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SCUOLA DI DOTTORATO DI RICERCA IN ECONOMIA E MANAGEMENT

CICLO XX

EVIDENCE ON ECONOMIC EVALUATION IN HEALTH CARE:
COST-EFFECTIVENESS ANALYSES OF HEALTH CARE PROGRAMS IN ITALY

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Abstract

Il presente lavoro considera il tema della valutazione economica in campo sanitario. Nello specifico vengono sviluppate due analisi di costo-efficacia con riferimento a due diversi tipi di programma sanitario. In primo luogo, si valutano gli effetti di diverse modalità di parto, esaminando in particolare la costo-efficacia dell'introduzione dell'analgesia epidurale in travaglio. In secondo luogo, si analizzano i costi e i benefici di un programma di screening per la prevenzione del tumore al colon-retto.

La dissertazione è articolata in cinque capitoli.

Il **primo capitolo** ha un carattere introduttivo e offre una breve rassegna aggiornata delle principali tecniche di valutazione economica.

Il **secondo capitolo** contiene una survey completa delle diverse misure di outcome e di qualità della vita degli interventi sanitari, considerando in particolare gli strumenti di indagine (questionari) utilizzati per valutare l'efficacia (impatti clinici e psicologici) dell'evento parto e dello screening del cancro al colon-retto. L'analisi è funzionale rispetto agli studi di costo-efficacia condotti poi nei capitoli 4 e 5.

Il terzo e quarto capitolo analizzano il tema delle diverse metodiche di parto, puntando l'attenzione su un fenomeno che di recente ha destato non poche preoccupazioni a livello mondiale e in particolare in Italia: il ricorso crescente, e talora non appropriato, all'utilizzo della pratica del taglio cesareo.

Il **terzo capitolo** effettua una analisi comparativa del livello di appropriatezza del ricorso alla pratica del taglio cesareo, confrontando l'Italia e il Regno Unito. Si analizzano le differenze di contesto sanitario e socio-demografico nei due Paesi e si considerano i fattori che potenzialmente potrebbero contribuire a spiegare una elevata frequenza e variabilità nell'utilizzo della pratica di taglio cesareo.

Il tema dell'appropriatezza nel settore analizzato appare particolarmente rilevante nell'ambito del dibattito generale in tema di sostenibilità del sistema sanitario pubblico. Negli ultimi anni, infatti, è stato registrato un incremento esponenziale della frequenza di utilizzo del taglio cesareo in Europa. Tale fenomeno non sembra peraltro essere pienamente giustificato e sottende sovente un grado elevato di inappropriatezza, essendo il taglio cesareo spesso praticato indipendentemente da ragioni cliniche o epidemiologiche.

Vengono considerati in particolare gli effetti che tale pratica può avere non solo in termini di spesa sanitaria pubblica, ma anche a livello sociale adottando una prospettiva più ampia, e si propongono misure di politica sanitaria e di governo clinico che possano consentire di controllare il fenomeno.

Viene esaminata, in particolare, la misura recentemente prevista in Italia con la proposta di introdurre l'analgesia epidurale tra i Livelli Essenziali di Assistenza (LEA)[1] allo scopo di contribuire a contrastare il tendenziale aumento dei parti cesarei[2].

Nonostante gli accesi dibattiti sull'argomento, pochi studi hanno tuttavia posto l'attenzione sui costi reali delle diverse metodologie di parto e la letteratura esistente è riferita ad un contesto, quello americano, estremamente diverso da quello italiano (Henderson J., 2001). Per questa ragione, nel **quarto capitolo** si sono analizzati i costi e i benefici di diversi metodi di parto (parto vaginale, con e senza analgesia epidurale, e parto cesareo) avendo come riferimento il contesto italiano.

L'analisi empirica è stata condotta considerando una azienda ospedaliera italiana, attraverso la raccolta diretta dei dati, la somministrazione di questionari e l'effettuazione di interviste alle pazienti.

E' stata effettuata una regressione logit per modellare la probabilità dell'evento "parto con taglio cesareo elettivo" come funzione di un insieme di caratteristiche cliniche e socio-economiche delle partorienti. I risultati ottenuti sembrano confermare l'ipotesi testata anche in altri studi secondo cui il taglio cesareo venga praticato per ragioni non-cliniche (Osborn J. and Signorelli C., 1995; Frost C., 2005).

Attraverso una analisi *micro-costing* sono stati valutati i costi diretti di ciascuna metodologia di parto, seguendo un approccio *activity-based costing*. Dall'analisi svolta è emerso che il parto cesareo è mediamente più costoso rispetto al parto vaginale, ma la differenza è marginale se si considera il costo-opportunità del tempo di assistenza durante il travaglio. Inoltre, le differenze tra i costi effettivi e le tariffe DRG utilizzate per il rimborso delle prestazioni sanitarie, potrebbe indurre comportamenti opportunistici in termini di pratica clinica.

I risultati dello studio dimostrano che l'introduzione dell'analgesia epidurale tra i LEA potrebbe avere certamente un impatto rilevante in termini economici, ma l'effetto complessivo finale non è chiaro: essa potrebbe contribuire a ridurre la frequenza di

[1] I LEA comprendono tutti gli interventi che il Servizio Sanitario Nazionale deve fornire a tutti gli assistiti in forma gratuita o tramite co-partecipazione alla spesa.

[2] In Italia più del 35% dei parti vengono praticati con taglio cesareo, mentre l'Organizzazione Mondiale della Sanità suggerisce che l'utilizzo di tale pratica non dovrebbe superare il 10-15%.

tagli cesarei inappropriati, ma nel contempo aumentare i costi legati a potenziali complicazioni.

Adottando una prospettiva sociale, sono stati considerati anche i costi indiretti, i costi intangibili (trasporto, medicazioni, assistenza, allattamento, perdite di tempo) e i benefici di ciascuna tipologia di parto[3].

L'analisi costo-efficacia mostra che in generale il parto vaginale con analgesia epidurale è preferito sia in termini di costi che benefici. Tuttavia, in molti casi l'analgesia epidurale può richiedere procedure d'emergenza, con risultati peggiori sia in termini di costi che di benefici.

Nel **quinto capitolo** viene effettuata una valutazione economica di un programma di screening per la prevenzione del tumore al colon-retto, con riferimento al territorio della provincia di Ferrara.

Il cancro del colon-retto (CRC) configura una delle forme di tumore più comuni nei paesi occidentali e rappresenta la seconda causa di morte per cancro in Europa (AIRT, 1998-2000). Numerose evidenze scientifiche suggeriscono che lo screening per la diagnosi precoce e la rimozione delle lesioni cancerose può ridurre l'incidenza del tumore del colon-retto e la connessa mortalità (Sonnenberg A., 2000, Lieberman DA., 1995) e aumentare la qualità di vita dei pazienti (Taupin D., 2006; Miles A., 2006).

La maggior parte della letteratura su questo tema è riferita al contesto americano, estremamente diverso da quello italiano. E' sembrato quindi opportuno e rilevante sviluppare uno studio specifico relativo ad una particolare realtà territoriale, per contribuire ad aumentare la conoscenza dell'efficacia e dei costi dei programmi di screening nella realtà italiana.

L'analisi svolta utilizza come caso-studio l'esperienza di un programma di screening iniziato nel 2005 in Provincia di Ferrara a seguito di un Piano Regionale di prevenzione del CRC, e ha l'obiettivo di determinare i costi effettivi del programma di screening, di confrontare i costi e l'efficacia delle tecniche adottate (test del sangue occulto e colonscopia), e di identificare i risultati attesi in termini di prevenzione del cancro.

[3] Il benessere della paziente è misurato attraverso appositi strumenti anonimi che considerano i cambiamenti delle dimensioni cliniche e psicologiche legate all'esperienza del parto. Gli strumenti utilizzati a tal fine sono: lo S.T.A.I. (state-trait anxiety inventory) forma Y e il Q.U.I.D. (Questionario Italiano del Dolore) prima e dopo il parto; S.T.A.I. e C.P.Q. (Childbirth Perception Questionnaire) nei due giorni successivi al parto.

Anche in questo caso, ai fini della valorizzazione di tutti i costi relativi a ciascuna fase del programma di screening è stata utilizzata una analisi *micro-costing*, seguendo un approccio *activity-based costing*, che considerasse tutte le attività svolte nel processo di assistenza.

L'efficacia dello strumento di diagnosi adottato, test del sangue occulto (FOBT) combinato con esame endoscopico, è stata valutata in termini di lesioni diagnosticate precocemente e di anni di vita guadagnati.

I risultati preliminari ottenuti mostrano che, a seguito dell'adozione e dell'avvio del programma di screening, il numero di nuovi casi individuati di polipi iperplastici, adenomi displasici e carcinomi è aumentato notevolmente. Inoltre, la diagnosi precoce ha permesso una diagnosi dei nuovi casi di tumore negli stadi Dukes meno avanzati.

Nel capitolo 5 vengono presentati i risultati preliminari dei primi due anni di attività di screening in termini di costi sostenuti per l'implementazione, sviluppo, organizzazione e gestione del programma di prevenzione e i costi di tutte le attività di diagnosi (FOBT ed esami endoscopici), del trattamento chirurgico, della terapia oncologica e del follow-up dei pazienti coinvolti nel programma.

I dati di costo e di efficacia raccolti sono stati infine utilizzati per stimare il costo per anno di vita guadagnato, utilizzando un Modello MISCAN-COLON[4].

[4] Il modello MISCAN-COLON è una versione riadattata del modello MISCAN, utilizzato per stimare l'impatto e la costo-efficacia dello screening al colon. Il modello MISCAN è una micro-simulazione di screening (Habbema, 1984) fondata su un modello di Markov, ma la cui formulazione permette un livello di semplificazione minore e quindi una maggiore flessibilità nell'esplorare diverse assunzioni.

Abstract

This thesis considers the topic of economic evaluation in health care.

Specifically we make a cost-effectiveness analysis of two different types of healthcare interventions. First, we evaluate the effects and cost-effectiveness of alternative methods of delivery associated with the introduction of epidural analgesia during labor. Then we analyse the costs and benefits of a colorectal cancer screening program.

The thesis consists of five chapters.

The **first chapter** introduces the study and provides a short review of the main economic evaluations techniques.

The **second chapter** contains a survey of different measures of outcome and quality of life of health care interventions. Namely, we discuss which instruments (questionnaires) can be used to evaluate the effectiveness (in terms of clinical and psychological outcomes) of the delivery event and the colorectal cancer screening. The analysis is fundamental to the cost-effectiveness studies treated in chapter 4 and 5.

The third and fourth chapters analyse the topic of alternative methods of delivery, with special attention to a recent phenomenon that has raised concerns worldwide, but especially in Italy: the increased use, at times not appropriate, of caesarean section practice.

The **third chapter** provides a comparative analysis of the appropriateness of caesarean section practice, comparing Italy and United Kingdom. We analyse the differences in terms of the healthcare system and the socio-demographic framework in the two countries and we consider the potential factors that might explain the high frequencies and variability of caesarean section practice.

The topic of the appropriateness of health care interventions plays a central role in the general debate surrounding public health care system sustainability. In recent years, in fact, an exponential growth in the frequency of caesarean sections has been registered in Europe. This phenomenon seems not to be completely justified by medical reasons suggesting inappropriate use, since caesarean section is practiced independently of clinical or epidemiologic reasons.

We consider the effects that such a practice can have, not only in terms of healthcare expenditure, but also from a broader societal perspective, and we suggest possible health policies and clinical governance measures to manage this malpractice.

Particularly, we examine the recent Italian proposal of introducing epidural analgesia among the Essential Levels of Assistance (LEA)[1] with the aim that this will help to counteract the rise of caesarean sections[2].

Despite the debates on this issue, few studies have paid attention to the real costs of alternative methods of delivery and the main literature refers to the American context, which is extremely different from the Italian one (Henderson J., 2001), both for epidemiologic and health care system characteristics. For this reason, in the **fourth chapter** we analyse the costs and benefits involved in alternative methods of delivery (vaginal delivery, with and without epidural analgesia, and caesarean section) in the Italian framework.

The empirical analysis has been conducted in an Italian university hospital, through direct collection of data, administration of questionnaires and direct interviews to patients and health staff.

A logistic regression has been used to model the probability of the event "delivery with planned caesarean section" occurring as a function of a set of clinical and socio-economic characteristics of the women. The results confirm the hypothesis that caesarean section is widely performed for non-medical reasons (Osborn J. and Signorelli C., 1995; Frost C., 2005).

A *micro-costing analysis* has been used to evaluate the direct health costs of each delivery method, following an *activity-based costing* approach. The analysis shows that caesarean section is, on average, more expensive if compared to vaginal delivery, but the difference is marginal if we take into account the opportunity-cost of time during labor. Since caesarean section is generally reimbursed more than vaginal delivery to cover the supposed higher costs of surgical intervention, differences between the real costs and the DRG tariffs may induce opportunistic behaviour in terms of clinical practice.

The introduction of epidural analgesia among LEA would certainly have a huge impact in economic terms, but the final effect is not clear: it may reduce the frequency of inappropriate caesarean sections, but also it may increase the costs due to complications.

From a societal perspective we consider also the indirect costs, the intangible costs (transport, medications, artificial feeding, time lost) and the benefits of each method[3].

[1] LEA are all the interventions that Nhs must supply to all citizens for free or through co-payment.

[2] In Italy more than 35% of deliveries are CS, while the WHO suggests an appropriate rate of 10-15%.

The cost-effectiveness analysis shows that, in general, vaginal delivery with analgesia provides better results both in terms of costs and benefits. Nevertheless, in many cases epidural analgesia can require emergency procedures, with worse results both in terms of costs and benefits.

The **fifth chapter** contains an economic evaluation of a colorectal cancer screening program in Ferrara Province.

Colorectal cancer (CRC) is one of the most common forms of cancer in western countries, and represents the second leading cause of cancer mortality in Europe (AIRT, 1998-2000). Evidence from several scientific studies suggests that screening for the early detection and removal of cancerous lesions can reduce the incidence of CRC, its resultant impact on mortality (Sonnenberg A., 2000, Lieberman DA., 1995) and improve patients' quality of life (Taupin D., 2006; Miles A., 2006).

The main literature on this topic refers to USA and few studies have been conducted in Italy. For this reason, the development of a specific study referred to a particular setting has been considered appropriate and relevant to increase the knowledge about the effectiveness and the costs of screening programs in the Italian framework.

This work uses as case-study the experience of a CRC screening program started in 2005 in the Province of Ferrara as part of the Regional Plan of CRC prevention and aims at determining the full cost of the screening program, at comparing the costs and effectiveness of the diagnostic techniques adopted (faecal occult blood and colonoscopy), and at the identification of the expected results in terms of cancer prevention.

Also in this case, we use a *micro-costing analysis* to identify and evaluate all of the costs involved in each phase of the screening program, following an *activity-based costing* approach to consider all the activities carried out in the assistance process.

The effectiveness of the diagnostic instruments used, FOBT combined with colonoscopy, is valued in terms of early detected lesions and years of life gained.

The preliminary results show that, after the screening implementation, a huge number of new cases of hyperplasic polyps, dysplastic adenomas and carcinomas are detected.

[3] The patient's wellbeing is measured through appropriate anonymous instruments that consider the changes in clinical and psychological dimensions due to the delivery experience. The instruments used are: S.T.A.I. (state-trait anxiety inventory) Y form and Q.U.I.D. (Pain Questionnaire) before delivery, S.T.A.I. and C.P.Q. (Childbirth Perception Questionnaire) two days after delivery.

Moreover, early diagnosis allows the detection of colorectal cancer at the earliest Dukes' stages.

In chapter 5 we present the preliminary results of the first two years of screening activity in terms of set up costs, the development, implementation and management of the prevention program and the costs of all the activities of diagnosis (FOBT and colonoscopy), surgery treatments, oncologic therapies and follow-up of the patients involved in the program.

Finally, we use the cost and effectiveness data collected to estimate the costs for year of life gained, using a MISCAN-COLON Model[4].

[4] The MISCAN-COLON model is an adapted version of the MISCAN model, used to predict the impact and cost-effectiveness of colon cancer screening. The MISCAN model is a micro-simulation screening analysis (Habbema, 1984) based on a Markov model, but it allows for less simplification and therefore more flexibility in exploring various assumptions and can be used to simulate all candidate screening tests.

CHAPTER 1

ECONOMIC EVALUATIONS OF HEALTH CARE PROGRAMS

1. Introduction

The economic evaluation of public healthcare programs and interventions is assuming an increasing role in the decision making process of public administrators. The healthcare context is becoming complex: the health care demand is increasing both in quantitative and qualitative terms and the public resources are scarcer. For this reason the policies adopted and the following decisional choices must be legitimated also from an economic perspective.

Economic evaluations of healthcare are considered a normal practice in many economic and political frameworks, but in the Italian context their diffusion is still limited. This aspect is reflected in the scientific literature, where the main studies are conducted in the American and English frameworks.

Concepts and instruments of economic evaluation are not a relevant issue in literature, especially in the international one. First applications of the economic evaluations of healthcare programs have been done in the 19th century, even if the systematic utilization and methodological formalisation have been done in the thirties of the last century in the United States during the New Deal period (this period was signed by strong public interventions for the economic and social support).

Public expenditure represents one of the prevalent factors of the introduction of the evaluation methods to attain both allocative and technical efficiency, maximizing the benefits obtained[1].

The economic evaluation of a program or public intervention recalls the fundamental principles of the *homo-economicus* action, efficiency -minimization of resources consumed with respect to the output obtained- and effectiveness - the ability to achieve a desired result. In the public organisations context, the efficacy concept is linked to the output one, as the ability to influence the needs and behaviours of the community. The economic evaluation, ex-ante and/or ex post, is an unavoidable moment,

[1]For an exhaustive historical and contextual analysis of the public organizations' framework, see Mussari (1999).

especially with refer of the scarce resources of which the public decision maker dispose, and that must be allocated among a multitude of possible alternative interventions.

The concept of economic evaluation must not be confused with the only efficiency, but it is aimed to the individuation of the most appropriate choices, including the change of the status quo, that maximizes the social value totally produced.

The economic component represents only a part of the evaluation process and sometimes not even the prevalent, but requires to be integrated with measures of efficacy in terms of result, and thus highlights all the method complexity that cannot ignore the presence of specific professions. Otherwise, in fact, we risk getting results appositely shaped to particular interests and not reliable.

In a review of economic evaluations for health care programs, Jefferson et al. (2002), highlights the diffuse presence of methodological errors. The same results were obtained by Neuman et al. (2000) with refer to the application of the cost-utility analysis done in healthcare from 1976 to 1977.

These aspects confirm the risk linked to an incomplete knowledge of the methodology to apply in the economic evaluation.

