtes obligé(e) de supprimer certains aliments :					
	Extrêmement mal	Mal	Modérément	Bien	Extrêmement bien
10. Durant les 5 derniers jours, vous avez été capable de surmonter les problèmes quotidiens :					
Durant les 5 derniers jours :	Toujours	La plupart du temps	Quelques fois	Rarement	Jamais
11. Combien de fois votre maladie vous a-t-elle rendu(e) triste ?					
12. Combien de fois avez-vous été anxieux(e) à cause de votre maladie ?					
	Jamais	Rarement	Quelques fois	La plupart du temps	Toujours
13. Durant les 5 derniers jours, combien de fois avez-vous ressenti la joie de vivre :					
Durant les 5 derniers jours :	Toujours	La plupart du temps	Quelques fois	Rarement	Jamais
14. Combien de fois avez-vous été frustré(e) à cause de votre maladie ?					

15. Combien de fois vous êtes-vous senti(e) fatigué(e) ?					
16. Combien de fois avez-vous été souffrant(e)					
	Toutes les nuits	5 ou 6 nuits	3 ou 4 nuits	1 ou 2 nuits	Jamais
17. Durant la dernière semaine, vous êtes-vous réveillé(e) pendant la nuit ?					
	Pour une grande part	Modérément	Un peu	Un tout petit peu	Pas du tout
18. Depuis que vous êtes malade, avez-vous été chagriné(e) par les modifications de votre apparence :					
	Enormément	Beaucoup	Un peu	Un tout petit peu	Pas du tout
19. A quel degré est-ce que la maladie a réduit votre condition physique en général ?					
	pour une grande part	Modérément	Un peu	Un tout petit peu	Pas du tout
20. A cause de votre maladie, vous avez perdu de votre endurance :					
	Majeure	Modérée	Minime	Insignifiante	Nulle vous êtes en forme
21. De par votre maladie, vous estimez la perte de votre tonus :					
	Jamais	Rarement	Quelques fois	La plupart du temps	Toujours
22. Durant les 5 derniers jours, combien de fois avez-vous été capable d'accomplir vos activités habituelles (travail, école, ménage, etc) ?					
23. Durant les 5 derniers jours, vous avez été capable de vaquer à vos loisirs habituels ou d'entreprendre de nouvelles activités :					
	Enormément	Beaucoup	Un peu	Un tout petit peu	Pas du tout
24. Durant les 5 derniers jours, avez-vous été incommodé(e) par le traitement médical ?					

	Pour une très grande part	Pour une grande part	Un peu	Un tout petit peu	Pas du tout
25. Dans quelle mesure votre maladie perturbe-t-elle vos relations avec les autres (famille ou amis) ?					
26. Dans quelle mesure votre maladie a-t-elle causé du tort à votre vie sexuelle ?					
Durant les 5 derniers jours :	Toujours	La plupart du temps	Quelques fois	Rarement	Jamais
27. Combien de fois avez-vous été incommodé(e) par des remontées de liquide ou d'aliments dans la bouche (régurgitations) ?					
28. Vous êtes-vous senti(e) obligé(e) de diminuer la vitesse avec laquelle vous mangez ?					
29. Vous avez eu des problèmes pour avaler					
3. Vous avez ressenti le besoin urgent d'aller à la Selle					
3. Vous avez été incommodé(e) par de la diarrhée :					
32. Vous avez été incommodé(e) par une constipation					
33. Vous avez été incommodé(e) par une nausée :					
34. Vous avez été inquiété(e) par la présence de sang dans les selles :					
35. Vous avez été incommodé(e) par une brûlure ou une acidité remontant dans la poitrine :					
36. Vous avez été incommodé(e) par une incontinence pour les selles :					

Appendix E

BAROS Questionnaire

Questionnaire de qualité de vie Moorehead-Ardelt II
Estime de soi et activités

Cochez les cases correpondant le plus à votre état

1. Estime de soi

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Je ne m'estime pas du tout

Je m'estime beaucoup

2. J'aime les activités physiques

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Pas du tout

Enormément

3. J'ai une vie sociale

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Pas du tout

Très riche

4. Je suis capable de travailler

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Pas du tout

Enormément

5. J'ai une vie sexuelle

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Aucune

Très active

6. La nourriture pour moi

❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑

Je vis pour manger

Je mange pour vivre

Protocole 12-002
Chirurgie bariatrique laparoscopique vs. robot-assistée

Questionnaire de qualité de vie Moorehead-Ardelt II
Estime de soi et activités
Scores

1. Estime de soi


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

2. J'aime les activités physiques


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

3. J'ai une vie sociale


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

4. Je suis capable de travailler


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

5. J'ai une vie sexuelle


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

6. La nourriture pour moi


❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑ ❑
-.50 -.40 -.30 -.20 -.10 +.10 +.20 +.30 +.40 +.50

-3 to -2.1	-2 to -1.1	-1	0	1	1.1 to 2	2.1 to 3
Très mauvaise	Mauvaise	Médiocre			Bonne	Excellente

Qualité de vie

Appendix F

Survey

IMAGE-GUIDED MINIMALLY INVASIVE SURGICAL INSTITUTE

Utility analysis of robotic assistance in laparoscopic surgery

1. In which specialty do you practice robot-assisted surgery ? _____

2. How many years have you been in practice? ___

3. Are you currently practicing robot assisted surgery ? ☐ No ☐ Yes

4. For how many years have you performed/been performing robot-assisted surgery ? ☐ <1 ☐ 1-5 ☐ 5-10 ☐ >10

5. Compared to laparoscopy, what impact does the robotic surgical system have on :

Patient recovery	☐ Negative	☐ No effect	☐ Positive	☐ Don't know
Your surgical skills	☐ Negative	☐ No effect	☐ Positive	☐ Don't know

6. Compared to laparoscopy, how did the introduction of surgical robots affect :

Room occupation time	☐ Decrease	☐ Equal	☐ Increase	☐ Don't know
Overall complication rate	☐ Decrease	☐ Equal	☐ Increase	☐ Don't know
Workplace safety for you and the OR team	☐ Decrease	☐ Equal	☐ Increase	☐ Don't know

Other effects on the surgery : _____

7. Compared to laparoscopy, how would you rank the importance of the following robotic surgical system's advantages ?

	Null	**Low**	**Medium**	**High**	**Don't know**
3D imaging	O	O	O	O	O
4 robotic arms	O	O	O	O	O
Improved ergonomics for surgeons	O	O	O	O	O
Increased range motion of instruments	O	O	O	O	O
Remote operations	O	O	O	O	O

Other advantages : _____

8. Compared to laparoscopy, how would you rank the importance of the following robotic surgical system's disadvantages ?

	Null	**Low**	**Medium**	**High**	**Don't know**
Higher cost	O	O	O	O	O
Lack of direct access to the patient	O	O	O	O	O

Other disadvantages : _____

9. For robotic surgery, how do you perceive the restricted number of instrument use ?

☐ Disadvantage ☐ Indifferent ☐ Advantage ☐ Don't know

10. How would you describe the impact of robotic surgery on your :

Teaching capacity	☐ Negative	☐ No effect	☐ Positive	☐ Don't know
Laparoscopic skills	☐ Negative	☐ No effect	☐ Positive	☐ Don't know
Scientific collaborations with other professionals	☐ Negative	☐ No effect	☐ Positive	☐ Don't know

Other activities : _____

11. What is your point of view regarding the future of the robotic surgical system ?

☐ It's promising
☐ It won't last long
☐ I'm indifferent
☐ Other (please specify) :_____

If you accept answering further questions, please specify your email adress : _____

The IHU Strasbourg team thanks you for filling out the survey.
For any questions, remarks or to return the survey please contact Imad Ismail at imad.ismail@ihu-strasbourg.eu.
You can also send a letter to :
IHU Strasbourg S/c IRCAD
1, place de l'Hôpital
67091 STRASBOURG Cedex

INSTITUT DE CHIRURGIE MINI-INVASIVE GUIDÉE PAR L'IMAGE

Utilité de l'assistance robotique en chirurgie laparoscopique

1. Dans quelle spécialité pratiquez-vous la chirurgie robot-assisté principalement? _____

2. Depuis combien d'années pratiquez-vous la chirurgie? __

3. Pratiquez-vous actuellement la chirurgie robot-assistée ? ☐ Non ☐ Oui

4. Depuis combien d'années pratiquez-vous (Pendant combien d'année avez-vous pratiqué) la chirurgie robot-assistée ?
☐ <1 ☐ 1-5 ☐ 5-10 ☐ >10

5. Comparé à la laparoscopie, quel effet exerce le système chirurgical robotique sur :

Rétablissement du patient	☐ Négatif	☐ Aucun	☐ Positif	☐ NA
Vos compétences chirurgicales	☐ Négatif	☐ Aucun	☐ Positif	☐ NA

6. Comparé à la laparoscopie, quel effet a eu l'introduction du système chirurgical robotique sur :

Taux de complications	☐ Diminution	☐ Aucun	☐ Augmentation	☐ NA
Temps d'occupation de la salle	☐ Diminution	☐ Aucun	☐ Augmentation	☐ NA
Sécurité au bloc opératoire pour vous et l'équipe	☐ Diminution	☐ Aucun	☐ Augmentation	☐ NA

Autres effets sur la chirurgie : _____

7. Comparé à la laparoscopie, comment évalueriez-vous l'importance des avantages suivants liés au système chirurgical robotique ?

	Nulle	**Basse**	**Moyenne**	**Elevée**	**NA**
Vision 3D	O	O	O	O	O
4 bras robotisés	O	O	O	O	O
Meilleure ergonomie pour les chirurgiens	O	O	O	O	O
Degré de liberté des instruments plus élevés	O	O	O	O	O
Opérations à distance	O	O	O	O	O

Autres avantages : _____

8. Comparé à la laparoscopie, comment évalueriez-vous l'importance des inconvénients suivants liés au système chirurgical robotique ?

	Nulle	**Basse**	**Moyenne**	**Elevée**	**NA**
Coût d'investissement	O	O	O	O	O
Absence d'accès direct au patient	O	O	O	O	O

Autres inconvénients : _____

9. Pour la chirurgie robotique, comment qualifieriez-vous la limitation du nombre d'utilisation des instruments ?
☐ Inconvénient ☐ Indifférent ☐ Avantage ☐ NA

10. Comment décririez-vous l'impact de la chirurgie robotique sur votre :

Capacité d'enseignement	☐ Négatif	☐ Aucun	☐ Positif	☐ NA
Compétence en laparoscopie	☐ Négatif	☐ Aucun	☐ Positif	☐ NA
Collaboration scientifique avec d'autres professionnels	☐ Négatif	☐ Aucun	☐ Positif	☐ NA

Autres activités : _____

11. Quel est **votre point de vue** concernant l'avenir du système chirurgical robotique ?
☐ Il est prometteur
☐ Il ne durera pas
☐ Je suis indifférent
☐ Autre (spécifiez) :_____

Si vous acceptez de répondre à des questions complémentaires, veuillez indiquer votre adresse mail : _____

L'équipe de l'IHU Strasbourg vous remercie d'avoir complété ce questionnaire.
Pour toute question, remarque ou pour retourner le questionnaire veuillez contacter Imad Ismail à imad.ismail@ihu-strasbourg.eu,
Ou à l'adresse postale suivante :
IHU Strasbourg S/c IRCAD
1, place de l'Hôpital
67091 STRASBOURG Cedex