With refer to the healthcare programs Kernick (1998) highlights some questions that must be put for an accurate economic evaluation:

- Have all the alternatives been considered?
- Have all the institutional point of view been considered? (Healthcare organizations, Minister, Regional Agency, practitioners)?
- Have all the costs effectively born been considered?
- Which outcome measures have been considered?
- Can results be generalized?

The evaluation problem cannot be faced without giving an answer to these questions, except with the risk of unreliable results, and thus, suboptimal choices, neither from an economic point of view, nor from the effectiveness of the program (Siegel J., 1996).

2. Economic evaluation methods

The main economic evaluation programs presented in literature are: cost-benefit analysis (CBA), cost-effectiveness analysis (CEA) and cost-utility analysis (CUA)[2]. Both the three approaches compare the resources consumed by the program (costs) and the outcomes obtained with a program with the same resources and outcomes obtained in absence of program (or with an alternative one) (Drummond M., 1997)

All these methods highlight the additional benefit produced by the program, or that would be generated with respect to the status quo. The element for which the three techniques differ is represented by the method chosen to measure outcomes.

In CBA some attempts are made to value the consequences of programmes in monetary terms, so as to make them commensurate to costs. The other two methods do not reach a monetary value. In CEA the consequences of programmes are measured in the most appropriate natural effects or physical units, such as years of life gained or correct diagnoses. In CUA the consequences of programmes are adjusted by health states preference scores or utility weights; that is, states of health associated with the outcomes are valued relative to one another. The most common measure of consequences in CUA is the "*quality –adjusted life-years*" (QALYs).

The choice of one of the three methods depends by many factors. The first choice factor is represented by the possibility to measure the outcomes in monetary terms. In healthcare services, in particular those where the public component is strong, the ability to give an economic value to the outcomes is neither immediate, nor possible in some cases. For this reason the use of cost-benefit analysis to evaluate healthcare programs is limited. Moreover, the cost-benefit analysis finds its highest utility and application for the efficient allocation of resources among alternative programs.

In many healthcare programs the problem does not consist in the opportunity of doing something or not, but in the choice of the most efficient way to do it. In this sense, cost-effectiveness and cost-utility analysis find complete application in the healthcare programs context to increase their technical efficiency (Mitton CR., 2003).

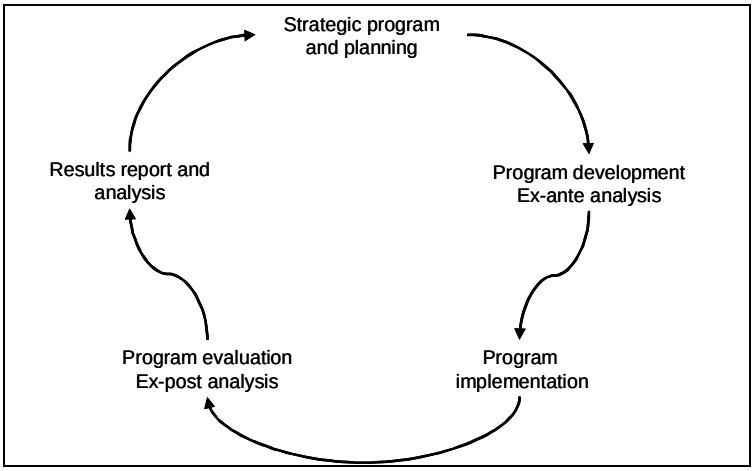
The process through which a program can be started and implemented is characterized, from a theoretical point of view, as a traditional planning and control process (fig.1).

The choice of a program came form a decisional process. This process, starting from the strategic priorities set by the annual planning, begins with an ex-ante evaluation,

[2] For further details see McDavid and Hawthorn (2006).

based on theoretical models and empirical analysis, in order to increase the probability of the intervention effectiveness. Then, an ex-post analysis verifies the obtained results, comparing them with the ex-ante objectives, and through a final report, evaluates the program effectiveness and the future decisions of continuing, changing or stopping the program.

Fig. 1 Logic process of introduction and evaluation of a program



Source: our elaboration

Cost effectiveness analysis (CEA) is one form of full economic evaluation where both the costs and consequences of health programmes or treatments are examined.

CEA is of most use in situations where a decision-maker, operating with a given budget, is considering a limited range of options within a given field[3]. This methodology is based on the assumption that the available resources in healthcare sector are limited both from a social and organizational point of view, and for the healthcare staff and patients.

Cost-effectiveness analysis compares alternative treatments when costs and outcomes are different. Costs are expressed in monetary units (dollars, euros, GBP), whereas the outcomes of the alternative treatments are expressed in non-monetary terms (years of life gained, cases treated with success, reduction of mmHG). For each alternative intervention the costs are compared with the related effectiveness measure. The lower is the ratio (cost/effectiveness) the higher should be the economic convenience for that alternative.

[3] For example, a person with responsibility for organizing cancer screening programmes might be interested in maximizing the number of cases detected.

Cost effectiveness analysis is an economic evaluation that takes into consideration the costs and the direct consequences of healthcare interventions and programmes. CEA allows the comparison of programmes having different consequences, thus is widely used in the healthcare sector.

The choice of a CEA requires that for each alternative is possible to evaluate the cost for effectiveness unit: the alternative with the lowest cost (and the same effectiveness), or the most effective (and with the same costs or cheaper) will be preferred.

This methodology is applied to solve optimization problems with refer to two particular situations:

- budget allocation choosing among a certain number of alternative programmes; having the aim of maximize the benefits (expressed in terms of effectiveness);
- reach a certain level of effectiveness bearing the lowest possible cost.

Although primarily a clinical issue, the availability of good quality data on the effectiveness of the programmes or treatments being assessed is crucial to the cost-effectiveness analyst. A major source of effectiveness data is the existing medical literature and systematic reviews but data can be obtained by expert opinions and clinical trials. In situations where no good clinical evidence exists, the cost-effectiveness analyst may proceed by making assumptions about the clinical evidence and than undertaking sensitivity analysis of the economic results to different assumptions.

The alternatives of CEA can be presented in a decisional tree, describing the available choices and consequences, where all the costs and effects can be expressed for each alternative.

CEA results can be expressed by a cost-effectiveness ratio (CER), where the effects of each intervention are compared with the costs. The intervention with the lowest cost (and the same effects) or the one with the highest effects (and the same costs) will be chosen as the more cost-effective.

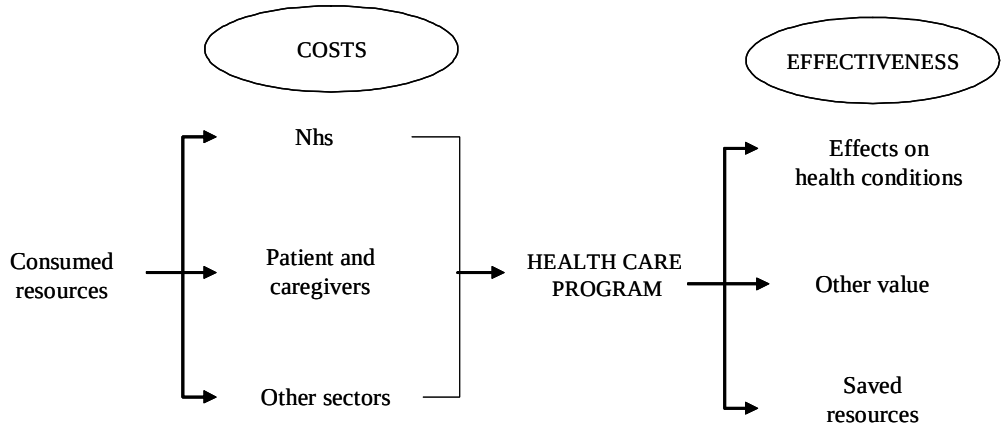
The incremental cost effectiveness ratio (ICER) is the ratio between the incremental cost and the incremental effectiveness of a program compared to an alternative one.

First, this method considers the direct costs and effects of a specific program/intervention, but does not consider the indirect costs and effect of the alternatives. Then, comparing the alternative interventions this analysis assumes that

results change in quantitative terms, without taking into account the qualitative changes.

According to a cost-effectiveness analysis an healthcare program should be analysed considering the costs (the resources consumed) and the effectiveness (in terms of created value) of the program (Figure 2).

Fig. 2 Cost-effectiveness analysis logic scheme



3. Evaluation of costs

Generally in costs evaluations three categories of costs can be identified:

- costs of healthcare resources: such as health materials, instruments, human resources, interventions, diagnostic exams, treatments; we can distinguish fix costs, variable costs and general costs; the identification can be done through direct measurement and the evaluation can be done using market prices, or more accurately the real costs of each resource;
- costs for patient and caregivers: private costs born to be treated (time lost, productivity costs, transport costs) and for assistance; these costs cannot be valued with market prices, but other evaluation methods must be applied (for example a human cost approach);
- costs of resources consumed in other sectors that may be directly affected by the intervention/program.

The main problem to be faced is the evaluation of the private costs for patients and caregivers, the intangible costs, as well as the costs in other sectors. In many cases the latest are not evaluated.

The identification, measurement and evaluation of all the cost items and the consequences must be done separately, therefore a unitary measurement of each phase and item must be done before further evaluations can be done.

For example, all the resources consumed in each phase of the health assistance process must be identified and accurately measured in unitary terms (number of physicians, nurses, time spent, material used, pharmaceuticals administered).

To this aim, the choice of the cost analysis method is extremely important.
According to the main literature (Drummond et al, 1997), the evaluation of the costs related to the intervention/program to be valued, should be done through a *micro-costing analysis*: this approach requires that all the single cost items must be identified, measured and evaluated.
This methodology, even if more laborious and less generalizable than a *gross-costing analysis*, gives a better and specific insight of the relation existing between the activities and the costs (Brouwer W., Rutten F., Koopmanschap M., 2001).
The individuation and measurement of each cost item should be done through direct measurement, with punctual collection of data from clinical record or through direct interview with physicians, nurses.
In the case-studies analysed in this work, we chose to evaluate the costs of procedures, intervention and health assistance using a micro-costing analysis, despite the lack of efficient informative systems. This choice, even though it requires more time, resources and faces more difficulties, has been supported by two reasons: first the reliability of the data collected and the measurements, then the innovative aspect assumed by this study, given the lack of similar studies done in our Country.
Another innovative aspect of this work is represented by the evaluation of the indirect costs for the patient and the caregivers. In the first case-study, where we evaluate the costs and effectiveness of alternative delivery methods, we considered not only the direct health costs of the delivery event, but also the costs born for the artificial feeding, the transport costs and the time lost by the patient and relatives.

4. Evaluation of effectiveness

With refer to the second dimension- the effectiveness- we can identify three types of consequences following a health program/intervention:

- changes in the health status of the patient (physical, social, emotional);
- other changes (reduction of anxiety);
- saved resources (reduction of future costs due to early diagnosis or prevention).

In the two case studies presented in this work, the effectiveness dimension is evaluated in a different an innovative way.

In the first case the effectiveness of the delivery methods is measured not only in terms of health status (i.e. Barthel index of disability) but also in terms of psychological changes and perception of the delivery experience. The instruments used for this evaluation are mainly psychological questionnaires that are not commonly used in cost-effectiveness analysis (for a more complete description see the next chapter).
In the second case the effectiveness of the screening program is measured in terms of early detected lesions, early diagnosis of cancer, number of avoided deaths and life years gained.

5. Case studies of cost-effectiveness evaluation

In this work we make a cost-effectiveness analysis of two different types of healthcare interventions.
In the first case-study we evaluate the costs and the effectiveness of alternative methods of delivery and we estimate the impact of the introduction of epidural analgesia during labor.
In the second case-study we evaluate the cost-effectiveness of a colorectal cancer screening program implemented in a specific Italian Province.

5.1. Costs and benefits of alternative methods of delivery

Aim of this work is to propose the results of a cost-effectiveness analysis of alternative methods of delivery in an Italian hospital.
After a short description of the study framework (the recent CSs increase in Europe and Italy) and the aim of the work, we describe the methodology of data collection and analysis. In this case-study we analyse the costs and benefits effectively involved in alternative methods of delivery- vaginal delivery (VD), with and without epidural analgesia, and planned caesarean.

A micro-costing analysis is used to evaluate the direct health costs of each delivery method, following an activity-based-costing approach.

From a societal perspective we consider the implicit indirect costs (transport, medications, artificial feeding, time lost) and the benefits of each method.

The effectiveness of each delivery method is measured using different instruments: we use the Barthel index to measure the disability before and after delivery, the Childbirth Perception Questionnaire to measure the mother's perception of the delivery experience, and finally we use the ability of natural breastfeeding as outcome measure.

The costs and effectiveness results are compared to calculate cost-effectiveness ratios.

5.2. Cost-effectiveness analysis of a screening program

Each public health policy, especially those involving a clinical intervention, such as a screening program or a preventive treatment, must be carefully evaluated to understand which potential advantages and disadvantages it can have both in health and economics terms.

The ethical principle for each clinical program is assuring that the potential benefits overcome the adverse effects. This is truer for the screening programs, because the persons involved are asymptomatic, therefore the program should give evidence on a hand of the potential advantages for the whole population, and on the other hand of the minimal risk for the individuals participating the program (Wilson J., 1968).

The World Health Organization (2006) defines the screening as "*a public health service in which members of a defined population, who do not necessarily perceive that they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of disease or its complications*"[4].

The first aim of an oncologic screening is the reduction of mortality and, where possible, the reduction of incidence, through the identification of individuals with pre-symptomatic lesions that can require further examinations and treatments.

[4] This is the most recent definition from the UK-NSC (Health Departments of the United Kingdom (2000). *Second Report of the National Screening Committee*, October).

An appropriate treatment of the cases identified by the screening must consents a high rate of recovery.

As the potential benefits of the program must overcome the disadvantages, a rigorous organization is necessary to insure that the available resources, even more limited, are used to provide an equal program and high quality services for the population.

According to WHO principles and actual recommendations, there are many aspects to take into account before implementing a screening program:

1. *frequency and distribution of cancer in the population*: incidence, survival rates and mortality for specific types of cancer differ from a Country to another, determining the priorities for prevention in different ways;
2. *knowledge of the natural history of the disease*: the tumour must have characteristics in terms of pre-malignant phases or limited invasion, that allow the utilisation of diagnostic techniques and the eradication of cancer in the early development and asymptomatic phases;
3. *quality of the screening test:* healthy individuals will be screened with a variable risk of disease, thus the test must be easily executed, acceptable, sensitive, specific and secure. The screening test cost must be sustainable for the health system;
4. *scientific evidence of theoretical and practical effectiveness of the screening test:* there is a real benefit only when the death for a given type of cancer can be avoided or delayed, so the test application should be able to reduce the disease incidence;
5. *identification of the target population:* the individuals that must be included in a screening program must be carefully identified (for gender, age, risk of disease);
6. *analysis of the advantages and disadvantages of the screening test:* the effectiveness of a cancer screening in reducing incidence and mortality is a necessary but not a sufficient condition to implement a screening program; all the screening programs can have side effects (such as false negative results that do not led to early diagnosis, false positive results that generate anxiety, or discomforting and painful follow-up tests);

7. *screening cost-benefit ratio:* the screening cost must be evaluated with refer to the whole health expenditure, including the time spent for the diagnosis and treatment.

These last two points represent the crucial point for the choices in the health sector: the limited resources available for the NHS must be carefully managed and rationalized to attain the effectiveness, efficacy and efficiency targets.

In order to achieve the objectives mentioned before, the health organisations must do proper economic evaluations that consent them to operate with concrete and reliable data.

5.2.1. Cost-effectiveness analysis of a colorectal screening program in Italy

Aim of this work is to propose the results of a cost-effectiveness analysis of a screening program for the colorectal cancer prevention in Italy.

Namely, we expose the case study of a screening program adopted in the Province of Ferrara, in Emilia Romagna Region.

After a short description of the colorectal cancer (CCR) characteristics, we describe the screening program implemented in the Province of Ferrara to prevent CCR and the methodology of data collection and analysis. Then we present some preliminary results of effectiveness in terms of incidence reduction and number of lesions detected. Finally, after a short description of the MISCAN (Micro simulation SCreening Analysis) model used to estimate the number of saved years of life with the screening program, we show the results of the cost-effectiveness analysis[5].

[5] The Miscan Model simulation has been conducted by the Department of Public Health, at the Erasmus University Rotterdam by J.A. Wilshut.

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CHAPTER 2

SURVEY ON DIFFERENT MEASURES OF QUALITY OF LIFE

Abstract[†]

To evaluate interventions in the field of health care, economists have begun to develop quality of life measures.

Here we present a survey of the most used instrument to measure effectiveness and quality of life in healthcare.

After a brief presentation of the concept of quality of life, we give some examples of outcome measures in general.

First we describe the general instruments reported in literature to measure the quality of life and then we illustrate specific instruments used for patients with cancer.

In the last part we descuss the instruments (questionnaires) used to evaluate the effectiveness, both in terms of clinical and psychological impacts, of the delivery experience.

1. Introduction

Recent developments in the fields of economics have intensified the interest of social scientists in particular aspects of quality of life (QoL).

Changes in the public sphere have also been important in focusing attention on quality of life. To justify new or continued funding projects or programmes must be shown cost-effective. Thus, measuring cost-effectiveness requires not only the relatively straightforward task of quantifying inputs to a program but also the more difficult task of evaluating its outcomes (Baldwin S., Godfrey C., Propper C., 1990).

To evaluate interventions in the field of health care, economists have begun to develop quality of life measures.

Here we present a survey of the most used instrument to measure effectiveness and quality of life in healthcare.

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2. The quality of life in healthcare

The quality of life is a notion that has been discussed, in various guises, throughout the history of philosophy. In recent times such notion has been variously employed by social scientists, for example by economists concerned with the question how society should best allocate resources.

The notion of quality of life appears in health care sector quite early and in the 60s-70s the health literature shows the initial interest for this concept, first theoretically and later with the first ideas about the measurement techniques and the development of questionnaires to be applied in practice (Niero M., 2002).

According to Apolone (1998) we can distinguish three outcome categories: clinical and epidemiologic, humanistic and economic (tab.1 appendix).

The components of the first type of outcome are measured by objective indicators, derived by diagnostic procedures such as clinical events, physic-metabolic measures and mortality.

The economic outcomes evaluate direct and indirect clinical aspects, such as hospitalisation, health examinations, resources consumption, working hours lost, productivity reduction.

The category of humanistic outcomes contains the measures mainly treated in this work: symptoms, functional status, wellbeing and quality of life.

These elements synthesise the main part of the variety that includes different approaches of QoL in health care.

According to Spilker (1990) QoL represents the functional effect of disease and therapeutic treatments on patient, in the way the patient defines it. Therefore QoL should be measured as the final status of a therapeutic treatment and must be considered one of the primary indicators of outcome (Fries JF., Spitz PW., 1990).

To define the quality of life some authors consider only a dimension of the humanistic outcomes, others include in the concept all the dimensions.

The World Health Organisation (1995) defines the QoL as the subjective perception that an individual has of his position in life, in a cultural setting and in a set of values in which he lives, in relation with his aims, expectations and worries. It refers a wide concept that can be modified by the perception of personal physical, psychological and

emotional health, by the level of independency, by the social relations and the interaction with the specific environmental context.

This definition highlights the main components of QoL, and creates a link among them.

In general, many authors have provided a definition of QoL that takes into account only one particular component, such as functional abilities (Patrick D., Smiths SJ., Miller JM., 1973), general satisfaction (Shumaker SA, 1995), wellbeing, and needs.

The subjectivity is the central concept of all these definitions, where the patient has an active role in the determination of his level of QoL.

All the definitions have been translated into measures, through standardised or semi-standardised questionnaires.

The employment of standardised questionnaires in healthcare is still controversial (Apolone, 1998), but it is necessary to compare outcomes of different experiences or interventions.

The use of questionnaires in medicine can be divided into four phases:

- in the first phase we find instruments to evaluate patients affected by chronic diseases, or cancer: the Karnofsky Performance Scale (1948) followed by the Activities of Daily Living and the Barthel Index (Mahoney, Barthel, 1965); in this period questionnaires are used also in psychiatry such as the Inventory to measure depression (Beck et al, 1961);
- in the second phase, from 70s-90s, many instruments have been developed starting from chronic disease questionnaires with contributions form social sciences; the measurements produced in this phase are widely employed today as general instruments of QoL;
- in the third phase, began in 90s, disease specific instruments are developed to measure the impacts of particular pathologies; in this period statistic techniques have been adopted to reinforce the validity and reliability of the existing instruments.

In 1996, the American Society of Clinical Oncology has declared the health-related quality of life one of the most important element to measure in patient with cancer.

Differently from other outcomes, such as toxicity, survival, physical reaction, the quality of life offers a unique perspective of the benefits that a patients can have during a clinical intervention (Conray, 2003).

Clinical studies often “undervalue the severity of the patients’ symptoms” and the evaluation of the patients can offer a deep knowledge of the symptoms of a treatment (Conray, 2003; Padilla, 1991)

Conray et al (2003) suggest that the quality of life is an element of the prognosis more useful than the performance status of a clinical exam to foresee the survival.

A clear and absolute definition of quality of life is not available yet. Even if the instruments linked to the quality of life consider a high quality of life as a good physical, social and emotional function, the patients do not give the same importance to these dimensions.

Smith and colleagues (1999) refer that the patients with chronic disease distinguish the *health status*, and the *perceived health* from the *quality of life:* for *the health status* they consider the physical dimension, for the quality of life they consider the mental status.

Smith and colleagues also state that, even if in some studies *health status* and quality of life are used to refer to the same concept, they are two clinical formulations that deeply differ. According to the authors, the quality of life is a multidimensional approach that measures the mental and physical status to get a general evaluation. From this perspective the social element is less important.

In general all the questionnaires used to measure the quality of life focus on the physical, social and emotional functioning (Conray, 2003). Sometimes the evaluation includes the pain dimension and the role limitation.

We can distinguish at least two main types of questionnaires:

- Generic questionnaires: used for a large number of diseases;
- Specific questionnaires: used for a specific type of disease.

There is not a unique questionnaire used in general for all the studies, but the selection of a questionnaire must be done according to the research aim and the psychometric proprieties to measure in the project.

3. General instruments to measure quality of life

Purpose of this section is to describe several instruments reported in the literature to measure the QoL in patients. The main characteristics are synthesized and presented in appendix (tab.2, 3, 4).

Many generic instruments to measure the QoL have been developed in the 1970's to satisfy the concept of health defined by the WHO in 1948 as "*a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity*"[14].

The multiplicity highlights that there is no common agreement on what is "quality of life". The continued development of instruments between the 70s and the early 90s, may signify a shift of ideas regarding QoL assessment.

The physical-psychological-social dimensions are present in the measures produced during that latter period, in particular the SF-36 (Brazier et al., 1992), the Sickness Impact Profile (SIP) (Deyo, Inui, 1982), the Nottingham Health Profile (NHP) (Hunt, McEwan, 1986).

The *Short Form Health Survey 36*, SF-36 (Ware and Sherbourne, 1992) is part of a larger project, the Medical Outcome Study (MOS), aimed to evaluate the effect of medical treatments on the wellness and the functionality of the US population (Stewart and Ware, 1992). The short questionnaire (36 items) evaluates 8 dimensions: the physical functions (10 items), the social functions (2 items), limitations due to physical problems (4 items), the limitations due to emotional problems (3 items), the mental health (5 items), the energy/vitality (4 items), the pain (2 items) and the perception of health in general (5 items). The 36th item explores the changes in health status with refer to the previous year.

The SF-36 evaluates the health status in general, so it can be used both for studies in the general population and for transversal/longitudinal studies concerning specific pathologies and treatments.

[14] Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948.

The scale of evaluation can be filled in 5-10 minutes and has a high degree of acceptability.

The evaluation of the items can be different for each area: some of them are dichotomous; others are valued with scales of 3, 5 and 6 levels.

Many studies have affirmed the good psychometric measures of the SF-36. The extensive use of this instrument has allowed a definition of the standard profiles and synthesis measures for an easier reading and interpretation of the results. This instrument has strong psychometric evidence that leaves no doubts on the internal and external validity and reliability of the scales. For this reason the SF-36 is a reference measure for the design and development of new instruments.

Moreover, this questionnaire has a solid structure, thus it is well accepted by the respondents and the probability of missing values is very low.

The SF-36 measures also positive health status and can be used for healthy population, not only for persons with disability or diseases; this is a characteristic that other instruments, such as the NHP and the SIP, does not have.

The SF-36 has been translated to almost 30 different languages and has been used in different countries obtaining good results, even if some concepts of physical vigour, energy, are more characteristic of the American culture than of the European in general (and South-European in particular).

Because of its characteristic of general questionnaire, the SF-36 needs to be combined with other specific questionnaires when particular patient populations are considered.

The *Nottingham Health Profile-NHP* (Hunt and McKenna, 1986), as the SF-36 has been designed to give a definition of health. This instrument has not been developed through the selection of previous questionnaires, but through a qualitative survey of the University of Nottingham at the end of 70ies on the English population. Almost 2.200 statements that people used to express the subjective sensations linked with health were collected during interviews.

It is composed by two parts, the first one of 38 items exploring 6 areas (pain, physical mobility, sleep, emotional reactions, energy and social isolation), the second one considers the perception of problems in 7 life sectors (reimbursed occupation, jobs near home, social relationships, social life, sexual life, hobby and holidays).

The validity and reliability of the NHP has been demonstrated in many studies and experiences developed in the last 20 years.
It has been translated in 13 languages obtaining good results.
This instrument is simple be administered and easy to be understood, thus it is useful for old people.
The questionnaire is composed by dichotomous answers (yes or no), so it is easy to be fulfilled, but the probability of missing values is high when persons are not able to make a defined choice.
The sensitivity of this instrument is very high, but tends to increase for worse health status. It can be used only to measure distress, thus it is not useful for normal persons in good health.
A short version of this measure, the *NHP-distress*, has been obtained from the previous one without the physical dimension (Hunt and McKenna, 1989).

Another general instrument to evaluate QoL is the *Sickness Impact Profile-SIP*, developed in his final version by Bergner in 1981.
The questionnaire measures the patient perception of his health condition. It was designed for different types and stages of disease and for varying demographic and cultural subgroups. It has been largely used as a measure of outcome in health studies in order to plan and develop assistance programs, to determine health policies and to monitor patient conditions during treatment (even if this instrument is not very sensitive to changes).
The SIP is a self-administered questionnaire to measure the physical and psycho-social activity and is composed by 136 items covering 12 areas (job, leisure, emotions, relationships, home and family, sleep, rest, diet, ambulation, mobility, communication and social interactions). The total score obtained by a series of calculations necessary to standardize the point of the different areas, may vary from 0 to 100: in a normal population is possible to obtain values of 2 or 3; in patients affected by strokes 30 point can be reached.
The peculiar aspect of this instrument is given by its ability to be adapted to many pathologic situations and substitute specific measures. Its length constitutes a disadvantage for its use. This instrument has been validated and translated in many languages (Carone M, 1999; Deyo et al., 1982).

Due to its length, this instrument was not useful for patients with serious illnesses thus, a shorter version of the questionnaire has been proposed, the SIP-68 items, in order to achieve better psychometric qualities than with the first version.

The *EuroQol* (EuroQol Group, 1990) represents the attempt to develop a general, standardized instrument to describe and evaluate the HRQOL independently from the specific disease. The EuroQol Group, composed by North-European researchers (England, Finland, Netherlands, Norway and Sweden) began the works in 1987 and published the results in 1990, with a final version of the questionnaire, called EQ-5D in 1991. The questionnaire considers 5 dimensions and an analogical self-evaluation scale.

The main characteristics of the EQ-5D are the following:

- it is a simple generic measure that considers only the areas common to the generic measures of health status;
- it explores each area with the lowest possible number of items;
- it gives a "health profile";
- it produces a unique general number, an index, of the health status.

This generic index can be assumed as reference element for the comparative evaluation of the costs of different intervention protocols to estimate the cost/benefits ratio and decide the allocation of the available resources for the health assistance.

Another instrument has been developed by the WHO to evaluate the QoL, the *WHO Quality of Life*- WHOQOL (WHOQOL Group, 1995), in two versions, an extended one of 100 items (WHOQOL-100), and a shorter one of 26 items (WHOQOL-BREF). Both instruments have been developed using a trans-cultural methodology, have subsequently been tested in 15 centres, and are available in 30 different languages.

These instruments give value to the subjective perception of the individual health status, giving the possibility to evaluate the disease non only in clinical terms, but also from a different perspective: the impact that disease and its treatment can have on social relationships, on job activities and on socio-economic conditions as perceived by the individual. The WHOQOL-100 explores the 6 areas; each section consists of 4 specific items and 4 general items that examine the total QoL and health status in general. The items are evaluated in a 5 points scale.

The WHOQOL-BREF examines only one item for each of the 24 sections, and 2 items of the general ones.

One of the main economic evaluation methods is the cost-utility analysis: it captures the implications of a new concept of health, in terms of value of life. This approach is based on the assumption that individuals make rational choices and express preferences comparing their health status with hypothetical health status. In these techniques the health status used to obtain utility, are based on scenarios, each of them generated by the combination of the main component elements of health. This health status can be generated by standard instruments of QoL, but are generally very short, to generate a limited number of combinations.
One instrument is the Health Utility Index - HUI (Furlong, 2001); it consists of 4 dimensions and generates 960 combinations (virtual health status).

The *Quality of Life Self Assessment Inventory* – QLS-100 (Skantze, 1993), consists of 100 items, divided in 11 sectors that explore the habitat status, the environment, the culture and the educational level, the relationships, the addictions, the internal experiences, the mental and physical health, the free time, the job and religion aspects. The subjects must express the satisfaction level that they get from either of these aspects. After the self-evaluation the physician checks, through a semi-structured interview, the scores that the patients assigned to each aspect and debates the implications for the following treatment. The authors sum the scores obtained in each sector to get a general index of Qol: the score will be one-dimensional with low probability, given the high heterogeneity of the sectors explored. The QLS-100 is not useful for clinical studies because of its length.

The *Quality of Life Inventory*- QOLI (Frisch et al, 1994) is an instrument to evaluate the QoL, based on the assumption that the general satisfaction is a result of the sum of the satisfaction in specific areas of life that the individual believes to be important.
Each of the 16 items represents a sector of life (health, job, friendships, home and others) and for each two dimensions are evaluated, the first to evaluate how much is important for the individual (from 0=not important at all, to 2=extremely important) and the second to evaluate the degree of satisfaction (from -3=very unsatisfied, to

+3=very satisfied). The patient is invited to make a list, for each item, of all the problems that are an obstacle for the achievement of the satisfaction.
The QOLI is short, simple to be complete and to be interpreted, and has an exhaustive manual but its psychometric evaluations are quite weak.

4. Specific instruments to measure quality of life

One of the first instruments proposed to evaluate the QoL is the *Quality of Life Scale-QOLS*, developed by Flanagan (1978) and adapted by Burckhardt et al. in 1989 for chronic diseases.
The scale is composed by 16 items, evaluated in a scale of 7 points, from "very pleasant" to "terrible", and has been used with good results in patients suffering of lupus erythematosus, rheumatic arthritis and similar diseases.

The *Quality of Life Index – QL-Index* (Spitzer et al, 1981) is a short (5 items) and simple instrument of hetero-evaluation (external), built to evaluate the results of treatments of cancer patients, but being very general it can be easily used also for other pathological conditions. However is not useful to evaluate subjects in good health. The QL- Index considers different items, such as: activities, daily life, health, support and humour, and gives a global judgment of the evaluator of the accuracy (and validity) of the evaluation. The evaluation scale is made by 3 points (0-2) and each level is accurately described; the highest scores correspond to the positive answers. Thus the higher is the index (from the sum of the single scores), the better is the quality of life. This instrument can give a valid starting point to evaluate risks and benefits of treatments and supports programs (such as palliative therapies) in patients with serious pathologies.

The *Quality of Life Interview-QOLI* (Lehman, 1988) is a semi structured interview, largely used in chronic psychiatric patients living in communities. The interview is composed of 143 items exploring the functions in daily life and the satisfaction that patients with serious mental illness derive from it. The QOLI gives objective indexes of the quality of life (stability of the living place, daily activities, frequencies of familiar and social contacts, job condition, subsidies and others) and subjective

indexes of quality of life (satisfaction with life conditions, leisure time, familiar and social relationships, security, legal problems, health problems and others). The psychometric characteristics have been largely verified. The same questionnaire is available in a short version of 78 items.

The *Psychological General Well Being- PGWB* (Dupuy, 1984) has been developed with the aim to supply an index to evaluate the subjective wellbeing or distress. It is composed by 22 items (each of them with possible answers from 1 to 6), that evaluate the frequency and intensity of the experience (6 for the best answer and 1 for the worst). The PGWB, that contains the SF-36 items, explores many dimensions: anxiety, depression, benefits, self-control, general health status and vitality.

The *Quality of Life Index*- QLI (Ferrans & Powers, 1992) takes into consideration the QoL in the 4 areas (health and functionality, socio-economic status, psychological/humour status and familiar life) generally considered as fundamental to define it. The scale used is defined as "discrepancy model", a technique that uses the patient's evaluation of the importance of an area or an event, to weight the evaluation of his/her satisfaction or impact in the same area. This technique can explain the impact of the factors connected to the evaluation of the measure of the QoL and allows a more accurate and detailed analysis. The questionnaire considers 34 items that measure the satisfaction of the subject in the different areas explored and the importance that he/she attached to each area. The QLI has been developed to be applied to patient in haemodialysis, but it has also been used for chronic psychiatric patients (Atkinson et al 1997). The QLI has shown good psychometric measures.

According to the Quality of Life Research Unit of the Toronto University, there are three main sectors to consider in order to determine the QoL: Being, Belonging and Becoming, each of them divided into three sections. On this premise a new instrument has been developed, the *Quality of Life Profile-Seniors Version*- QOLP-SV (Raphael et al, 1995, 1996), dedicated to senior subjects, because "aging of population is associated to an increment of chronic diseases and, as a consequence, to an increasing demand of services for old people".

The QoL is an essential element for those who must supply these services, as it represents a means to rationalize them and to evaluate their effectiveness.
The QOLP-SV takes into consideration the three sectors and the nine sections considered essential for the definition of the QoL. For each section must be determined its importance for the individual and the satisfaction level he/she can obtain from it.
For each of the 9 sections the degree of control is evaluated that the individual has on them and whether he/she has the opportunity to improve or change them. The validation studies gave good results.
A specific instrument for adolescents has been developed by the same group, the *Quality of Life Profile- Adolescent Version*- QOLP AV.

The *Lancashire Quality of Life Profile* – LQL (Oliver, 1996) built from the Lehman QOLI, is an instrument developed according to the hypothesis that the quality of life is a complex concept, that cannot be described by a single measure and that must be valued only through a profile of various indicators, that differ for the measurement scale, the temporal interval used, the type and number of required indications" (Ruggeri, 1998). The scale, proposed to evaluate health and wellness of patients with mental pathologies, takes into consideration three different variables: the individual characteristics of the patients (demographic and economic indicators such as age, gender, origin, social class), the objective indicators of QoL (social indicators, behavioural and psychopathological treats), and the subjective measures of QoL.
The LQL is a self-evaluation instrument, composed by 100 items exploring 13 sections: patient's characteristics, general wellbeing (two sections), job-education, leisure time, religion, financial situation, housing conditions, legal and security status, familiar relations, social relations, health and self esteem. The period of time considered might vary with respect to the items, from the last 2 weeks to the last year. The Italian version of the LQL has been developed and validated by the Psychiatric Institute of the University of Verona.

The *Quality of Life Enjoyment and Satisfaction Questionnaire*-Q-LES-Q (Endicott et al, 1993) is a self-reported questionnaire developed to obtain a sensible measure of the pleasure and satisfaction degree that the individual has in the different sectors of daily life. These measures seem to be related to the severity of pathology (especially in

depression) and contribute to highlight important differences that other types of measure are not able to explore.

The Q-LES-Q is composed of 58 items exploring five areas: physical health (13 items), subjective sensations (14 items), leisure time activities (6 items), social relationships (11 items) and general activities (14 items). There are also 3 other scales related to the work activity (paid work, house keeping and student). The items are evaluates on a 5 points scale and the higher scores express the greater satisfaction and pleasure. In addition to these items there are other 2 items that must be evaluated separately and express, satisfaction with treatment (if the subject receives any) and the person's general satisfaction and fulfilment.

4.1. Specific instruments used to measure Quality of Life in patients with cancer

The Nottingham Health Profile and the *Short-Form Health Survey* (SF-36) are the most used general instruments to evaluate QoL. Specific instruments have been developed to capture the effects of specific diseases, such as cancer.

An example of specific instrument is The European Organization for Research and Treatment (EORTC) Quality of Life Questionnaire (QLQ-C30). Differently from the SF-36 that can be used for different diseases, the EORTC QLQ-C30 has been validated for patients with cancer. It consists of 30 questions divided into nine parts, that measure: physical health, role functioning, cognitive health, emotional and social health, tiredness, pain, sickness, vomit, and one question about health in general. For patients with colorectal cancer this questionnaire is linked to the QLQ-CR38, which is specifically designed for this form of cancer (Aaronson, 1999). The EORTC QLQ-30 is one of the most important questionnaires as it measures the changes in health status, even if it does not distinguish the different stages of the disease. This questionnaire has been validated with patients of different nationalities and cultures and allows for comparisons between countries (Aaronson et al 1993).