Appendix G

EvaRIO Measures

TYPE OF EFFECT		DESCRIPTION OF EFFECTS / INDICATOR
Direct effects ***Mainly Monetary***	**Standard** *Volume of activities corresponding to the research projects using RI* ***Monetary***	***R&D projects linked to RI use**: amount of budget of the projects and/or research contracts related to RI use, or equivalent in jobs* ***Training**: budget for training on RI, equivalent in number of trainees and training time* ***Collaborative agreements with RI:** amount of budget of collaborative agreeements, equivalent in jobs* NB: including follow-up projects on RI
	Comparative Advantage ***Monetary as well as non monetary***	***Direct advantage from using the RI compared to alternative means (opportunity cost):*** *No alternative means for doing research,* *Time/cost sparing, better results, other qualitative advantage,...*
Capacity effects *increase in generic capacity resulting from RI activity* ***Non monetary*** *potential (not necessarily exploited)*	**S&T** *Science and technology knowledge and competences*	***Increase in knowledge signaled by:** publications as (co-)autho, patents, thesis; new or improved prototype, product, demonstrators, pilot, process, equipment (physical artefact), databases...* ***Other gain in knowledge (qualitative description)***
	Network *Knowledge and competences regarding relations with other actors and to ties with other actors*	***Collaborations**: Number of* **EU projects**, of different partners and new EU partners; idem for pre-competitive, academic or **industrial projects**; *Signals of collaborations such as **co-publications** and co-invention of **patents**.* ***Other network enrichment (qualitative description)t**: new contacts, higher visibility in the network, relational ability:, know-who-is-doing-what, know-how to work with others, strenghthening quality of links*
	Reputation *Reputation assets*	***Prizes, awards**; invitations to conference as keynote, round table, position in ranking* ***Citations** in specialised or general press* ***Other reputation enhancement:** qualitative description of events or factors signalling reputation increase, for instance TV or press broadcasts including those for general audience.*
	O&M *Competences in management / organisational changes*	***Existence of dedicated** service/ dedicated FTE-full time equivalent (how much) for: managing RI activities; quality, Techno Transfers* ***Formal tools** in: project management; accounting / cost procedures; Quality management, evaluation and strategic planning, etc. linked to RI* ***Significant organisational changes***
	Human Capital *Enlargement / diversificat° of staff*	*Number and origin (univ, industry…cf inward-mobility) of **staff** (scientific/engineers/technicians) recruited or maintained for operating/using/designin&building the RI ; **qualification** and **turnover***
Indirect *Re-deployment of the gains in capacity identified above...* *... outside RI* *ie in activities not using the RI* ***Monetary***	**S&T**	***Valuation of gains in S&T capacity** in a new research projects or in new products/services/process, measured in revenue (sales, royalties, new contracts, scientific prize,...) or cost/time savings.*
	Network	***Valuation of gains in networking capacity:** idem*
	Reputation	***Valuation of gains in reputation:** idem*
	O&M	***Valuation of gains in organisation and method**: idem*
Effect on performance *... on RI* *Exploitation of the gains in capacity for enhancing the performance as a user of the RI*	***Monetary*** ***as well as*** ***non monetary***	***Valuation of the gains in experience/new skills/contacts** acquired in a first use of the RI (learning by using), as it is re-used in the same RI, measured in terms of time / cost savings when using the RI again, or raising funding for a new RI project,...* ***Better ability to use the RI** via adhoc indicators (specific to the RI): variety, quantity & renewal of RI services, nb of internal users, training,...*

Résumé en Français

1 Introduction générale

La santé est un droit fondamental et unique, universellement considéré comme n'ayant pas de prix. Cependant, comme tout autre bien économique, la santé a un coût qui ne cesse d'augmenter avec l'évolution des techniques médicales et le vieillissement de la population.

La maîtrise des dépenses de santé est devenue une préoccupation primordiale pour les pouvoirs publics qui concentrent leurs efforts sur trois axes principaux : réorganisation de la gestion de l'assurance maladie, réforme du financement de l'assurance maladie et réorganisation des soins. Face à un déficit de la Sécurité Sociale de 11.6 milliards d'euros en 2004 et 12.5 milliards en 2013 (DREES), le besoin d'évaluation et d'évolution des pratiques médicales a vu l'instauration en 2004 de la Haute Autorité de Santé (HAS) - structure nationale dédiée à ces analyses.

Historiquement, chaque dispositif médical faisait objet d'une évaluation globale dans le cadre du parcours de prise en charge du patient. Avec l'instauration de la HAS et la Commission Nationale d'Évaluation des Dispositifs Médicaux et des Technologies de Santé (CNEDiMTS), chaque dispositif devrait dorénavant être évalué individuellement afin de déterminer sa valeur ajoutée comparée aux pratiques habituelles. Il est ainsi devenu indispensable d'intégrer les discussions d'impacts socio-économiques dans le processus de développement des dispositifs médicaux innovants.

Créée en 2012 suite au programme "Investissements d'Avenir", l'Institut Hospitalo-Universitaire de Strasbourg (IHU)[1] représente la volonté de l'Etat à parier sur l'avenir

[1] Connu, par ailleurs, sous le nom d'Institut de Chirurgie Mini-Invasive Guidée par l'Image.

d'un nouveau type de chirurgie mini-invasive, qualifié d'"hybride". Ce concept innovant vise à bouleverser les pratiques traditionnelles en fusionnant des spécialités jusque-là considérées comme distinctes : radiologie interventionnelle, chirurgie laparoscopique et endoscopie interventionnelle.

L'IHU Strasbourg est ainsi un centre médico-chirurgical dédié au traitement des pathologies de l'appareil digestif en employant les techniques les moins invasives possible. De plus, en tant que centre de recherche, il regroupe des équipes qui conçoivent et développent les instruments et les procédures du futur. Prenant exemple sur les pratiques de l'Institut de Recherche Contre les Cancers de l'Appareil Digestif (IRCAD), maison-mère de l'IHU, l'institut cherche aussi à se positionner comme un centre international de formation accueillant des professionnels et des étudiants pour l'enseignement des pratiques mini-invasives.

Le concept des technologies "hybrides" provient de la complexité et de la variété des maladies de l'appareil digestif qui nécessitent la mobilisation de plusieurs spécialistes. Les chirurgiens se concentrent sur la résection des organes et leur réparation, les gastro-entérologues se focalisent sur les thérapies médicales et endoscopiques et les radiologues interventionnels sur les procédures guidées par l'image. La chirurgie hybride cherche à combiner l'expertise de ces trois types de spécialités afin d'améliorer l'efficacité de la prise en charge des patients.

Les innovations en chirurgie mini-invasive hybride sont ainsi directement concernées par les évaluations d'impacts d'autant plus qu'elles risquent, de par leur complexité, d'augmenter significativement le coût des soins. Cependant, elles offrent de nombreux avantages que l'IHU souhaite mettre en valeur, parmi lesquels la possibilité de réduire la durée de séjour, d'augmenter l'attractivité de la région ou de réorganiser les prises en charge afin de les rendre, globalement, plus efficientes.

Objectif et plan de thèse

Par définition, l'IHU cherche à mener des activités de soins, de recherche-développement et d'éducation fortement interdépendantes, axées sur les innovations chirurgicales hybrides. Chaque activité, selon l'institut, devrait générer des impacts sur différents types

d'acteurs. Or, il existe actuellement peu d'outils permettant l'évaluation de ces impacts. Plus particulièrement, nous n'avons identifié aucune méthodologie qui permettrait d'évaluer les trois activités et de combiner leurs impacts dans un ratio coût-bénéfice unique.

Dans notre travail de thèse, nous nous concentrons principalement sur l'évaluation des impacts de la **création** et de l'**utilisation** des technologies innovantes sachant qu'elles étaient, au moment de conduire l'analyse, les deux activités les plus développées de l'institut. Cette évaluation inclut aussi bien l'impact de ces activités sur les partenaires de l'IHU, les patients et la société que sur l'économie de manière générale.

Cette thèse s'articule donc autour d'une question principale : comment procéder afin d'évaluer l'efficience ainsi que l'impact socio-économique des innovations chirurgicales? Afin d'y répondre, nous proposons une série de développements méthodologiques décomposée en trois chapitres, portant sur l'analyse :

- de l'impact sur le coût de l'introduction d'une innovation chirurgicale dans la salle d'opération ;
- du bénéfice pour les patients, l'hôpital et l'économie découlant de l'utilisation de l'innovation chirurgicale ;
- de l'impact du processus de recherche et développement qui a conduit à la création de l'innovation chirurgicale utilisée .

Malgré le fait que, chronologiquement, le processus de recherche et développement (R&D) survient avant l'utilisation d'une innovation, nous avons analysé cette activité en dernier. En effet, l'impact que nous cherchons à évaluer nécessite une certaine période de "maturité" avant de s'exprimer et donc de devenir mesurable.

Le chapitre introductif de la thèse présente le cadre général en détaillant les raisons qui ont motivé le travail, les bases scientifiques sur lesquelles il s'est appuyé ainsi qu'une description de l'IHU, initiateur de cette étude.

Le deuxième chapitre est dédié à l'élaboration d'une méthodologie de calcul du coût d'une opération chirurgicale employant des technologies hybrides. Après identification

des pratiques courantes de calcul de coût dans la littérature et une description des pratiques mises en œuvre à l'Hôpital de Strasbourg, nous avons développé notre propre méthodologie en utilisant le système de chirurgie robotique Da Vinci Si comme cas de figure. Notre choix pour cette technologie repose sur sa considération par les praticiens hospitaliers comme étant l'exemple type d'une innovation mini-invasive, ainsi que sur la possibilité d'accéder directement à une base de données créée par l'IHU.

Le troisième chapitre se focalise sur les mesures d'efficacité et de coût que la littérature considère comme étant pertinentes pour l'évaluation d'une prise en charge chirurgicale. Nous élargissons ainsi l'analyse de coût du deuxième chapitre en couvrant le parcours complet du patient et fournissons certains éléments quant à l'impact positif des innovations chirurgicales mini-invasives aussi bien sur l'hôpital que sur la société.

Le quatrième chapitre s'intéresse principalement à l'évaluation des impacts du processus de création des technologies chirurgicales hybrides. Ainsi, nous mettons en valeur la possibilité et la nécessité d'inclure l'impact de la R&D dans une évaluation d'impact des innovations chirurgicales.

Le dernier chapitre conclut notre travail en rappelant l'objectif de la thèse ainsi que nos contributions pour l'atteindre. Nous présentons différentes pistes de travaux futurs qui permettront, selon nous, d'avancer les discussions autour de l'évaluation des impacts des innovations chirurgicales mini-invasives.

2 Connaissances exploitées

Notre analyse de l'impact socio-économique des innovations chirurgicales hybrides a nécessité l'acquisition et la mobilisation de connaissances dans quatre domaines : l'économie de la santé, les sciences de gestion, l'économétrie et l'économie de l'innovation. L'objectif principal était de créer un premier cadre conceptuel mettant en avant la complémentarité entre ces différents domaines pour l'évaluation des innovations chirurgicales.

Les connaissances en gestion, ou plus particulièrement en gestion des coûts, ainsi que les connaissances en économie de la santé et en économétrie ont été principalement mobilisées pour l'évaluation du coût et des bénéfices des pratiques chirurgicales. Les connaissances en économie de l'innovation ont permis d'élargir notre évaluation, jusque-là restreinte à l'impact de l'utilisation des innovations en chirurgie, en incluant l'impact de l'activité de recherche et développement.