Since its development in the 1990s, this instrument has been translated into several languages and is widely used in international trials in oncology (Efficace, 2004). During this time, however, the treatment for CRC has evolved to include the use of radiotherapy, chemo-radiation before surgery, minimal access surgery and new chemo-therapy regimens.

The QLQ-CR38, therefore, may no longer sufficiently cover the effects of current treatments. In addition problems using the questionnaire have been reported relating to missing data and lack of specificity.

This instrument contains specific scales to particular patients' subsets, and it is not possible to directly compare issues between these groups. Finally, the QLQ-C38 was only tested for its psychometric performance in the Netherlands, but not internationally (Sprangers, 1999). For these reasons, a new module, the QLQ-CR29 has been developed by the EORTC QoL Group and it is available in six European languages. It will undergo psychometric examination in an international field study to ensure that it is an appropriate and psychometrically tested instrument to be used in international clinical trials in patients with cancer of the colon and rectum

Bouchet et al compared the SF-36, the Nottingham Health Profile and the Dukes Health Profile (DHP) and shown that the SF36 is the most reactive and the most useful to distinguish between healthy persons and patients with disease. Both give also good results in terms of reproducibility and are easy to be used, but DHP is the best in this special field (Bouchet, 2000).

Even if the evaluation of the quality of life has the potential to supply new evidence with regarding to health and health care, there are still many problems with respect to the methodology and the interpretation of the results.

The use of different instruments and the presence of not validated instruments are some of the limitations in the evaluation of the quality of life (Byrne, 2007). Conray and colleagues explain that the interpretation of data is limited by the statistic analysis that does not include the distribution of the basic level of the quality of life (Efficace, 2004; Byrne, 2007). They suggest the definition of a standard method to allow the publication of precise data.

Another significant limit in the use of these questionnaires is the lack of data, both because patients can be too ill to complete them, and because there is no structure for an efficient distribution and collection of questionnaires in clinical centres (Conray, 2003).

The methodology of data collection for the quality of life presents many obstacles.

From a review of the literature about quality of life of patients affected by colorectal cancer, between 1980 and 2003, Efficace and colleagues found that 74% of all studies do not state their hypothesis before starting the survey, and thus they do not obtain relevant data.

On the other hand there is no uniform approach for the interpretation of the results of quality of life and in particular, rarely the reasons are explained why one instrument is used instead of another.

Moreover, there is a problem of the presentation of the basic level of quality of life and the timeout at which it is established. For screening studies this aspect must be taken into particular consideration. For example, in order to do a precise analysis and to represent the basic level status, it must be stated if the questionnaire has been completed immediately before the screening or some weeks before.

Moreover, few attentions have been done to study the clinical importance of the changes in each single individual. Wyrwich (1999) and colleagues used statistical analysis of a clinical study of 605 patients with cardiac problems to define a standard for *minimally important clinical differences* in the questionnaire of Chronic Heart Failure (CHQ) and the SF-36. They used the standard error measure (SEM) to determine the degree of change required for a significance change and found that for the three dimension of the CHQ a unique SEM criterion is required (generally is used 1.96 at 2.77 SEM). The Wyrwich analysis suggests that a SEM must be used for the CHQ, but that more research must be done before generalizing the results to other questionnaires.

In a short review of the literature, Wedding et al (2007) show some limits in the measure of the quality of life of old patients. In the oldest, the analphabetism, the weak hearing, the tiredness and a bad performance status decrease the compliance with the study. Dementia and other cognitive problems can limit the comprehension of the questionnaires. The presence of other diseases can confound the cancer or the screening impact on the quality of life. Often the studies that validate the questionnaires do not consider oldest patients (Wedding, 2007).

4.2. Specific instruments to measure the effects of delivery methods

Delivery, differently from other health care interventions (therapies and surgical operations) does not change the health conditions or the quality of life of the patient.
Pregnancy can certainly cause temporal discomforts in physical terms, due to vomit, nausea, or headache but can also cause long-term conditions such as hypertension, diabetes, vascular problems.
Vaginal delivery is painful and can have bad physical consequences (vaginal lesions due to lacerations or episiotomy), but generally it does not improve the quality of life.
If delivery is done with caesarean section, it becomes a surgical intervention and can be used for therapeutic reasons, for example to remove fibro-adenomas or cysts, with improvements in health conditions; it can also have complications and woman's health status can get worse, for example in case of incontinence, uterine injuries, or hysterectomy in the worst cases. Psychological changes can also occur after delivery: postpartum depression is one of most known (McKee MD., 2001).
Changes in the quality of life due to delivery are limited to the labor period, the delivery moment and the postpartum period.
Therefore the general instruments used in the economic evaluations (such as QALYs, EuroQol (EQ-5D) and the questionnaires SF_36 o SF_12 (Jomeen J., Colin T., 2005) are not useful in this case.
A first index of women clinical status before and after delivery is the *Barthel index* (Mahoney F, Barthel D, 1965) to measure disability. The index consists of 10 dimensions and for each dimension it assigns points from 0 to 10 to physical conditions, such as the ability to walk, eat, dress. The final scores can vary from 0 to 100 (where 0 is the higher disability and 100 is the perfect health status).
According to the main literature, the instruments used to evaluate the impact of delivery on woman's well being must be clinical and psychological instruments.
The psychological determinants that may give information about the maternal status are anxiety, pain perception and maternal satisfaction of the delivery event.
The instruments used to this aim are the State-Trait Anxiety Inventory- S.T.A.I. Form Y (Scale A-B) (Spielberger C., Gorusch, 1970), the Italian Questionnaire of Pain - Q.U.I.D. , (De Benedittis, 1988) and the Childbirth Perception Questionnaire –CPQ (Padawer et al., 1988).

Specific instruments to measure the effects of delivery methods are described in details in the following paragraphs.

4.2.1. The State-Trait Anxiety Inventory – STAI

The State-Trait Anxiety Inventory (STAI) is the most known and widely used instrument to evaluate the level of anxiety in adults under stress.

In general anxiety is defined as "a subjective state of internal discomfort, dread and foreboding, accompanied by nervous system arousal. Different from fear, anxiety tends to occur without conscious or apparent stimulus" (Gurian B. and Miner J.).

The distinction between the "trait" anxiety and the "state" anxiety introduced by Cattel and Scheider (1961), has been elaborated by Spielberger et al in 1970, to develop a self-evaluation scale. The theoretical background of this concept is the distinction of anxiety as transitional status and anxiety as stabile trait of the personality.

Briefly, "the personality status" is a temporal section in the lifetime that can be expressed through emotional reactions. Whereas, the "treats" of personality can be described as durable differences between individuals in the way they perceive the world and in the way they react or predictably behave (Spielberger, 1983).

The "state anxiety" thus can vary of intensity and change over time as function of the external threats perceived, whereas the "trait anxiety" reflects the individual differences in the frequency and intensity with which the anxiety states have occurred in the past and the probability they can occur in the future.

A first test has been designed in 1964 with the elaboration of a unique group of items, administered in different ways, to assess both the state and treat anxiety. In a second moment the theoretical developments of the anxiety concept and the results of empirical research required a change in the items and procedures of the test.

A form X of the STAI has been developed with 40 items divided in two subscales, that take into consideration the distinctive factors of the state A and the treat A.

In 1979 a substantial revision of the scale X has been done, changing the items more linked to depression and giving much more importance to the cognitive aspect of anxiety. In 1983, after 10 years of application, the STAI-Y form (evolution of the X form) has been published. The revised form, STAI-Y, is easy to be administered and

can clearly distinguish the state and trait anxiety, and thus is the most used instrument to assess anxiety.

The questionnaire consists of 40 items, and the individual must answer in terms of intensity using a Likert scale of 4 points (where 1 is no intensity and 4 is the highest intensity). Items are grouped in two scales, one to explore how patients feel in general and the other one for specific moments.

The two scales are: the state anxiety, where anxiety is a specific experience, a feeling of in security, of impotence facing a threat, which can lead to concern or to escape; the treat anxiety, which consists in the tendency to perceive stressing situations as dangerous and threatening and to react to such situations with a different intensity.

In the study we chose this instrument to assess the effects that the delivery experience can have in terms of anxiety conditions in women. This instrument has already been validated in the Italian framework (Pedrabissi L, Santinello M, 1989), and it is easy to be administered and interpreted, and thus it has been chosen for this study.

Following the instructions of the STAI manual, the questionnaire has been administered in three steps, to assess changes in the anxiety status.

4.2.2. Pain dimension: the Italian Questionnaire of Pain - QUID

The diagnosis and measurement of pain is extremely important in clinical and experimental research. The quantification of observable data is essential to transit from a qualitative to a quantitative science. Thus, in the last year the assessment of pain has assumed an exceptional importance.

The precise quantification of a subjective factor, as pain, presents many limits: we can not rely on the exclusive verbal description of the patient, as the experience of pain qualitatively and quantitatively depends by cognitive, emotional determinants. This means that for the measurement of pain we must consider the multidimensionality of the experience.

There are many scales to quantify the clinical level and intensity of pain, some are simple categorical or ordinal scales (Keele, 1966), others are magnitude or estimation scales (Sternbach, 1974).

The categorical scales consist in verbal descriptor, used to quantify and qualify pain in the simplest way. They require the best choice of the verbal descriptor (slight, strong,

atrocious). The disadvantages of these scales are the limited number of possible answers and the tendency of many patients to polarize their choices on median or extreme values of the scales, introducing a distortion in the evaluation and reducing the possible answers.

Among these scales we can find:

- the Visual Analogue Scale-VAS- by Scott, Huskisson (1976) is easy to be used and more sensitive and reliable if compared to other descriptive scales, even if it reduces pain to a one-dimensional measure;
- the Verbal Rating Scale (VSR) by Keele and Armstrong (1964) is easy to be used and administered but has a low sensitiveness;
- the Numeric Rating Scale (NRS) by Sternbach (1974).

The semantic multidimensional scales consider also qualitative aspects of life experience, cognitive and emotional aspects.

The main used instrument to evaluate pain is the *McGill Pain Questionnaire (*MPQ) by Melzack (1975). It uses 20 groups of descriptors. Adjectives are included in sub-groups and increase for intensity while they describe a pain (the first adjective has value 1, the second 2 and so on). The patient must specify the pain intensity in a numeric verbal scale of 6 points. Four indexes are obtained:

- the Pain Rating Index Scale: the total sum of the value of each adjective chosen;
- the Pain Rating Index Rank: refers to the ordinal position that each descriptor have in its sub-group;
- the Number of Chosen Words: number of descriptors chosen by the patient to describe the pain;
- the Present Pain Intensity: indicates the pain intensity at the moment of questionnaire fulfilment.

This instrument has a high sensitivity and seems to be the most appropriate to distinguish the sensorial quality from the affective and cognitive quality of the pain experience.

From a statistic point of view, many studies confirm the reliability and validity of this instrument. One of the structural limits of this questionnaire is given by an internal disproportion that prefers the sensorial dimension to the affective and cognitive.

This instrument is widely used in the Anglo-Saxon countries and it has been translated and validate in many languages, even if with some semantic limits.

In Italy many versions of the MPQ have been proposes before the final version of the *Italian Questionnaire of Pain (QUID) (Questionario Italiano del Dolore),* (De Benedittis, 1988).

This instrument, based on the original MPQ method, has been designed with the aim of developing an efficient and reliable instrument for Italian patients. The QUID reliability has been measured with a test-retest method and shows a very high accuracy in the choice of the single descriptors (84% of reliability; even higher than the original MPQ). Also the reliability of the sub-groups descriptors is very high, between 76% and 100%.

The questionnaire validity has been valued for many aspects:

- construct validity[15]: the inter-correlation among the main QUID indexes are statistically significant and compared to the original MPQ;
- internal validity[16]: the QUID has even a better internal proportion among the main dimensions of pain experience that the MPQ;
- convergent validity[17]: the QUID has a satisfactory validity if compared to the VAS and the MPQ.

For its reliability and validity, we choose to use the QUID to measure the pain after delivery, as one of the dimension to value the effectiveness of the alternative delivery methods.

4.2.3. Maternal satisfaction as a measure of effectiveness: the CPQ

The term satisfaction is generally used to define a subjective experience of pleasure, constitutes by the emotion felt reaching an aim. This concept refer both to a positive response towards an event and to its pleasing acceptance (Hoddnett, 2002).

In general an individual can be satisfied for some aspects of one experience and unsatisfied for others; positive and negative factors can co-exist.

The theoretical framework shows the multidimensional characteristic of the satisfaction.

[15] In Psychometrics it is the extent to which a test measures a specified construct or hypothetical construct, determined by interpreting the psychological meaning of test scores and testing implications of this interpretation.

[16] The extent to which the conclusions of an empirical investigation are true within the limits of the research methods and subjects or participants used

[17] A form of validity that, together with discriminant validity provides evidence of construct validity. It is based on the assumption that different measures of the same hypothetical construct ought to correlate highly with one another if the measures are valid.

If we apply this definition to the health context, we can observe how a positive reaction towards a specific clinical treatment cannot be considered an absolute category of the satisfaction perceived by the subject.

This issue has been introduced for the first time in UK with the Health System reform of 1980, when the hospitalised patients' satisfaction was evaluated with the aim of improving the health services to be provided.

Lavander (1999) emphasized how this new guidance was important for the maternal satisfaction of the delivery event, predisposing trained professional figures and adequate services for the satisfaction of women and their relatives. After these changes the maternal satisfaction increased and the birth mortality decreased.

Nowadays the main part of the future mothers have positive expectations for the delivery event: these are partially confirmed after delivery, but partially denied for many unpredicted factors, such as an emergency caesarean or the uncontrolled pain.

Maternal satisfaction can be evaluated considering three independent dimensions (Robinson et al., 1998):

- the first one refer to the enthusiasm and happiness associated to delivery;
- the second one is represented by negative emotional reactions and by contrasting feelings of relax and panic;
- the third one indicates the physical discomfort and refers also to pain.

Satisfaction should be measured with a multidimensional instrument, but almost all the evaluation methods investigate the single dimensions separately. In some cases two dimensions are explored in bi-dimensional correlations.

The *Mackey Childbirth Satisfaction Rating Scale* (Goodman, 2003), for example, measures the birth satisfaction through 34 items, and investigates the behaviour during delivery and the feelings of the experience.

Another instrument is the *Perception of Birth Scale* (POBS) (Fawcett, 1996), developed to measure woman's perception of the delivery experience. The questionnaire consists of 25 items, divided in subscales: delivery experience, labor experience, delivery result, partner interaction and mother consciousness. This instrument has been designed after a wide literature review and refers to other instruments: the *29-Items Questionnaire* and the *Questionnaire Measuring Attitudes about Labour and Delivery Experience* (QMAALD, 1979).

The first items of this last instrument refer to labor (ability, relax, control, partner support), the others investigate the birth moment, others refer to expectations and the clinical staff involvement, the last three refer to the first contact with the baby.
A modified version of the QMAALD has been developed by Cranley (1983) to use the questionnaire with women having a planned caesarean, substituting the labor items with others concerning the moment of preparation to the surgical intervention.

The Childbirth Perception Questionnaire (CPQ) was designed by Padawer et al. (1988) to assess women's satisfaction with their childbirth experience. Past research studies have used open-ended interviews or single-item scale to assess women's satisfaction (Affonso, 1980; Cranley et al, 1983; Lipson, 1980), whereas the CPQ is innovative as it uses a multiple-item scale. The CPQ is multidimensional and can measure many aspects involved in the perception of the childbirth experience.
The CPQ consists of three subscales corresponding to concerns and satisfaction regarding many dimensions (tab.4 appendix). The first one regards the woman's physical appearance/sexuality during pregnancy, childbirth and after birth (5 items, range of possible scores was to 5 to 30); an example of item is: "I felt embarrassed about my physical appearance during labor and delivery". The second subscale investigates the delivery mode (Caesarean versus vaginal) and the woman's conduct during the labor and delivery (13 items, range of possible scores was 13 to 78), an example is "I am satisfied with the way I delivered". The last part explores the interaction with partner during childbirth (9 items, range of possible scores was 9 to 54); for example "I felt my husband was aware of my needs during the childbirth experience".
Respondents indicate the extent of their agreement or disagreement with each item using 6-point Likert-type scales (end points are (1) agree completely to (6) disagree completely). Scores for each sub scale are obtained by summing the women's responses (1 to 6) across the items for that scale.
In Padawer study Cronbach's alpha reliability coefficients for the three scale were 0.58 (satisfaction with physical and sexuality), 0.82 (satisfaction with delivery and labor) and 0.75 (satisfaction with partner interaction).
The choice of using the CPQ in the study is due to many reasons. First of all this instrument is multidimensional and allows the evaluation of many dimensions related

to pregnancy and delivery. In second place, the CPQ can be easily administered and analysed: differently from other instruments, that must be administered during labor or delivery, the CPQ can be completed shortly after the birth. Finally, the CPQ can be easily obtained without specific permissions or requirements.

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Appendix

Tab. 1 Examples of outcome measures (Apolone, 1998)

Outcome	*Events*	*Examples*
Clinical epidemiologic	Clinical events Physic metabolic measures Mortality	Infections, myocardial broke Hypertension, tumour markers Specific deaths (tumours), all causes
Humanistic	Symptoms Functional status Health status Well being QALY	Symptoms Check List, pain scales Karrnofsky Index, ADL SF-36, SIP, NHP Psychological General Wellbeing Utility measures in terms of QoL
Economic	Direct medical aspects Indirect medical aspects	Hospitalisation, resource consumption Productivity lost, work hours lost

Tab. 2 General measures of QoL

General instruments

Instrument, *main reference*	**Number of items**	**Dimensions (items)**	**Evaluation**
Short Form Health Survey 36 - SF-36 , *Ware & Sherbourne, 1992*	36	Physical functions (10), social functions (2), limitations due to physical problems (4), limitations due to emotional problems (3), mental health (5 items), energy/vitality (4), pain (2), perception of health in general (5). The 36th item explores the changes in health status with refer to the previous year.	Self-reported
Nottingham Health Profile – NHP, *Hunt & McKenna, 1989*	38	Pain, physical mobility, sleep, emotional reactions, energy and social isolation. Considers the perception of problems in 7 life sectors (reimbursed occupation, jobs near home, social relationships, social life, sexual life, hobby and holidays).	Self-reported
Sickness Impact Profile - SIP *Bergner et al., 1976, Deyo, Innui et al, 1982*	136/68	Job, leisure, emotions, relationships, home and family, sleep, rest, diet, ambulation, mobility, communication and social interactions.	Self-reported
Health Utility Index- HUI *Torrance et al, 1995*	23	Health status	Self-reported
EuroQoL *EuroQoL Group, 1990*	5	Generic health status	Self-reported
WHO Quality of Life – WHOQOL, *WHOQOL Group, 1995*	100/26	QoL, health status, physical area, psychological area, independence level, social relationships, environment, spiritual aspects.	Hetero-evaluation
Quality of Life Self-Assessment Inventory-QLS-100 *Skantze et al., 1992*	100	Habitat status, environment, culture and the educational level, relationships, addictions, internal experiences, mental and physical health, free time, job and religion aspects.	Self-reported
Quality of Life Inventory – QOLI *Frisch et al., 1992*	16	Health, job, friendships, home and others	Self-reported

Tab. 3 Specific measures of QoL

Specific instruments			
Instrument, *main reference*	**Number of items**	**Dimensions (items)**	**Evaluation**
Quality of Life Scale – QOLS *Flanagan, 1978*	16	QoL	Self-reported
Quality of Life Index - QL-Index *Spitzer et al., 1981*	5	Activities, daily life, health, support and humor	Hetero-evaluation; 3 points (0-2)
Quality of Life Index – QLI *Ferrans & Powers, 1992*	34	Health and functionality, socio-economic status, psychological/humour status and familiar life	Self-reported
Quality of Life Enjoyment and Satisfaction Questionnaire- Q-LES-Q *Endicott et al., 1993*	58 (+33)	Physical health (13 items), subjective sensations (14 items), leisure time activities (6 items), social relationships (11 items) and general activities (14 items). There are also 3 other scales related to the work activity (paid work, house keeping and student). Other 2 items evaluate satisfaction with treatment (if the subject receive any) and the persons general satisfaction and fulfillment	Self-reported
Quality of Life Interview – QOLI, *Lehman, 1983*	143	functions in daily life and satisfaction that patients with serious mental illness derive from it. The QOLI gives objective indexes of the quality of life (stability of the living place, daily activities, frequencies of familiar and social contacts, job condition, subsidies and others) and subjective indexes of quality of life (satisfaction with life conditions, leisure time, familiar and social relationships, security, legal problems, health problems and others).	Semi-structured
Psychological General Well-Being – PGWB *Dupuy, 1984*	22	anxiety, depression, benefits, self-control, general health status and vitality	Self-reported
QLQ – C30 *EORCT* QLQ-CR38, *Sprangers MAG, Aaronson, 1999*	30	Physical health, role functioning, cognitive health, emotional and social health, tiredness, pain, sickness, vomit, and one question about health in general.	Self-reported
Quality of Life Profile - Seniors Version - QOLP-SV *Raphael et al., 1995*	111	QoL in elderly	Self-reported
Lancashire Quality of Life Profile – LQL *Oliver, 1991*	100	Patient's characteristics, general wellbeing (two sections), job-education, leisure time, religion, financial situation, housing conditions, legal and security status, familiar relations, social relations, health and self esteem	Self-reported

Tab. 4 Specific measures for delivery

Specific instruments for delivery			
State-Trait Anxiety Index- STAI *Spielberger et al, 1970*	40	Items are grouped in two scales, one to explore how patients feel in general and the other one for specific moments. The two scale are: the state anxiety, the treat anxiety	Self-reported Using a Likert scale of 4 points
McGill Pain Questionnaire *Melzack (1975)* QUID- Questionario Italiano del Dolore *De Benedittis, 1988*	60	Pain Rating Index Scale: the total sum of the value of each adjective chosen; Pain Rating Index Rank: refer to the ordinal position that each descriptor have in its sub-group; the Number of Chosen Words: number of descriptors chosen by the patient to describe the pain; the Present Pain Intensity: it indicates the pain intensity at the moment of questionnaire fulfilment.	Self-reported
Mackey Childbirth Satisfaction Rating Scale *Goodman, 2003*	34	Behavior during delivery, feelings	Self-reported
Perception of Birth Scale (POBS) *Marut and Mercer, 1996*	25	delivery experience, labor experience, delivery result, partner interaction and mother consciousness	Self-reported
Questionnaire Measuring Attitudes about Labour and Delivery Experience QMAALD, *Cranley 1979*	29	ability, relax, control, partner support during labor and birth, expectations and clinical staff involvement; first contact with the baby	Self-reported
Childbirth Perception Questionnaire- CPQ *Padawer et al.,1988*	27	Physical Appearance/Sexuality; Satisfaction with Delivery and Conduct During Labor/Delivery; Satisfaction with Interaction with Spouse During Childbirth	Self-reported

Tab. 5 The three subscales of the Childbirth Perception Questionnaire

Satisfaction with Physical Appearance/Sexuality

- I felt embarrassed about my physical appearance during pregnancy(*)
- I am concerned that I will not be as physically attractive as I was before I had a baby(*)
- Sexual activities or desire frequently decreases for the first 6-8 weeks after delivery: I worry about how this will affect the next few months(*)
- I felt embarrassed about my physical appearance during labor and delivery (*)
- Sexual activity or desire frequently decreases for the first 6-8 weeks after delivery: I worry about how this will affect our marriage in the long run (*)

Satisfaction with Delivery and Conduct During Labor/Delivery

- I feel satisfied about my conduct during labor and delivery
- I lost control of myself emotionally during labor (*)
- I feel that I did not deal with the physical pain during labor as well as other women do (*)
- I am satisfied with the way I delivered (vaginal or caesarean)
- As a result of my childbirth experience, my self-respect has gone up
- I feel disappointed about my conduct during labor and delivery(*)
- I was satisfied with how much control I had over decisions made during my childbirth
- I am satisfied with the amount of drugs/medications I used during labor and delivery
- I am disappointed by my childbirth experience (*)
- As a result of the labor and delivery experience, I feel I do not cope very well with pain (*)
- I thought that the labor and delivery would be easier for me than they were (*)
- I did things during labor and delivery that I am now embarrassed by (*)
- As a result of my childbirth experience I feel less self-confident (*)

Satisfaction with Interaction with Spouse During Childbirth

- I felt my husband was aware of my needs during the childbirth experience
- I felt emotionally close to my husband during labor
- I think the experience of pregnancy has strengthened my relationship with my husband
- I am worried that the baby will in some ways have a bad effect on my relationship with my husband (*)
- I think the experience of labor has hurt my relationship with my husband (*)
- I feel that my husband was as helpful as he could have been during the childbirth experience
- I am satisfied with how my husband and I communicated during labor
- I think the baby will have a good effect on our marriage
- My husband is spending as much time as possibly can visiting me in the hospital.

(*) asterisked items were reverse-scored.

CHAPTER 3

SUSTAINABILITY AND APPROPRIATENESS OF PUBLIC HEALTH CARE SYSTEMS: THE MEDICAL PRACTICE OF CAESAREAN SECTION IN ITALY AND UNITED KINGDOM

Abstract

This chapter provides a comparative analysis of the appropriateness of caesarean section practice, comparing Italy and United Kingdom.

We analyse the differences in terms of the healthcare system and the socio-demographic framework in the two countries and we consider the potential factors that might explain the high frequencies and variability of caesarean section practice.

The topic of the appropriateness of health care plays a central role in the general debate surrounding public health care system sustainability. In recent years, in fact, an exponential growth in the frequency of caesarean sections has been registered in Europe. This phenomenon seems not to be completely justified suggesting a high level inappropriateness use, since caesarean section is practiced independently of clinical or epidemiologic reasons.

We consider the effects that such a practice can have, not only in terms of healthcare expenditure, but also from a broader societal perspective, and we suggest possible health policies and clinical governance measures to manage this phenomenon.

Namely, we examine a recent measure provided in Italy that proposes the introduction of epidural analgesia among the Essential Levels of Assistance with the hope that this will help to counteract the rise of caesarean sections.

1. Introduction

Caesarean Section (CS) practice has registered a huge growth in all the European countries, but especially in Italy, where the 37.8% of CSs over all deliveries has overcome the appropriate rate of 10-15% suggested by the WHO (ISTAT, 2004).

In June 2006, after the publication of the ISTAT report about "Pregnancy, delivery and breastfeeding", all the main journals, newspapers and media reported the Italian primate in Europe for the CS rates[1].

This phenomenon has raised strong concerns among politicians and public opinion that many caesareans were not necessary and not appropriate.

In Italy there is also a strong variability in the use of CS, in particular in the Southern Regions, where demographic and logistic characteristics seem to explain the frequencies of CS practice.

The increase in CSs rates seems not to be justified: CS is practiced independently from health conditions or epidemiological reasons, but more often for physicians' induction or mothers' demand (Dranove D, 1995).

Physicians might have a higher preference for planned caesarean because they can reduce the risks of natural deliveries and thus avoid legal problems (Dubay L., 1999), and they can better organise and manage health and human resources (Brown H., 1996)[2].

Mothers might prefer a delivery with caesarean, because they think it is safer and can limit the risks for them and the baby, but especially because they think they can avoid the pain of a natural delivery. This aspect seems to be even more evident in UK, where the increment of CSs is lower than in Italy, but mainly referred to patients demand (so to be mentioned as "*too posh to push*" phenomenon).

This tendency has certainly an impact in terms of equity and healthcare expenditure and new policies must be implemented to counteract the rise, suggesting alternative forms of delivery assistance.

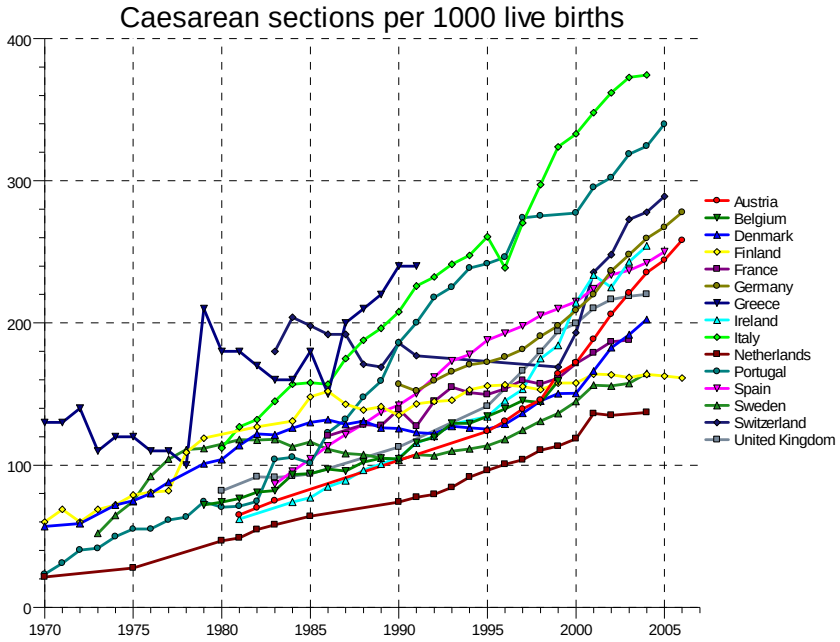
[1] For example see the titles of the newspaper *Corriere della Sera* (6 June 2006) "Italia prima in Europa per i parti cesarei" ("Italy the first in Europe for caesareans") and *Repubblica* (5 June 2006) " Parti cesarei è boom. L'Italia prima in Europa" ("A boom of caesarean sections. Italy the first in Europe").

[2] Especially in those hospitals where the constant presence of anaesthetists is not granted, and there is lack or health staff and beds.

2. Caesarean Section frequency

An increase in the frequencies of CSs has been registered in all the European countries since 1970 to 2006 (Fig. 1). In some states, such as France, Finland, Sweden and Netherlands, CSs are less than 200 per 1000 live births, in other states, such as Austria, Denmark, Germany, Ireland and United Kingdom, the number of CSs is between 200 and 260 per 1000 live births, whereas in Italy and Portugal, CS is practiced in more than 300 per 1000 live births[3].

Fig. 1 Caesarean Sections Trend in Europe (CSs over1000 live birth)

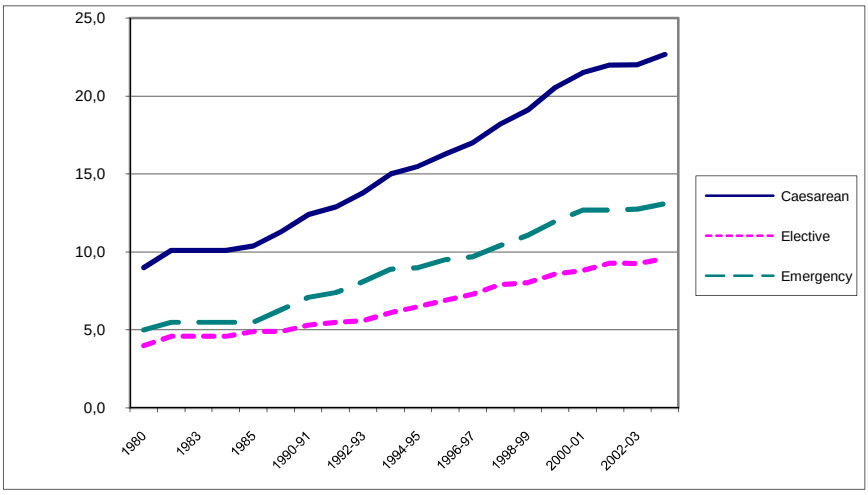


Source: Database Health for All Europe 2008 - June 2008

As shown in Fig. 2 (and tab. A1 appendix) in UK the percentage of the CSs practiced over all the deliveries increased from 9% in 1980 up to 22,7% in 2005, but the increment is attributable most to the urgent CSs (increate from 5 to 13.1%) than to the elective CSs (increased from 4 to 9.6%).

[3] If we analyse the percentage variation in the last 20 years we observe a general increment in all the Countries: up to 40% in Denmark, France and Finland and not proportional in Ireland (141%), Portugal (74%), UK (95%) and Italy (82%).

Fig. 2 Caesarean Sections frequencies in UK, 1980-2003

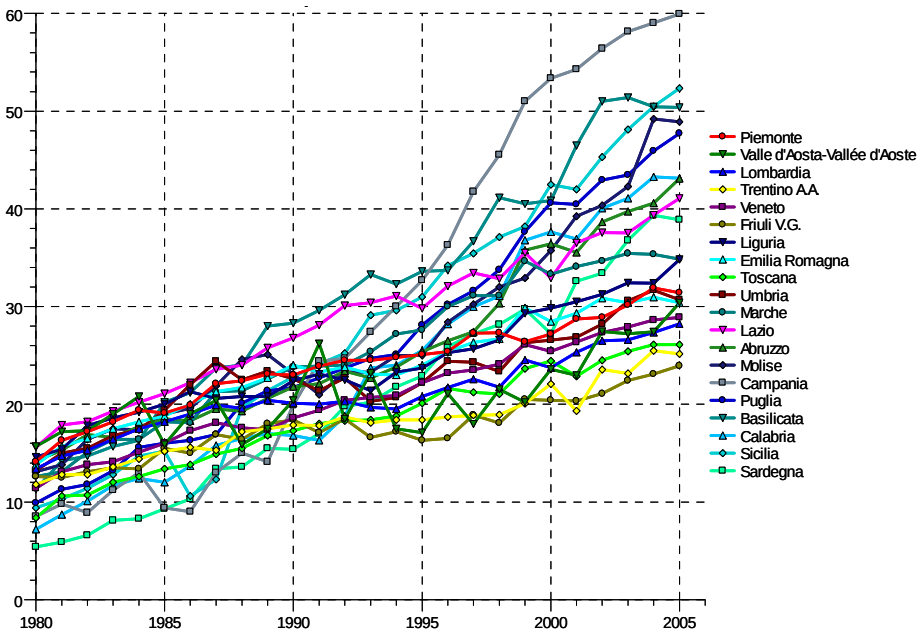


Source: Department of Health UK 2006

In Italy the CSs procedures over all deliveries are increased from 11.2% in 1980 up to 38.32% in 2005.

As shown in Fig.3 there has been a general increment in all the Italian Regions, but not in the same measure.

Fig. 3 Caesarean Sections frequencies in the Italian Regions 1980-2005



Source: Database Health for All Italy 2008

Since 1980 to present, the increment has been contained in some Regions such as Val d'Aosta, Trentino, Friuli and Lombardy (below 100%), whereas in other Regions the increase has reached the 500%, such as in Campania, Sardinia and Sicily.

There is a high difference in the frequencies of CS practice between Regions and in the hospitals within the same region. If we observe the frequency of CSs over all deliveries in Veneto Region, in 2000-2001 (Fig. A1 in appendix), we see a substantial difference among the structures: in particular there is a huge difference between the Local Health Organisation of Treviso (where CS is practice in 16.7% of deliveries) and the Local Health Organisation of Chioggia (where CS is practice in 44% of deliveries).

The two main aspects to be analyzed and debated are the following:

- The increment of CS rates over all deliveries has overcome the appropriate CS rate suggested by the WHO, reaching in some Regions values higher than 50%. There is concern in terms of appropriateness of this medical practice and about the economic impact that it can have.
- The high variability of the practice at national level among the different Regions and also at regional level among the different local health organizations: a different utilization of CS practice within the same Region, if the epidemiologic framework is the same, is not justified and can lead to inefficiencies and inequities (McPherson K., 1990; Phelps C., 1995)

3. Analysis of the factors that might explain the increased rates of CSs

Many factors might contribute to explain the high frequency and variability of CS practice:

- Epidemiologic, demographic and clinical factors: i.e. the birth rate (natality) and fertility rates, the average age of women at delivery, the plurim deliveries, the mortality rates during delivery (both for mothers and babies);
- Non clinical factors: healthcare resources (human resources, available hospital beds), socio-economic status of mothers, education level, financial incentives.

We will see in details if and how these aspects might contribute to explain the huge increment in the CS practice.

3.1. Clinical factors

Starting from the literature and statistic data available for Italy and United Kingdom, we try to investigate possible clinical factors that might have an impact in the CSs increment.

Among the epidemiologic reasons, the birth rate[4] and the fertility rate[5] might have contributed to increase the frequency of CSs.

For example, the increment of the birth rate leads to an increment of births and deliveries and thus it might contribute to a higher use of the CS's practice.

In percentage, however, the proportion of CSs over all deliveries should remain the same.

The Italian and English data of the CSs rates every 1000 births in the period 1980-2003 (Fig.A2 in appendix) and the birth rates and fertility rates (Fig.A3-A4), show a countertendency trend: the number of CSs increases exponentially in both the Countries, while the birth rate and fertility rate keep a negative trend till the 2000 and register a low increment only in the last years. Thus, birth rate, fertility rate and delivery method seem not to be related.

Nevertheless, if we take into consideration the fertility rate and the number of children for each woman, there might be a non linear relation between the birth rates and the CS rates. After a first delivery with caesarean, in fact, the following deliveries tend to be practiced with another caesarean to avoid complications, thus, in the Regions where women have more than one baby and where caesarean section is already widely used, there will be an exponential increment of this practice over time.

Often CS is practiced for multiple deliveries (for twins), but if we look at the data of the multiple deliveries in both Countries (Fig.A5 in appendix), despite the increasing trend, the variation in percentage is not significant.