Rappelons que l'économie de la santé est un domaine en émergence qui se positionne soit à l'échelle macro- soit micro-économique. La macro-économie de la santé se focalise sur l'analyse de la production et de la consommation des soins à l'échelle nationale tout en évaluant la santé des populations, l'équité dans l'accès aux soins et les politiques de santé plus généralement. La micro-économie de la santé, moins connue, se concentre sur l'étude des pratiques des professionnels et institutions de santé en se basant sur des méthodes d'évaluations plus détaillées.

Tenant compte du fait que l'IHU se focalise principalement sur les pratiques aussi bien du chirurgien ou de l'hôpital que du chercheur ou du développeur, notre objectif d'évaluation de l'impact socio-économique des innovations chirurgicales hybrides s'inscrit plutôt dans une approche micro-économique. Notre exploration des fondements de cet aspect d'économie de la santé nous a permis d'identifier quatre pratiques principales d'évaluation : minimisation des coûts, coût-efficacité, coût-utilité et coût-bénéfice.

Chacune des quatre méthodes d'évaluation citées se distingue par son analyse des mesures d'efficacité. La première ne s'intéresse qu'aux coûts et aux pratiques qui permettent de les diminuer. La deuxième compare le coût d'utilisation d'une technologie à son effet sur une mesure "brute" d'efficacité telle que le poids perdu ou les années de vie gagnées. La troisième méthode compare le coût d'utilisation à l'impact qu'elle peut avoir sur une

mesure d'utilité telle que, par exemple, les années de vie gagnées ajustées par la qualité (QALYs[2]).

La méthode coût-bénéfice s'intéresse à la comparaison des coûts et des impacts qu'une technologie peut avoir sans imposer une limite quant au nombre ou au type de mesures d'efficacité. Cependant, deux conditions se posent lors de l'application de cette méthodologie : respect de l'éthique et capacité à exprimer tout impact en valeur monétaire. Étant donné notre objectif de combiner l'impact de différentes activités, la méthode coût-bénéfice nous semble être la plus pertinente pour notre sujet.

L'analyse du coût des opérations chirurgicales se base sur les principes de la comptabilité analytique et des méthodes de calcul des coûts de production. En parallèle, nous exploitons nos connaissances en langage informatique, particulièrement le logiciel statistique R, afin de créer les algorithmes nécessaires à l'automatisation des calculs.

Afin d'exploiter les bases de données mises à disposition par l'IHU et l'hôpital, nous avons aussi eu recours aux méthodes économétriques, notamment durant nos analyses comparatives de l'efficacité des technologies chirurgicales. Les modèles linéaires hiérarchiques, peu utilisés dans la littérature chirurgicale, se sont révélés particulièrement adaptés à la structure de nos données.

L'économie de l'innovation, quant à elle, nous a permis d'introduire une dimension dynamique dans notre analyse en prenant en compte l'évolution dans le temps de l'impact des innovations sur les chirurgiens, chercheurs et partenaires industriels de l'IHU. Nous nous sommes particulièrement intéressés aux mesures de gains en capacité (gain en connaissances techniques ou de management, réseau relationnel, réputation etc.) suite au processus de R&D, ainsi que l'élaboration d'une méthode permettant leur évaluation.

[2]Quality Adjusted Life Years

3 Évaluation du coût des technologies chirurgicales mini-invasives : les méthodes existantes et notre contribution

Après introduction du cadre général de la thèse, notre analyse débute par une étude des points forts et points faibles du système de santé français mettant en avant l'absence de méthodologies de calcul d'impact des innovations sur le coût des opérations chirurgicales. Dans ce chapitre, nous avons cherché à créer les bases pour une telle méthodologie couvrant ainsi la première partie (coût) de l'évaluation de l'impact qu'une innovation peut avoir sur la prise en charge du patient.

3.1 Revue de la littérature

La revue de la littérature sur les méthodologies de calcul de coût débute par une mise en comparaison des différentes recommandations nationales et internationales en économie de la santé. Nous nous sommes focalisés principalement sur l'identification des points communs afin d'établir une base solide pour une comparaison des différentes publications scientifiques ainsi que pour la création de notre propre méthodologie.

Une deuxième revue de la littérature, spécifique aux publications par les chirurgiens, portant sur l'analyse du coût d'une opération chirurgicale, a révélé un manque de rigueur dans les calculs ainsi que dans leur publication. Nous avons ainsi pu justifier la nécessité de créer et de publier une méthodologie de calcul de coût mise à la disposition des chirurgiens, des hôpitaux et de l'IHU.

3.2 Méthode

Notre analyse du coût d'une opération chirurgicale mini-invasive guidée par l'image se base sur quatre formules, développées dans le cadre de la thèse, couvrant aussi bien les coûts fixes que les coûts variables. Dans la catégorie coûts fixes, nous incluons le coût des équipements médicaux et du personnel tandis que dans la catégorie coûts variables nous incluons les instruments réutilisables et consommables.

L'application et la validation de nos formules se basent sur une comparaison entre deux types de chirurgie mini-invasive interchangeables, à savoir : le *bypass* gastrique assisté

par robot (Da Vinci) et le *bypass* gastrique laparoscopique traditionnel. Deux approches ont été suivies durant l'application afin de démontrer l'utilité de notre méthodologie dans le cas d'indisponibilité ou de disponibilité d'une base de données exhaustive.

3.3 Résultats

Les résultats d'application de notre méthode de calcul de coût démontrent qu'on peut précisément déterminer l'impact de l'introduction d'une technologie chirurgicale mini-invasive sur le coût d'une opération chirurgicale. Deux applications des formules de calcul de coût nous ont permis de développer un algorithme, basé sur le logiciel statistique R, capable de calculer rapidement et avec précision le coût de toute opération chirurgicale.

Nos applications mettent en avant la flexibilité de notre méthodologie de par l'existence de deux approches différentes. La première approche repose sur un nombre minimal d'informations basées essentiellement sur l'expérience des chirurgiens. La deuxième approche permet d'exploiter une base de donnée complexe afin d'en tirer un nombre maximal de conclusions. L'algorithme ainsi développé existe sous deux versions dont le choix dépend du moment d'évaluation (*ex ante* ou *ex post* vis-à-vis de l'adoption de la technologie étudiée) et de la disponibilité des données.

Notre comparaison de la chirurgie assistée par robot *versus* la laparoscopie traditionnelle montre que l'introduction du système chirurgical robotique augmente significativement le coût par opération jusqu'à atteindre 225% de celui de la laparoscopie. L'analyse de la chirurgie robotique comme cas de figure a mis en évidence un manque important de considération pour le coût des innovations chirurgicales. En effet, en se fiant à nos calculs, il nous semble inconcevable qu'une technologie qui engendre un coût plus de deux fois plus élevé que son alternative soit adoptée sans justification de son efficacité.

3.4 Apports et limites

Un des apports majeurs de ce chapitre est le développement de deux algorithmes permettant à toute personne intéressée de déterminer l'impact d'introduction d'une innovation sur le coût de la salle d'opération. Cependant, bien que ce calcul se fasse en un clic, l'extension ainsi que l'adaptation de ces algorithmes nécessitent des connaissances en

statistique, gestion des coûts et programmation, peu présentes dans le monde chirurgical.

La méthode développée suite à cette analyse est particulièrement adaptée à l'évaluation des innovations en chirurgie mini-invasive, qui ont servi comme base pour sa construction. Néanmoins, les formules qui composent cette méthode peuvent être appliquées dans d'autres domaines, que ce soit en imagerie, en pharmaceutique ou en médecine générale.

Notre étude présente plusieurs limites, dont certaines sont techniques. L'application de notre méthodologie de coût, par exemple, est limitée par un manque d'accès aux données ne permettant pas la prise en compte des frais généraux. Par ailleurs, le manque d'accès aux données de l'hôpital implique la nécessité d'établir certaines hypothèses afin de rendre l'analyse possible. Notons que tout changement d'hypothèse et toute décision d'inclure des frais généraux, généralement spécifiques à chaque institut, peut nécessiter un développement supplémentaire ou une adaptation des algorithmes.

4 Évaluation médico-économique des technologies médicales

En économie de la santé, le calcul de coût ne constitue que le premier élément de trois des quatre principales pratiques d'évaluation médico-économique (coût-efficacité, coût-utilité et coût-bénéfice). Le deuxième élément nécessaire à la constitution de la méthode coût-bénéfice est, logiquement, l'impact des innovations chirurgicales en terme de "bénéfice".

4.1 Revue de la littérature

Notre revue de la littérature pour ce chapitre débute donc par une identification des mesures d'impact qui peuvent refléter, dans le cas des chirurgies mini-invasives ou hybrides, un bénéfice pour la société ou l'économie. Pour ce faire, nous avons comparé les recommandations internationales afin d'identifier les mesures généralement considérées comme représentant un bénéfice dans le domaine de la santé.

Chaque mesure a ensuite fait l'objet d'une analyse spécifique afin d'identifier les différentes méthodes de calcul présentées dans la littérature. Nous nous sommes aussi particulièrement intéressés aux ajustements nécessaires pour leur prise en compte dans une évaluation d'impact (coût-bénéfice) plus globale.

4.2 Méthode

Suite à la revue de littérature, nous avons pu identifier six mesures d'impact que nous considérons comme étant pertinentes pour notre analyse, à savoir l'impact sur : les complications, la durée de séjour, le tourisme médical, le présentéisme, l'absentéisme et la qualité de vie. Chaque mesure a été évaluée selon la disponibilité des données et la permission d'accès, soit en se basant sur les données d'un protocole clinique de comparaison robot versus laparoscopie (déjà utilisé dans une de nos approches de calcul de coût), soit sur des données IHU portant sur d'autres opérations mini-invasives.

Notre étude d'impact du tourisme médical a fait l'objet d'une recherche de données dans la base IHU relative à la patientèle internationale. Nous avons effectué une analyse

coût-bénéfice spécifique en ayant comme objectif principal de calculer le retour sur investissement de chaque euro dépensé par l'IHU, aussi bien en termes de bénéfices qu'en termes d'impacts sur le territoire.

L'analyse des données de qualité de vie a été réalisée en utilisant un modèle linéaire hiérarchique, peu employé dans le domaine chirurgical. Nous avons détaillé les méthodes couramment utilisées dans la littérature pour des évaluations *ex post*, afin de montrer l'ambiguïté qui existe sur l'utilité de certains modèles statistiques et justifier notre choix.

Étant donné le rôle important des chirurgiens dans le choix des technologies chirurgicales, nous nous sommes aussi intéressés aux raisons qui motivent l'adoption d'une innovation et plus particulièrement d'un système de chirurgie robotique. Nous avons ainsi créé un questionnaire d'évaluation spécifique au robot Da Vinci nous permettant de mettre en évidence les facteurs qui influencent leurs décisions.

4.3 Résultats

L'exploitation des données du protocole clinique comparant le *bypass* gastrique robot assisté et son équivalent laparoscopique nous a permis de tester la pertinence de certaines mesures de bénéfice. Les résultats démontrent une différence non statistiquement significative dans la durée de séjour hospitalière, de l'absentéisme et de la qualité de vie. Le système de chirurgie robotique, considéré comme une innovation sans précédent, ne semble donc pas offrir d'avantages dans ces trois dimensions malgré son coût élevé.