An aspect that could explain the rise of CSs in the last decades is the average age of mother at delivery.

In 1980, in fact, Italian women had the first baby at 27 years of age, whereas in 2004 the average age at delivery is 31 years.

[4] The birth rate is the number of living born in the population over 1000.

[5] The World Health Organization defines the fertility rate as the "average number of babies that would be born for each woman, if all the women would have lived till the end of their *childbearing years* and gave birth babies, according to a given set of age-specific fertility rates. This rate is given by the sum of the fertility rates for all ages, multiplying for the interval into which ages are grouped".

The United Kingdom is the European Country with the youngest mothers at first delivery: 7,9% of women has the first baby at 20 years age, whereas in Italy only 2% of mothers are so young.

The percentage of women having a first baby over 35 years of age is increased from 5,65% to 19,26% in 1975-2004 in UK and from 8,76 to 17,78% in 1981-1997 in Italy (Fig. A6 in appendix.).

Having a baby after a certain age can certainly have an impact in the frequency of CS practice. On one hand, older women have a higher risk of complications during pregnancy and delivery, and thus require a caesarean. On the other hand, getting pregnant late is more difficult and may require artificial procreation devices, often very expensive. In these cases babies are considered “precious” and the delivery must be the less risky as possible to avoid risk of complications, thus the CS is the most preferred delivery method.

A high incidence of CS might be explained by an increment of delivery complications and maternal deaths.

If we look at the maternal mortality rates in the last 20 years we observe a reduction from 53 to 3 dead mothers every 100.000 births in Italy and from 18 to 8 dead mothers every 100.000 births in UK (Fig.A7 in appendix).

We do not exclude an endogeneity problem in the data, as the possibility of practice CS could have lead to a reduction in the number of maternal deaths.

3.2. Non-clinical factors

If we consider the non clinical factors, such as the health care resources, we observe a reduction of the number of hospital beds in the maternity units, both in Italy and United Kingdom (Fig. A8). This could explain the use of caesarean section practice only if planning the surgical intervention can lead to a better and simpler organization and management of the delivery unit and the available human resources. Actually, a study by Brown et al. (1996) shows that deliveries with a planned caesarean section are practiced from Monday to Friday, in the morning hours, avoiding weekends and holidays. In this way the delivery event can be planned in moments in which all the staff is available, reducing the probability of emergency interventions at every hour, as normally occurs in case of natural delivery.

The international literature shows the existence of many other factors that could explain the tendency of caesarean sections.

As mentioned before, a delivery practiced with caesarean allows for a better allocation and management of healthcare resources, but especially of physicians' time.

With regard to this last aspect, gynaecologists may prefer planned caesareans to natural deliveries because they can better organise their time, in particular if they work both in public hospital and in the private sector (Shelton, Brown, 1996).

Moreover, the CS practice can reduce the risk of possible complications during delivery, and thus the probability of judicial litigations (Dubay L. et al, 1999)[6]. Thus, caesarean section can be included among the interventions of preventive medicine.

A large body of evidence and econometric work is available upon demand induction in surgical procedure, and caesarean section is probably the most studied procedure.

A wide field of literature sustains the hypothesis that increment of CS rates could be due by the Supply Induced Demand effect (SID) and the financial incentives of the reimbursement system (Dranove D, 1996, Gruber J, 1996, 1999).

The "induced-demand" model states that physicians may exploit their agency relationship with patients by providing excessive care in presence of negative income shocks (McGuire and Pauly, 1991). This model is based on the assumption that physicians derive utility from income and leisure and disutility from inducing demand for unnecessary services. The disutility may also arise from reputation effects.

Thus, physicians will exploit their agency relation with patients to perform more remunerative procedures if the marginal benefit of a specific intervention outweighs the associated marginal costs (Brent W., 2005).

In this context, CS is reimbursed more than vaginal delivery to cover the higher costs of the surgical intervention, but in specialized hospitals, where the costs of planned caesarean can be contained, there is an incentive to practice this type of delivery because of the highest positive margins that the reimbursement system can lead.

In Italy, for example, the DRG tariff to reimburse a caesarean section delivery is very high if compared with a natural one, thus there is a high tendency to practice this intervention because of the financial incentives. A study by Fabbri and Monfardini (2000), demonstrates that physician choice of treatment intensity is quite responsive to the financial environmental he faces. The study, relying on a natural experiment on

[6] With regard to this aspect, the insurance premium for physicians is recently increased.

fees reduction, suggests that risk adverse providers overused caesarean delivery relative to the level that would be chosen by a financially disinterested provider.

The caesarean practice induction cannot be ascribed only to physicians: there is also a certain propensity to caesarean in patients.

In the United Kingdom the so called "*too posh to push*" effect seem to support the existence of a relation between social status and women' desire to deliver without pain. Rich women seem to ask for a caesarean section because they do not want to suffer. Actually, this relation has been denied by a study by Barley and Aylin (2004) using the Nhs data of hospitalisations in 2001.

The social status does not seem to influence women preferences for CS, neither does the education level[7].

Nevertheless, women may prefer planned caesarean because they are no completely informed: they think that caesarean can reduce the risks of complications and the pain during labor, but they are not aware that it is not risk less (Grant D., 2005).

Caesarean section is a proper surgical intervention and can have serious consequences: it can cause not only abdominal pain, but also urethral damages, uterus lesions, haemorrhages and in the worst cases hysterectomy.

The recovery after a CS is more suffering and long if compared with a natural delivery: woman is treated with painkillers, must stay in bed for all the following day and cannot take care of her baby.

Women delivering with caesarean section should wait at least a couple of years before getting pregnant again: the uterine must scar to avoid following lesions. Waiting so long could be an opportunity cost too high to be born for some women.

Caesarean section affects also the possibility of natural breastfeeding. After delivery, in fact, the baby should be attached to the mother's breast as soon as possible, to stimulate the production of milk: this could be difficult to be done after a caesarean, because the mother must recover after the surgical intervention. Women having a caesarean can have more difficulties to interact with the baby because of the wound, the pain, the residual effect of anaesthesia, and this can limit the possibility of breastfeed. This can certainly have a negative impact both in woman's health and her psychological status, but also in economic terms.

[7] A study done in Emilia Romagna Region using the CEDAP data show that the level of education and the delivery methods are not significantly related.

Finally, the woman's desire to face the delivery event without pain is increased, but is not having sufficient answer from healthcare structures.

Recent scientific researches show the many advantages of epidural analgesia in pain reduction during labor (Giron G, 1992). Differently from other European countries where epidural analgesia is quite used, in Italy its diffusion is still limited by social and cultural factors, but especially by economic constrains.

In the United Kingdom, epidural analgesia is practiced in almost the 35% of vaginal deliveries, in the 47% of instrumental deliveries and in the 57% of the induced deliveries. (Tab. A2-A3 appendix.).

In Italy only the 20% of women have epidural analgesia and only the 4% of them in public hospitals, whereas the other must pay for it out-of pocket or do it in private structure.

In October 2006 the Italian Minister of Health has proposed the introduction of this practice among the Essential Level of Assistance, so that it can be provided for free at NHS charge.

4. Estimate of the economic impact of caesarean section practice for NHS

The increasing rates of CSs practiced in the last decades in Italy have raised huge concerns at institutional level for the costs that the public sector must bear for such practice.

The costs borne by the hospital for the delivery are reimbursed with tariffs defined at regional level[8].

Delivery with caesarean section is more expensive and therefore more generously reimbursed than natural delivery, thus a reduction of CSs rates could represent a huge saving in economic terms for the NHS.

In this work we try to evaluate the economic impact and the potential savings that a reduction of inappropriate CSs could have both in Italy and UK.

To this aim, an "appropriate" rate of CSs must be defined, and we considered an "optimal rate" the 10-15% recommended by the World Health Organization[9].

[8] In the Italian National Health Service health services are provided by four main types of hospitals: teaching public trust (university hospital, AO), big and small public hospitals (ASL) and private authorized hospitals (private). They are financed according to two different payment schemes: private and AO are paid prospectively with DRG based tariffs; ASL received a reimbursement drawn from a capitation system, covering a large set of treatments and conditions.

We used the official ministerial data regarding the hospitalisations frequencies for the delivery event, classified by the Diagnosis Related Groups and Health Related Groups in Italy and UK respectively. We calculated the percentage of "CSs without complications" (DRG 371 and HRG N11) over all deliveries in both Countries, and we reduced the percentage to the one suggested by the WHO (so we decreased the number of planned caesareans at the "appropriate" rate). Then we estimated the savings in terms of healthcare expenditure for the NHS for the avoidable CSs, using as proxy the difference between the tariffs for a caesarean delivery and a natural delivery without complications (DRG 371-373 in Italy and HRG N11-N07 in UK).

As shown in tab.1, reporting the Italian and English tariffs for the delivery procedures, in both countries a CS without complications is reimbursed almost € 1.100 and £ 731 more than a vaginal delivery.

Tab. 1 DRGs (HRG) tariffs in 2005-2006 in Italy and United Kingdom

Delivery Description	Italy	UK
370 C-CAESAREAN SECTION W CC (HRG N10)	€ 3.425,89	£ 2.067
371 C- CAESAREAN SECTION W/O CC (HRG N11)	€ 2.397,45	£ 1.489
372 M- VAGINAL DELIVERY W CC (HRG N06)	€ 1.937,46	£ 1.490
373 M- VAGINAL DELIVERY W CC (HRG N07)	€ 1.286,30	£ 758

Source: TUC 2006, DoH UK.

The assumptions made to estimate the savings are the following:

- we assumed that the potential inappropriate caesarean sections must be deliveries without complications;
- we assumed that the potentially "avoidable" caesarean section can be practiced with vaginal delivery without complications;
- we assumed that the "optimal" rate of CSs is the one suggested by WHO, 15-20% over all deliveries.

Reducing the CSs rates registered in 2003 in Italy and UK to the appropriate rate of 15% and assuming that the deliveries could be vaginal, the potential savings in tariffs

[9] The WHO recommendations on appropriate technology for birth suggest that "there is no justification in any specific geographic region to have more than 10-15% caesarean section births".

terms is almost more than € 88.000.000 in Italy and £ 17.000.000 in UK. In tab. 2 we calculated the savings also for the previous years[10].

Tab. 2 Savings in terms of tariffs reimbursement in Italy and UK

ITALY					UNITED KINGDOM			
2003	**DELIVERY**	total nr deliveries		total reimbursed	**2004**	**DELIVERY**	total nr deliveries	total reimbursed
370	CAESAREAN S. w cc	15.720	€	53.007.054,00	N10	CAESAREAN S. w cc	19.682	£ 40.682.694,00
371	CAESAREAN S. w/o cc	182.541	€	430.740.172,29	N11	CAESAREAN S. w/o cc	108.100	£ 160.960.900,00
372	VAGINAL w cc	7.748	€	17.382.560,52	N06	VAGINAL w cc	21.302	£ 31.739.980,00
373	VAGINAL w/o cc	324.973	€	484.034.284,58	N07	VAGINAL w/o cc	349.733	£ 265.097.614,00
374	VAG+steriz	8.599	€	16.729.268,51	N08	VAG+steriz	5.850	£ 10.196.550,00
375	VAG + other	991	€	3.017.624,73	N09	VAG + other	58.215	£ 61.707.900,00
	TOTAL DELIVERIES	**540.572**	€	1.004.910.964,63		TOTAL DELIVERIES	**435.100**	£ 570.385.638,00
	CSs over all deliveries	37%				CSs over all deliveries	127.782	
	% CSs w/o cc	34%				% CSs w/o cc	23%	
2003	OMS suggested 15%	81.086			**2004**	OMS suggested 15%	84.432	
	difference 371-15%	101.455				difference N11-15%	23.668	
	difference tariff €	870,23				difference tariff £	731	
	saving €	**€ 88.289.358,70**				saving £	**£ 17.301.088,70**	
2002	OMS suggested 15%	79.422			**2003**	OMS suggested 15%	82.674	
	difference 371-15%	93.463				difference N11-15%	23.320	
	difference tariff €	870,23				difference tariff £	731	
	saving €	**€ 81.334.306,49**				saving £	**£ 17.047.248,95**	
2001	OMS suggested 15%	77.864			**2002**	OMS suggested 15%	79.685	
	difference 371-15%	82.929				difference N11-15%	21.540	
	difference tariff €	870,23				difference tariff £	731	
	saving €	**€ 72.167.477,72**				saving £	**£ 15.745.666,90**	

Source: our elaboration using TUC 2006 and DoH UK data.

The reliability of these results is certainly limited by many factors that must be carefully examined. First of all we must take into account the fact that the Italian DRG tariffs are defined at regional level and can change during time, so the evaluation should be done for each Region, considering the specific setting in a giving period.

Actually, in many Regions the difference between the tariffs for each delivery method are more evident, such as in Veneto, Tuscany or Basilicata, whereas in other Regions the difference is marginal or the tariffs are the same, as in Lombardy.

In some Regions tariffs may vary with respect to the size and type of hospital classification and if they are public or private structures. In addition, in some Regions tariffs are adjusted year by year, whereas in others tariffs have never been changed since 2000, the year in which the national tariffs introduced with the 1997 D.M. have been converted in Euro currency.

Moreover, the evaluation has been done taking into account only the potential savings for the National Health Service, from a narrow perspective. The same analysis should be made adopting a broader point of view, considering also the costs for society (Drummond M., 1997).

[10] We considered the 2004 data only for the UK because the 2004 data were not available for Italy.

Another aspect to be mentioned is the possibility that the WHO appropriate rate could not be correctly defined.

To this aim we considered the clinical guidelines in Italy and UK[11], to have a better knowledge of the cases in which the caesarean section should be practiced (i.e. for placenta previa, for breech presentation of twins, when the mother is positive for HiV or hepatitis C) and the cases in which CS is not advised (i.e. twins delivery, pre-term delivery, when mother is positive for hepatitis B/C, short baby) (tab. A4 all.).

If we define the "inappropriate" caesarean sections according with the national guidelines instead of WHO rates, we can do the analysis again, but in a more accurate way. For the UK, where delivery data are contained in a detailed database, the analysis can be done in a more specific and reliable way.

We used the hospitalisation data at patient level contained in the English database HES (*Hospital Episode Statistics*) registered in 2004[12]. We extracted all the episodes containing the word "delivery" in the codification and we identified all the deliveries practiced with caesarean sections over all deliveries. We distinguished all the episodes that in the "primary diagnosis" or "secondary diagnosis" codes refer at least one of the circumstances in which the caesarean section is considered appropriate according to the NICE guidelines. Then we identified the proportion of potentially inappropriate caesareans.

Starting from 1.367.715 observations, 107.004 cases of CS deliveries without complications have been extracted. We identified the cases in which a planned caesarean is recommended by the guidelines and the cases for which a vaginal delivery would have been more appropriate.

Only 81.659 caesareans over 107.004 presented at least one of the conditions for which the guidelines suggest a planned CS. This means that almost the 24% of the CSs could be avoided, with a potential saving of £ 18 million (tab.3).

In Italy there is no database providing such detailed information at patient level, thus the analysis has been done in a specific setting.

We considered a Local Health Organisation of the Veneto Region and we used the data of hospital demission reports (SDO) registered in 2005 and referred to the delivery episodes.

[11] The Italian guidelines are based on the English guidelines.

[12] The HES database contains all the hospitalisation data at single patient level and information of the HRG classification of the episodes, the diagnosis and interventions done during the hospitalisation, the complications occurred, the clinical status and the previous diseases, the anamnestic information of the treated patients.

Starting from 906 observations, all the DRG-371 cases of "CSs without complications" have been extracted.

Of 300 cases of CS (33% of all deliveries), only 90 recorded at least one of the conditions for which CS is required, according to the guidelines.

We used the difference between the Regional tariffs for CS and vaginal delivery without complications (in Veneto Region the difference was €1.237,00 in 2005), and we estimated a potential saving of € 259.770 (tab.3).

Tab. 3 Potential saving using the guidelines as indicator of inappropriate CSs

	HES data UK	ULSS Veneto Region
Total Observations	1.367.715	906
Caesarean Sections w/o cc	107.004	300
Appropriate CSs	81.659	90
Potential avoidable CSs	25.345	210
Difference of tariffs	£ 731,00	€ 1.237,00
Potential savings	£ 18.527.195,00	€ 295.770,00

Source: our elaboration

5. The economic impact of CS practice from a broader perspective

In order to evaluate the economic impact of CS from a societal point of view, we should adopt a broader perspective and consider many other aspects (Sculpher M, 2005).

First, we should estimate the real cost of the procedure and not its tariff. Actually, the DRG tariffs, do not reflect the real costs of an healthcare service, because they are calculated as an average value of the costs born by a sample of health organizations and then applied to each health structure using appropriate weights (Nonis M., 2003; Taroni F., 1997).

A more accurate evaluation can be done using a *micro-costing analysis* in a specific setting, to calculate the effective costs of the delivery procedures.

The length of the in-stay for a vaginal delivery is usually shorter than for a caesarean (on average three days versus five days), thus in the period spent in hospital the costs increase both for the hospital and for the patients and their caregivers.

The analysis should take into account not only the direct health costs of the delivery (materials and pharmaceuticals, human resources, instruments and structures

involved), but also the non-health direct costs (transport costs, time lost during the in-stay and for medications, time lost by the caregivers) (Petrou, 2002).
The intangible costs should be carefully analysed too: such as the pain felt during labor or after the surgical intervention and the differences in terms of clinical and psychological impacts for the patient.
As mentioned before, we should also take into account the opportunity costs in the long term of waiting at least two years before getting pregnant again after CS and the costs of the inability of natural breastfeeding.
Finally, we should consider all the health and non-health costs due to the increased risk of complications.

6. Possible strategies to change the medical practice in Italy

The possible strategies to try to change the medical practice in Italy are certainly referable to clinical governance instruments, based on clear and defined guidelines.
Caesarean section should be practiced only in emergency, to save mother's life of her baby, but actually the utilization of this intervention is left to physicians' discretion.
In many European Countries vaginal delivery is usually adopted also ,in the same circumstances for which Italian physicians practice a planned caesarean: for example when the previous delivery was a caesarean or in presence of particular pathologies.
Therefore, physicians and health staff should be "re-educated", incentivising the diffusion and knowledge of all the available scientific evidence on this issue.
Italian women are not free to ask for a caesarean section as a preferred method of delivery, because this practice must be prescribed by a physician (they can decide to deliver at home, in water into a pool, or in other particular settings), but it is also well known that in many cases there is an implicit agreement between private gynaecologists and patients and even in absence of medical indications women can have a planned caesarean if they prefer. These women in many cases are not completely informed of the real consequences of such a practice, therefore it would be essential to reduce the information asymmetry, making them aware of all the benefits and potential risks that this surgical intervention can have.
The number of caesarean sections has been considered in many cases a "sentinel event", to be taken into account when evaluating the hospital performances.