Suite à l'analyse de l'impact de la procédure mini-invasive "Peroral Endoscopic Myotomy" (POEM) en terme de tourisme médical, nous avons déterminé que chaque euro dépensé par l'IHU génère, au minimum, 1,82 euros injectés dans l'économie locale et 1,18 euros dans celle de l'hôpital. La même analyse pour le *bypass* gastrique laparoscopique nous a permis de déterminer que chaque euro dépensé par l'IHU génère, au moins, 1,82 euros pour l'économie locale et 3,30 euros pour celle de l'hôpital plus particulièrement. Il est ainsi possible d'évaluer l'impact d'une procédure ou technologie innovante sur le tourisme médical et la région plus précisément.

L'analyse des 29 réponses au questionnaire d'évaluation du système de chirurgie robotique démontre que, malgré le coût élevé d'investissement nécessaire à l'acquisition du système robotique, la majorité des répondants lui sont favorables. Selon notre analyse,

les avantages les plus importants de ce système chirurgical semblent résider dans son utilisation en tant que simulateur et outil d'enseignement.

4.4 Apports et limites

De notre point de vue, la littérature a jusque-là fortement négligé certaines mesures d'impact telles que le tourisme médical ou le présentéisme dans l'évaluation des technologies chirurgicales. Nos revues et applications permettront aux décideurs de compléter notre méthodologie de calcul de coût initiale, rendant ainsi possible l'application d'une évaluation coût-bénéfice. Nos recherches sur les méthodes économétriques pour l'évaluation de la qualité de vie devraient aussi permettre aux chirurgiens et aux statisticiens d'améliorer la validité de leurs études de qualité de vie.

Dues à un manque de données non collectées par l'hôpital ou l'IHU, certaines mesures de coût et d'efficacité de la chirurgie robotique n'ont pas pu être estimées dans le cadre de la thèse. Par conséquent, notre analyse a été fractionnée en se basant sur différents types de chirurgies, limitant notre capacité à effectuer une analyse complète d'une seule et même technologie.

Étant donné le nombre peu élevé de réponses au questionnaire "Da Vinci", les résultats de notre application quant à la mesure des raisons qui motivent l'adoption d'une innovation sont peu représentatifs. Néanmoins, notre approche peut servir comme premier exemple pour effectuer une évaluation plus détaillée.

Les techniques d'évaluation en économie de la santé, nos méthodes incluses, se focalisent sur l'évaluation du coût et des impacts à un moment donné. Or, si on considère les effets d'apprentissage et l'impact des innovations incrémentales, les résultats d'une évaluation peuvent changer tout au long de la durée de vie d'une innovation.

5 Impact de la recherche et du développement dans le domaine de la santé

L'introduction des innovations chirurgicales dans la salle d'opération survient seulement après le processus de R&D qui permet la création de ces technologies. Une évaluation d'impact socio-économique d'une technologie chirurgicale hybride ne doit donc pas se limiter à l'usage de l'innovation dans la salle d'opération mais doit aussi inclure la totalité du processus nécessaire à sa création et les effets qui en dépendent.

En tenant compte de l'intérêt que l'IHU porte à l'usage des technologies hybrides qu'elle développe, l'analyse de l'activité de recherche et développement fait partie intégrante de l'évaluation de la prise en charge mini-invasive des patients. De surcroît, elle permet d'introduire une dimension dynamique dans notre méthode d'évaluation de par son analyse des gains en capacité (expliqués plus bas) tout au long de la durée de vie des projets de recherche.

5.1 Revue de la littérature

L'analyse d'impact du processus de recherche et développement débute par une synthèse des différentes catégories d'innovation présentes dans la littérature médicale, à savoir : incrémentale, radicale et de rupture. La compréhension des différences qui existent entre ces catégories et l'analyse des origines de chaque type d'innovation nous ont permis de déterminer les principaux "points de départ d'impacts" à inclure dans notre évaluation.

En effectuant une revue de la littérature des méthodes d'évaluation des activités de R&D, nous avons pu constater un manque de documentation significatif qui limite leur reproductibilité systématique. Néanmoins, une analyse de leurs principales caractéristiques nous a permis de mieux positionner la méthode "EvaRIO", développée par le BETA[3], que nous avons adaptée à l'activité de R&D de l'IHU. Notre choix de la méthode EvaRIO repose sur la possibilité de bénéficier de l'expérience d'un nombre important de chercheurs à l'origine de son développement ainsi que sur la capacité de cette méthode à exprimer les impacts en termes monétaires (nécessaire à leur inclusion dans une étude coût-bénéfice plus globale).

[3]Bureau d'Economie Théorique et Appliquée

5.2 Méthode

L'extension de notre analyse au processus de R&D se base sur la création d'une adaptation de la méthode EvaRIO, nommée "EvaRIO Reworked", pour l'évaluation des infrastructures de recherche. La méthode et son adaptation se focalisent sur la mesure des gains en capacité et leur exploitation afin de générer des impacts économiques, mesurables en termes monétaires.

Le terme "gain en capacité" se décompose en : la création de connaissances scientifiques et techniques, la création/renforcement des liens avec d'autres acteurs, le gain en réputation, le développement de nouvelles techniques d'organisation et de management, et l'augmentation du capital humain. Théoriquement, les partenaires de l'IHU développent leur capacité à travers les collaborations et les projets de recherche menés avec l'institut. De plus, il est possible d'exploiter cette augmentation de capacité soit avec l'IHU, soit sans (effets indirects), générant ainsi des impacts économiques considérables.

Après identification des différents partenaires industriels et scientifiques de l'IHU, nous avons effectué un total de 15 interviews dont la synthèse critique a permis d'identifier les points forts et points faibles de la collaboration avec l'institut. Cette analyse a aussi permis d'évaluer la pertinence de l'application de la méthode EvaRIO et la mesure des gains en capacité dans le cadre d'une infrastructure de R&D chirurgicale telle que l'IHU.