If it would be possible to publish the statistics of interventions and the results in performance terms of all the healthcare structures, hospitals and physicians, as it happens in UK, we will probably register a change in the caesarean section frequencies.

Another possible attempt to reduce the number of caesarean sections could be done at economic level. As mentioned before, there is a financial incentive to practice CSs, because of the positive margin between tariffs and costs (CS is more generously reimbursed than VD), thus a change in the reimbursement system and a reduction of fees could certainly disincentive the use of CS when it is not really necessary.

Finally, women should have the possibility to deliver in the way they think is more appropriate and less painful, introducing alternative delivery methods and devices at NHS charge. The introduction of epidural analgesia among the LEA, for example, has been proposed to this aim and with the hope that this could counteract the tendency of practice too many CSs, increasing women wellness and reducing the public healthcare expenditure.

6.1. Epidural analgesia as a possible solution

Women' desire of deliver without pain has been the stimulus for the development and improvement of specific technique of analgesia and anaesthesia.

Recent scientific evidence show the advantages of analgesia during labor: it reduces pain and determines a reduction of the metabolic needs, increasing the placental perfusion, with huge benefits both for the mother and the foetus (Bocci A., 1995).

In particular epidural analgesia can be considered the most reliable technique and the gold standard for the pain reduction during delivery labor (Giron G., 1992).

Despite the evidence, in Italy the diffusion of this method is limited by socio-cultural factors and economic constrains that limit the creation of appropriate health service of analgo-anaesthesiology assistance in the obstetric units.

In addition to this aspect, there is a certain concern among clinicians that analgesics devices can cause prolong labours with an increased risk of operative and emergency deliveries. Thorp et al (1993) refer an increment of emergency caesareans for women who had epidural analgesia. Another retrospective study done in Austrian show that epidural analgesia can cause an increment in the use of instrumental deliveries, but the

probability of emergency caesarean is the same for women delivering without analgesia (Ploeckinger B., 1995).

According to an Australian study babies born with this technique can not be immediately attached at mother's breast, they face more difficulties in the first week of life and they stop breastfeeding earlier that the other babies (Torvaldsen S., 2005)[13].

Epidural analgesia doesn't seem to be risk less and cannot be practiced in any circumstance. Besides the clinical cases for which this method is not indicated, there is a defined temporal interval in which epidural analgesia can be done during labor.

According the Italian Obstetric Anaesthetists Association, in Italy only 20% of women have epidural analgesia, against the 90% in USA, 70% in England and France and 38% in Spain.

In England epidural analgesia is the most used type of anaesthetic during delivery and its use has increased in the last years (tab. A2, A3 appendix).

The differences registered in Italy may be due to the fact that this practice is not granted by the NHS and not reimbursed: only 4 % of Italians get epidural in public hospitals for free, the others must pay out of pocket in private (between € 800-1000).

The importance of safeguarding the woman's choice to control pain during labour, according to the National Committee of Bioethics and the National health plan, has been confirmed the 18th October 2006, by the National Committee of the Essential Levels of Assistance (LEA), with the approval of a document[14] that underlines the essential role of analgesic procedures during delivery.

The Italian Minister of Health has proposed the introduction of epidural analgesia not only to give to all women the possibility to reduce pain during labour, but also with the hope that this will help to counteract the caesarean section (CS) rates, reducing costs for the NHS.

Nevertheless any study has been done in the Italian framework to evaluate the real cost of alternative methods of delivery, and the economic impact that the introduction of epidural analgesia would have for the NHS.

Moreover, the impacts in terms of psychological and clinical wellness for the women are not clear yet: epidural analgesia, reducing the pain during labor can lead to a better

[13] The study has been conducted at the University of Sidney by S. Torvaldsen and colleagues on a sample of 1300 women. Over the 416 that have had epidural, 172 have had CS and only the 53% of babies born with epidural was breastfed at 24 weeks, versus the 75% of babies born without epidural.

[14] In that occasion has been approved the document "Controllo del dolore durante il travaglio ed il parto vaginale tramite procedure analgesiche" (Pain control during labour and vaginal delivery through analgesic procedures).

perception of the delivery experience and a higher ability of coping with this event, but it is not risk less.

7. Discussion and conclusions

The increase in CSs rates registered in Italy and Europe in the last years is not justified both from a clinical and epidemiologic point of view.

Especially in Italy, there is no evidence to explain the increase and the variability in the CS frequencies. The increased use of this practice seems to be due to other factors, such as risk reduction (preventive medicine) and financial incentives.

This phenomenon certainly has a huge impact in terms of healthcare expenditure for the NHS, but we should also take into account the social costs that it might have from a broader perspective.

In economic terms, CS is considered more expensive if compared to a vaginal delivery: this is confirmed by literature data but also by the DRGs tariffs.

Nevertheless, the main studies done in this field refer to the American context, which is deeply different from the Italian one (Petrou S., 2001, Henderson J., 2001).

Some studies show that there is a difference in costs between caesarean section and vaginal delivery, but it is marginal (Malkin J.D., 2001); therefore a reduction of caesareans would not allow so much saving.

Despite the debates, few studies have put the attention on the real costs of the delivery methods, especially in the Italian framework. It would be the time to evaluate if there are relevant differences in costs among delivery methods, and quantify them.

This would allow, on one hand, to understand if the DRGs tariffs truly represent the real cost of interventions and if tariffs' differences are justified (in Lombardy vaginal delivery and caesarean are reimbursed the same amount), and on the other hand to estimate the impact that the introduction of epidural analgesia could have in economic terms for the public system.

The knowledge of the real costs of health interventions is essential not only for financial reasons but also for a better awareness of the economic implications that new law proposals could have.

At the same time it is also important to evaluate how the delivery methods can impact on women, on their health status and their mental and psychological conditions.

The higher cost of a health intervention can be justified only if it is necessary to increase the patient's health status, to avoid complications or risks, or because it can reduce pain, suffering and allow a better and shorter recovery both in clinical, mental and social terms.

All these aspects will be treated in the following chapter, as extension of this study[15].

To conclude, we cannot define an "optimal" rate of caesarean sections (Cyr R., 2006), but we should adopt strategies that allow the practice of an "appropriate" rate.

[15] An experimental study has been developed in a University hospital in Veneto Region, with the aim to estimate the real costs of different delivery methods- vaginal delivery with and without epidural analgesia and caesarean section- and the benefits in terms of psychological impacts for the patients.

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Appendix

Tab. A1 Methods of delivery practiced in UK in 1980-2003

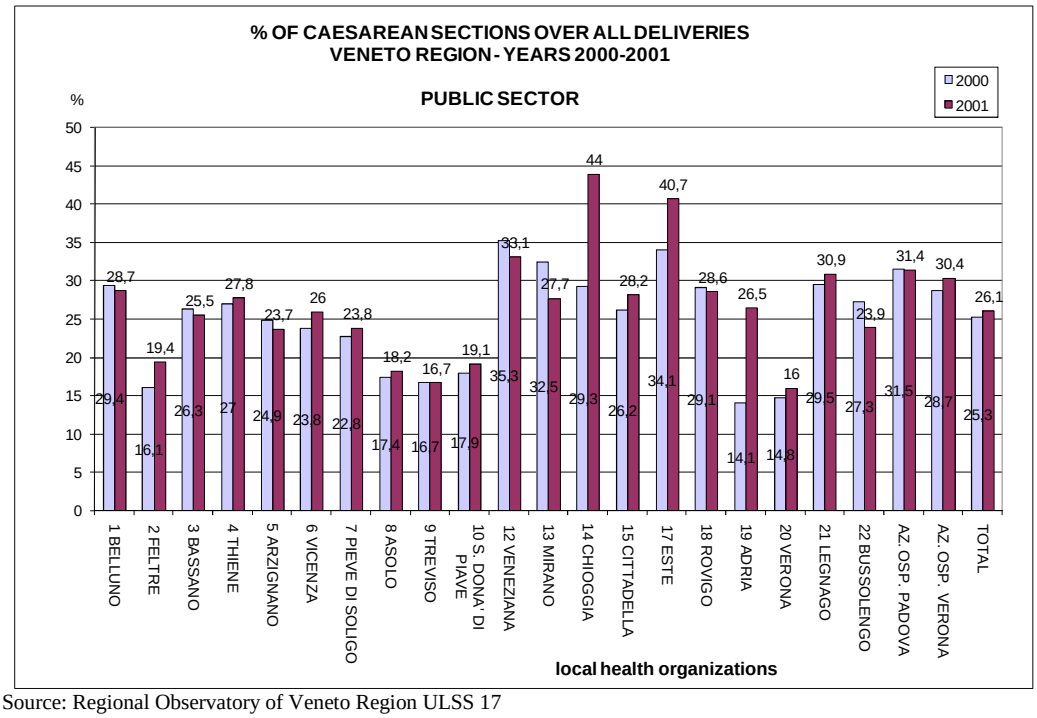
NHS hospital deliveries: method of onset of delivery, 1980-2004

England *percentages %*

	Total nr of cases 100%	Method of delivery											
		Spontaneous		Forceps		Ventouse	Breech	Breech extract.	Caesarean			Other
		Vertex	Other	Low	Other				Total	Elective	Emergency	
1980	601.500	75,5	1,0	6,2	5,1	0,7	1,2	1,3	**9,0**	4,0	5,0	0,1
1982	574.600	75,8	1,1	5,7	4,6	0,6	1,0	1,0	**10,1**	4,6	5,5	0,0
1985	605.100	75,4	2,5	5,3	3,8	0,7	0,9	0,9	**10,4**	4,9	5,5	0,1
1989-90	633.500	76,7	1,4	3,9	3,9	1,6	0,8	0,3	**11,3**	4,9	6,3	0,2
1990-91	652.100	75,6	1,1	4,0	3,5	2,1	0,8	0,3	**12,4**	5,3	7,1	0,2
1991-92	643.800	75,1	1,2	3,9	3,0	2,7	0,8	0,2	**12,9**	5,5	7,4	0,2
1992-93	624.600	74,4	1,1	3,6	3,0	3,1	0,7	0,2	**13,8**	5,6	8,1	0,2
1993-94	620.200	72,5	1,3	3,5	3,0	3,7	0,7	0,2	**15,0**	6,1	8,9	0,2
1994-95	604.300	71,5	1,3	3,3	2,5	4,8	0,7	0,2	**15,5**	6,5	9,0	0,2
1995-96	592.600	70,8	1,5	2,8	2,3	5,4	0,7	0,2	**16,3**	6,9	9,5	0,1
1996-97	594.500	70,6	1,1	2,4	2,1	5,9	0,7	0,1	**17,4**	7,3	9,7	0,3
1997-98	585.000	69,2	1,0	2,2	1,7	6,5	0,5	0,1	**18,2**	7,9	10,4	0,5
1998-99	577.500	67,7	1,2	2,0	1,7	7,1	0,5	0,1	**19,1**	8,0	11,1	0,6
1999-00	565.300	66,3	1,1	2,0	1,8	7,4	0,4	0,1	**20,6**	8,6	12,0	0,4
2000-01	549.600	65,1	1,5	2,1	1,7	7,2	0,5	0,1	**21,6**	8,8	12,7	0,4
2001-02	541.700	65,6	0,9	2,0	1,5	7,2	0,3	0,1	**22,0**	9,3	12,7	0,3
2002-03	548.000	65,9	1,0	1,9	1,5	7,1	0,3	0,1	**22,0**	9,3	12,7	0,2
2003-04	575.900	65,5	1,0	1,7	1,6	7,0	0,3	0,1	**22,7**	9,6	13,1	0,2

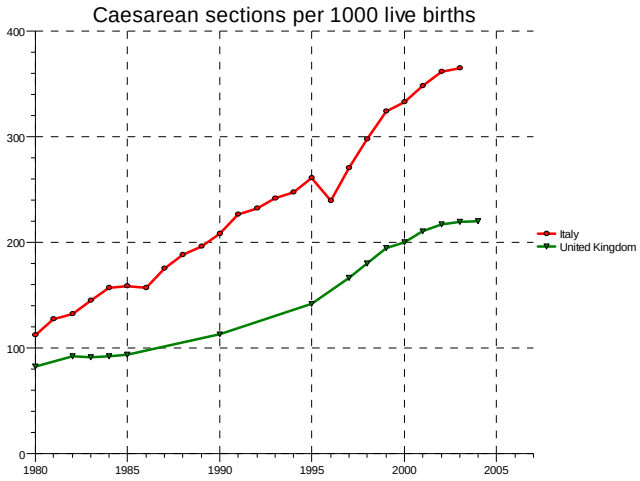
Source: HIPE,HES

Fig. A1 Percentages of CSs over all deliveries in Veneto Region in 2000-2001



Source: Regional Observatory of Veneto Region ULSS 17

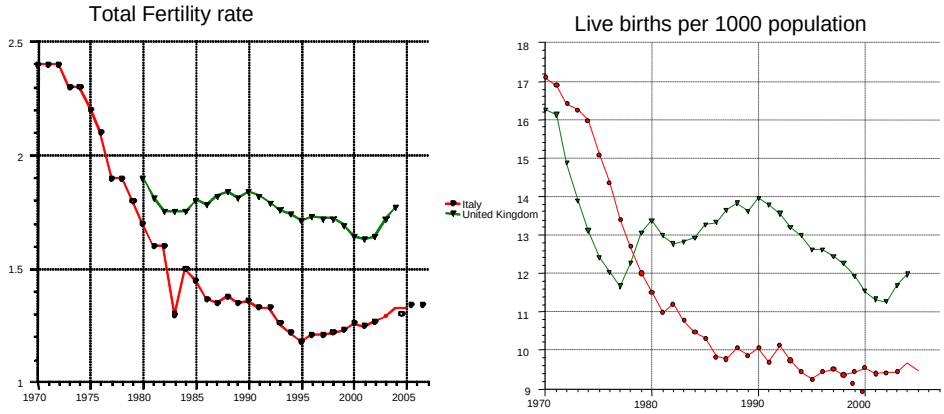
Fig. A2 Caesarean sections practiced over 1000 live births in Italy and UK



Source: HFA-Europe 2007 data

Fig. A3-4 Fertility rate and live birth rates

A3 *A4*



Source: HFA-Europe 2007 data

Fig. A5Multiple deliveries in Italy and UK 1980-2004

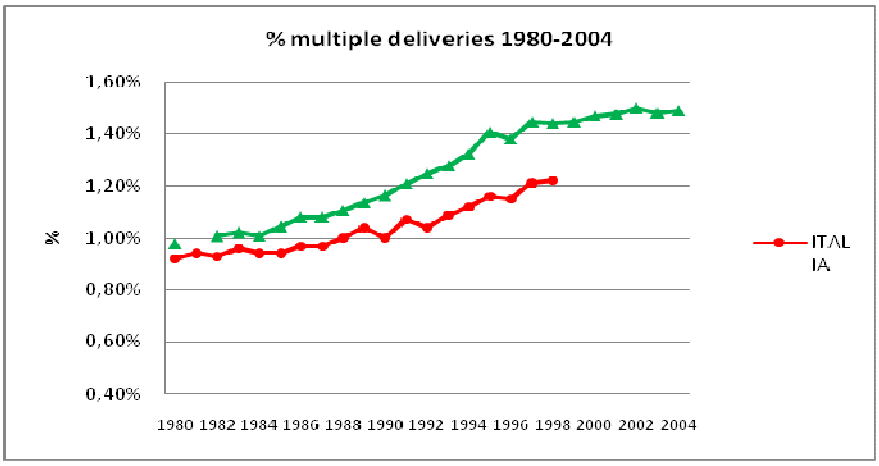
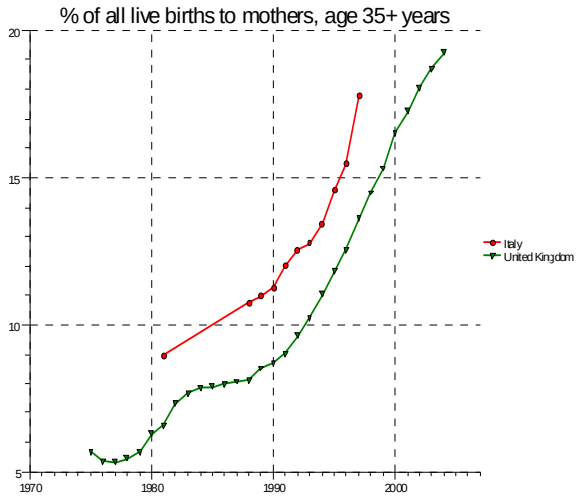
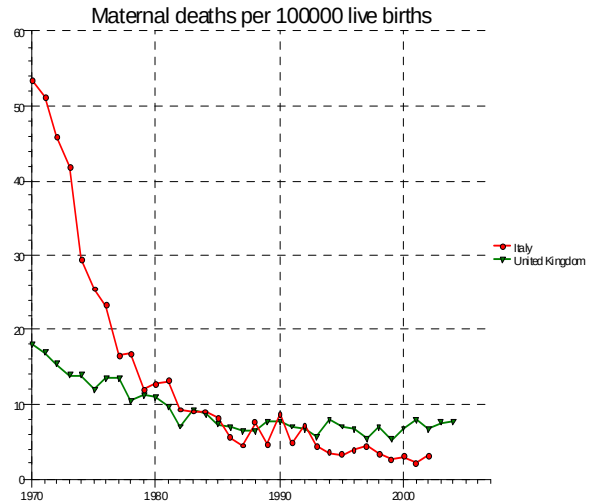


Fig. A6 Percentage of all live births to mothers, over 35 years old in Italy and UK in 1980-2004
Fig. A7 Maternal deaths over 100000 live births in Italy and UK, 1970-2004

A6



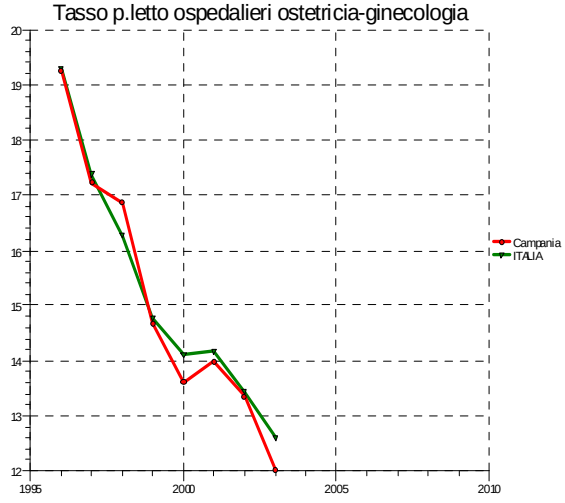
A7



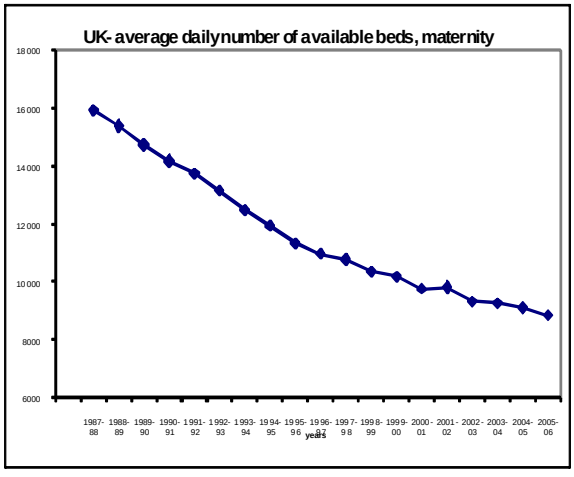
Source: HFA-Europe 2007 data

Fig. A8 Bed rates in obstetrics and gynaecology units in Italy
Fig. A9 Average daily number of available beds in maternity units