5.3 Résultats

En s'intéressant à l'impact de la R&D des chirurgies mini-invasives guidées par l'image, nous avons pu mettre en évidence plusieurs départs d'impact des collaborations entre l'IHU et trois types de partenaires : entreprises, laboratoires de recherches et chirurgiens chercheurs IHU/IRCAD. Bien que de nombreux effets positifs et gains aient été relevés (science et technologie, network et capital human), certains acteurs ont signalé des difficultés notamment en terme de réputation et d'organisation. De manière générale, les partenaires industriels et les chirurgiens chercheurs IHU/IRCAD semblent tirer le plus profit de cette collaboration tandis que les laboratoires de recherche ne parviennent pas toujours à l'exploiter dans toutes ses dimensions.

Suivant notre application de la méthode EvaRIO et la revue des méthodologies d'évaluation de la recherche dans le domaine de la santé, nous avons pu créer une adaptation plus orientée par projet. Nous avons ainsi établi un cadre de référence qui permettra à l'IHU d'effectuer dans le future une analyse plus précise de son activité de R&D, dont les résultats complèteront utilement l'analyse coût-bénéfice développée dans les chapitres précédents.

5.4 Apports et limites

L'évaluation d'impact de l'activité de R&D de l'IHU sur ses partenaires a rencontré quelques obstacles, liés au degré de confidentialité de certains informations. Ainsi, certains résultats peuvent être considérés comme imprécis. Mais le problème principal provient de l'impossibilité de déployer la méthode sur la totalité du processus dans le temps : en effet, les projets R&D analysés sont encore en cours, or l'exploitation d'un gain en capacité nécessite du temps. Ceci explique la faiblesse apparente de l'impact lié à l'exploitation de gains de capacité.

Néanmoins, nous avons pu établir le cadre théorique d'une nouvelle méthodologie qui se focalise sur une analyse projet par projet. Cette spécificité permet aux décideurs de tracer l'impact aussi bien de l'utilisation que du développement d'une innovation chirurgicale précise.

La qualité des résultats de l'application d'EvaRIO, ainsi que son adaptation, repose fortement sur l'expérience des évaluateurs, ainsi que sur le temps investi dans la préparation et la synthèse des résultats. En effet, notre étude a nécessité un investissement considérable en temps, d'autant plus qu'il s'agit d'un travail exploratoire et à l'échelle micro-économique.

6 Conclusion générale

En tant qu'institut spécialisé dans le développement et dans l'utilisation des innovations chirurgicales, l'Institut Hospitalo-Universitaire de Strasbourg sera confronté à un besoin constant d'évaluation de son activité. Cette thèse vise à répondre à ce besoin en contribuant à l'élaboration d'une méthodologie d'évaluation d'impact adaptée, focalisée sur l'impact socio-économique des innovations chirurgicales hybrides.

L'évaluation d'impact des chirurgies mini-invasives guidées par l'image doit être considérée comme un **processus**, durant lequel une idée se transforme en projet, puis en produit et enfin en prise en charge de patients. La création et l'introduction d'une technologie chirurgicale innovante dans la salle d'opération peut donc avoir un impact à plusieurs niveaux.

Le premier niveau observable se manifeste par un changement du coût de la prise en charge médicale que le système français de collecte et traitement des données actuel ne permet pas d'évaluer correctement. Notre proposition d'une méthode de calcul de coût contribue à résoudre ce problème en permettant à toute personne d'accéder à un algorithme de calcul rapide et simple d'utilisation.

Le deuxième niveau d'impact affecte aussi bien la société que l'économie en améliorant la santé et la productivité de la population tout en augmentant l'attractivité de l'activité de soins. La littérature chirurgicale a jusque-là fortement négligé certains de ces impacts, peu d'études les prennent tous en compte dans une même évaluation. Nos synthèses et discussions des différentes mesures d'impact fournissent des éléments de réflexion quant à la possibilité de combiner ces mesures.

Un point particulièrement innovant de cette thèse réside dans la volonté d'intégrer l'impact du processus de recherche et développement (troisième niveau) dans l'équation coût-bénéfice déterminée dans les chapitres précédents. Pour remplir cet objectif, nous avons créé une adaptation de la méthode EvaRIO développée au BETA, permettant l'évaluation de l'activité de R&D de l'IHU projet par projet.

Notre travail a ainsi permis de contruire plusieurs méthodologies d'évaluation complémentaires afin de déterminer un ratio coût-bénéfice. Une telle analyse ne se contente pas d'évaluer l'impact de l'utilisation d'une nouvelle technologie sur l'acte chirurgical, sur le patient

et sur l'économie mais prendrait aussi en compte les impacts du processus de **création** de cette innovation.

Afin d'élargir notre méthode, il serait indispensable de développer davantage les outils d'évaluation pour certaines mesures d'efficacité. Le tourisme médical, par exemple, a été évalué en suivant une méthode coût bénéfice tandis qu'une méthode input-output pourrait s'avérer plus large. Par ailleurs, l'analyse de l'impact d'une technologie chirurgicale sur les capacités d'apprentissage et d'enseignement pourrait représenter une réelle valeur ajoutée. En effet, une des particularités en chirurgie est l'importance du gain d'expérience, sa transmission et son impact sur la prise en charge des patients. Pour compléter nos méthodologies, il serait indispensable d'étudier les possibilités d'évaluer l'impact qu'une technologie chirurgicale pourrait avoir sur la formation ainsi que sur l'apprentissage des chirurgiens.

Enfin, un axe de recherche future consisterait à tester la complémentarité de nos méthodes en les appliquant sur une technologie chirurgicale unique et si possible créer une méthode unifiée. Pour ce faire, une condition nécessaire serait de mettre en place un système de collecte de données adapté pour rendre de telles analyses possibles.