A8



A9



Source: HFA Italy 2007, UK Statistics and HES

Tab. A2 Types of analgesia used during delivery in UK 2003-2004

NHS hospital deliveries: anaesthetics used before and during delivery by method of onset of labour and delivery

England *percentages %* 2003-2004

Method of onset of labour	Method of delivery	Total nr of cases (thousands) 100%	Types of anaest. Analgesic used before and during delivery					
			general	epidural	spinal	general &epidural	general & spinal	epidural & spinal
Total all deliveries		**575,9**	**2**	**19**	**12**	**0**	**0**	**2**
Spontaneous	spontaneous	305,9	0	11	1	0	0	0
	instrumental	45,3	0	42	5	0	0	2
	caesarean	43,2	10	29	33	2	1	5
Induced	spontaneous	77,6	0	23	1	0	0	1
	instrumental	17,2	0	54	3	0	0	2
	caesarean	24	8	38	28	3	1	5
Caesarean	caesarean	62,9	6	7	67	0	1	9

Source HES

Source: HES data

Tab. A3 Types of anaesthetics used during delivery in UK in 1989-2004. (HES)

NHS hospital deliveries: anaesthetics used by method of onset of labour and delivery, 1989-2003

England *percentages %*

	Types of anaest. Analgesic used before and during delivery					
	general	epidural	spinal	general &epidural	general & spinal	epidural & spinal
All deliveries						
1989-90	7	16	1	1	0	0
2003-04	2	19	12	0	0	2
Onset and delivery spontaneous						
1989-90	0	9	0	0	0	0
2003-04	0	11	1	0	0	0
Onset spontaneous & instrumental del.						
1989-90	2	44	1	0	0	1
2003-04	0	42	5	0	0	2
Onset spontaneous & caesarean del.						
1989-90	59	22	3	9	0	1
2001-02	13	31	28	3	1	6
Onset induced and delivery spontaneous						
1989-90	0	20	0	0	0	0
2003-04	0	23	1	0	0	1
Onset induced & instrumental del.						
1989-90	1	57	1	0	0	1
2003-04	0	54	3	0	0	2
Onset induced & caesarean del.						
1989-90	54	26	2	13	0	0
2003-04	11	41	21	3	1	6
Elective caesarean						
1989-90	53	31	11	1	0	1
2003-04	6	7	67	0	1	9

Source HES

Tab. A4 Guidelines for the practice of Caesarean Section

<table>
<tr><th>English guidelines NICE in 2004</th><th>Italian Guidelines</th></tr>
<tr><td>Caesarean Section should be planned for:
- Breech presentation at term
- Breech presentation for twins
- mother with HIV
- mother with HIV and hepatitis C
- Genital Herpes in the third week
- Placenta previa 3rd or 4th degree</td><td rowspan="3">The Italian guidelines are designed at regional level by the Health care Regional Agency, according to the main international researches and studies.

The Italian guidelines follow the English NICE principles and suggest caesarean section in the same cases.

The choice of the most appropriate delivery methods is up to the clinician, in order to safeguard the patient’s health status.</td></tr>
<tr><td>Caesarean Section should not be advised for
- Multiple delivery
- Pre-term delivery
- Too little baby for the gestational age
- mother with hepatitis B
- mother with hepatitis C
- Genital Herpes at term</td></tr>
<tr><td>There is any evidence that a caesarean delivery should be followed by another caesarean section.</td></tr>
</table>

CHAPTER 4

AN ESTIMATE OF COSTS AND BENEFITS OF ALTERNATIVE METHODS OF DELIVERY: AN EMPIRICAL ANALYSIS IN AN ITALIAN HOSPITAL

Abstract[†]

The recent large increase in caesarean sections (CSs) in Europe seems not to be completely justified: CS is practiced independently from epidemiological reasons (physician's induction or mother's demand).

In Italy the introduction of epidural analgesia among the Essential Levels of Assistance (LEA) has been proposed with the hope that this will help to counteract the rise of CSs. This work aims at analyzing the costs and benefits effectively involved in alternative methods of delivery- vaginal delivery (VD), with and without epidural analgesia, and planned caesarean.

The empirical analysis is conducted in an Italian hospital, where a wide range of individual variables are collected from clinical records, questionnaires and interviews.

A logistic regression is used to model the probability of the event "elective-CS" occurring as a function of women characteristics (clinical and socio-economic) to confirm that CS is widely performed for non-medical reasons (Signorelli, 1995).

A micro-costing analysis is used to evaluate the direct health costs of each delivery method, following an activity-based-costing approach. CS is on average more expensive than VD, but the difference is marginal taking into account the opportunity-cost of time during labor.

From a societal perspective we consider the implicit indirect costs (transport, medications, artificial feeding, time lost) and the benefits of each method.

The cost-effectiveness analysis shows that in general VD with analgesia is preferred both in terms of costs and benefits, but the final effect of its introduction is not clear: it could reduce inappropriate CSs, but also increase the costs due to complications.

[†] This chapter has been developed in collaboration with the Department of Gynaecology and Reproductive Sciences and the Gynecology and Obstetrics Clinic, University Hospital of Padua.

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1. Introduction

In the last years Caesarean Section (CS) practice has registered a huge increase in all the European countries, but especially in Italy, where the 37.8% of CSs over all deliveries has overcome the appropriate rate of 10-15% suggested by the WHO (Istat, 2004).

In Italy there is also a strong variability in the use of CS, in particular in the Southern Regions, where demographic and logistic characteristics seem to explain the frequencies of CS practice.

The increase in CSs rates seems not to be justified: CS is practiced independently from health conditions or epidemiological reasons, but more often for physicians' induction or mothers' demand, because safer and less painful.

This tendency has certainly an impact in terms of equity and healthcare expenditure and new policies must be implemented to counteract the rise, suggesting alternative forms of delivery assistance.

The importance of safeguarding the woman's choice to control pain during labour, according to the National Committee of Bioethics and the National health plan, has been confirmed last 18 October 2006, by the National Committee of the Essential Levels of Assistance (LEA), with the approval of a document that underline the essential role of analgesic procedures during delivery.

In 2007 the Italian Minister of Health has proposed the introduction of epidural analgesia not only to give to all women the possibility to reduce pain during labour, but also with the hope that this will help to counteract the caesarean section (CS) rates, reducing costs for the Nhs.

In recent years new specific analgesic techniques has been developed and implemented to satisfy the women' desire to deliver with less pain.

The most recent scientific knowledge shows the advantages of the introduction of epidural analgesia during labour: the pain reduction determines a decrease of the metabolic needs and an increase of placenta perfusion with huge benefits for mother and child homeostasis (Bocci A., 1995).

Despite epidural analgesia can be considered the *gold standard* in the reduction of pain during labour (Giron G., 1996) for its reliability and efficacy, in Italy the diffusion of this practice is limited by social and cultural factors and by economic aspects.

Economic and logistic problems are an obstacle for the creation of centres of anaesthesiology assistance in the obstetrics units.

Moreover there is concern among physicians that analgesic methods may prolong labour length and increase the rate of operative deliveries.

A study conducted by Thorp (Thorp J.A., 1993) refers an increment of urgent CSs after epidural analgesia, whereas an Austrian retrospective study shows that the use of epidural is correlated to instrumental deliveries, but CS frequencies are the same for deliveries that do not use analgesia (Ploeckinger B.,1995).

According to Torvaldsen (2006), children born with epidural analgesia have more problems at breastfeeding in the first week of life, and are the first to stop breastfeeding in the following months[1].

Epidural analgesia is not risk less and cannot be practiced in every occasion: besides the clinical condition for which it is not suggested, epidural can be done by an anaesthetist and only into a defined temporal range during the labor (5 cm of dilatations).

According the Italian Obstetric Anaesthetists Association, in Italy only 20% of women have epidural analgesia, versus the 90% in USA, 70% in England and France and 38% in Spain.

The differences registered in Italy may be due to the fact that this practice is not granted by the Nhs and not reimbursed: only 4 % of Italians get epidural in public hospitals for free, the others must pay out of pocket in private (between € 800-1000).

From an economic perspective, if epidural would help to reduce CS rates in Italy, it is not clear which would be the impact in terms of costs for the Nhs.

Caesarean section is more expensive if compared to a vaginal delivery and also the DRGs tariffs to reimburse hospitals are higher for CS[2].

The main part of the studies on this issue refers to the American context, which is extremely different from the Italian one (Petrou S., Hendersen J., 2001). Some studies show that there is a difference in costs between CS and VD, but it is marginal, and a policy aiming to reduce CS rates would not lead to significant savings (Malkin JD, 2001).

[1]The study has been conducted at the University of Sidney by S. Torvaldsen and colleagues on a sample of 1300 women. Over the 416 that have had epidural, 172 have had CS and only the 53% of babies born with epidural was breastfed at 24 weeks, versus the 75% of babies born without epidural.

[2] Generally the national DRG tariff to reimburse hospitals is higher for CS. In Veneto Region the tariff VD without complications is € 922,94, while CS may vary between € 2.197,78 and € 3.472,52 (respectively without and with complications).

Despite the debates, few studies have paid attention to the real cost of alternative methods of delivery – CS, VD with and without epidural analgesia- in the Italian framework.

This work aims at evaluating and comparing the differences in costs among the delivery methods. The results allow on a hand to understand if the DRGs tariffs truly represent the real cost of each practice and if differences are justified[3] (in Lombardy VD and CS without complications have the same tariffs) and on the other hand to estimate the impact in terms of costs that epidural would have for NHS.

The aim of the study is extremely interesting if we take into consideration the new laws proposal and the increasing interest for the pain during labour.

We also analyse the impact in terms of benefits that each delivery method can have. It is well known that epidural analgesia reducing pain allows for a better perception of the birth experience and a higher ability to cope the situation.

According to the main literature an intervention with a higher cost is justified only if is necessary to grant a higher level of health status for the patient, avoiding risks and complications.

2. Materials and methods

The methodological approach used in the study is part of the methods used in cost analysis. It aims at determining all the activities done during the hospitalisation to evaluate the full cost of the alternative delivery methods.

An empirical analysis is done to evaluate the cost of different methods of delivery: vaginal delivery (VD) with and without epidural analgesia and caesarean section (CS). We evaluate the direct health costs, but also the indirect (health and not) costs and the outcomes of each procedure through direct administration of questionnaires to a sample of patients[4].

We administered an anonymous questionnaire containing personal information about individual characteristics (age, origin, religion, civic status, education level,

[3] The DRGs tariffs are defined at regional level, with appropriate weights, but they do not represent the real cost of interventions. The amount of the tariff DRG-371 (for CS) at national level in France, is almost twice if compared to the VD tariffs DRG-373. A study of Fabbri Monfardini shows that this differences may induce to opportunistic behaviors in terms of clinical practice (Fabbri D., Monfardini C., 2000).

[4] We administered an anonymous questionnaire containing personal information about individual characteristics (age, origin, religion, civic status, education level, profession, individual and familiar income), clinical information (pathologies during pregnancy, procreation method, number of check-up during pregnancy, tests done), information about the delivery method.

profession, individual and familiar income), clinical information (pathologies during pregnancy, procreation method, number of check-up during pregnancy, tests done), information about the delivery method.

2.1. The setting and the sample of patients

The empirical analysis refers to a specific hospital of Veneto Region (the University hospital A.O. of Padua), where the frequencies of deliveries and the case-mix are sufficient to conduct a study with a significant sample.

The choice of this hospital instead of a hospital of local health organization (Asl) is due to the fact that epidural analgesia is practiced with a certain frequency.

The university hospital considered has a numerous staff and the constant presence of anaesthetists that can practice epidural in every moment (whereas in other hospitals there is a huge lack of anaesthetists and human resources).

The study refers to a sample of women that have given birth in the Obstetrics and Gynaecology unit of the AO hospital.

The women invited to complete the questionnaires have been selected consecutively among the patients hospitalised in a period of three months, reaching a sample of 250 women[5].

The study compliance has been of 80,4%, whereas 10% refused to be part of the study and 9,6% did not return the questionnaire [6](tab.1).

Tab. 1 Compliance to the study

Compliance	***patients***	***%***
fulfilled	201	80,40%
Refused	25	10,00%
Not fulfilled	24	9,60%
TOTAL	250	100%

Source: our elaboration

[5] The questionnaire has been administered after delivery, through direct interviews explaining the aims of the study, the data collection mechanisms and the fulfillment instructions. The questionnaires were left to the patients for the auto-fulfillment and collected the day after (or left in a box before the demission from the hospital). The questionnaire has been disposed also in English version for the strangers. The questionnaire was anonymous to increase the level of attendance of the answers, but through a codification we could match the data collected through questionnaires and the data from records.

[6] In many cases patients did not completely fulfill the questionnaire because strangers with language problems, in other cases they fulfilled it only in part or they forgot to return it before exit.

All women have been considered eligible to the study and no restrictions have been made to the sample in terms of age, origin, race or number of deliveries.

Nevertheless, the presence of many foreigner women caused a reduction in the compliance rates due to language problems.

In tab.2 we show a summary of the women characteristics. In particular we can notice that average age at delivery, 32 years old, is quite high, confirming the average data referred to Italy of 31 years (ISTAT, 2006). The youngest mother delivers at 20 years old, the oldest at 46 years old.

The main part of patients are Italians (78%), followed by Rumanian (8%), Philippians and Moldavian (3%), and only in lower part Albanian or Moroccan (less than 1%) (tab.3). The prevalent religion is Christian-catholic, the minor Orthodox and Muslim (tab. 3).

Tab. 2 Patients age

Var	**Observ.**	**Mean**	**Std. dev**	**Min**	**Max**
age	208	32.6	5.09	20	46

Source: our elaboration

Tab. 3 Origin and religion

Origin	**Freq.**	**Percent**	**Cum.**
Albanian	3	1.43	1.43
Congolese	2	0.48	2.38
Philippine	7	3.33	5.71
Italian	165	78.57	84.29
Moroccan	4	1.90	86.19
Nigerian	4	1.90	90.48
Pakistani	1	0.48	90.95
Polish	1	0.48	91.43
Rumanian	17	8.10	99.52
Moldavian	6	2.38	100.00
Total	210	100.00	

Religion	**Freq.**	**Percent**	**Cum.**
N.R.	28	13.33	13.33
atheist	3	1.43	14.76
catholic	146	69.52	84.29
Christian	11	5.24	89.52
evangelist	1	0.48	90.00
Islamic	1	0.48	90.48
Muslim	6	2.86	93.33
orthodox	14	6.67	100.00
Total	210	100.00	

Source: our elaboration

Women have a high level of education: more than 42% has a high school degree, the 30% has a graduation degree or a higher title (PhD), the 12% a university diploma or short graduation degree, only the 8% ended the study after secondary school and more than 1% at the primary school (tab. 4).

More than 32% of patients are employed, the 11% are home keepers or entrepreneurs, and the 8% unemployed or owners (tab. 5a).

Tab. 4 Level of education

Education	Freq.	Percent	Cum.
N.R.	10	4.76	4.76
diploma	1	0.48	5.24
primary	3	1.43	6.67
laurea	65	30.95	37.62
laurea_br	24	11.43	49.05
med_inf (secondary)	17	8.10	57.14
med_sup (high school)	90	42.86	100.00
Total	210	100.00	

Source: our elaboration

Tab. 5a Professional condition

Profession	Freq.	Percent	Cum.
Not declared	10	4.78	4.78
other	16	7.66	12.44
autonomous	16	7.66	20.10
home keeper	24	11.48	31.58
manager	11	5.26	36.84
unemployed	18	8.61	45.45
professor	1	0.48	45.93
employed	68	32.54	78.47
entrepreneur	23	11.00	89.47
nurse	1	0.48	89.95
teacher	2	0.96	90.91
musicals	1	0.48	91.39
worker	16	7.66	99.04
student	2	0.96	100.00
Total	209	100.00	

Source: our elaboration

The personal income of the patients is for the 40% lower than €15.000, the 24% earn between € 15.000 and € 30.000, the same percentage has no income and only the 1% has an income higher than € 50.000. The results are better if we consider the familiar income (tab. 5b).

Tab. 5b Level of individual and familiar gross income for year

Income	Individual		Family	
	Freq.	Percent	Freq.	Percent
0	40	22.10	8	4.85
<15000	72	39.78	23	13.94
15000-30000	44	44.31	56	33.94
30000-50000	22	12.15	42	25.46
> 50000	3	1.66	36	21.82
Total	165	100.00	165	100.00

Source: our elaboration

2.2. The frequencies of alternative delivery methods

If we analyse the frequencies of the alternative delivery methods we can see that in the hospital the CS rate is very high: 42% of all deliveries are practiced with CS. Planned CS are 26%, whereas only the 16% of CS are in urgency (tab.6).

Almost the 33% of induced deliveries and the 14% of deliveries practiced with epidural analgesia have complications that require urgent CS.

The registered rates of CS are higher if compared to the national average (about 37,8%).

Tab. 6 Frequencies of the alternative methods of delivery

Delivery method	*Freq.*	*Percent*	*Cum.*
ces_el	54	25.84	25.84
ces_urg	33	15.79	41.63
vag	122	58.37	100.00
Total	209	100.00	

CS	*Freq.*	*Percent*	*Cum.*
ces_urg	33	15.79	41.63
Induced	17	32.69	
Epidural	6	13.95	

Source: our elaboration

Such an elevate rate is certainly due to the case-mix[7]: the AO hospital has the most complicated cases and may requires for CS with higher frequency. This partly confirms the results of a study that affirmed the importance of the case-mix as a factor that can explain the CS rates (Frost C., Thomas J. 2005). Nevertheless the value is still too high if we consider the CS rates registered in similar hospital (A.O.) at national level (34,52%) and regional level (29,32%).

[7] The AO treats all the most risky and complex cases, because the hospital is very specialized and has a neonatal center to assist babies with complications.

2.3. A model to estimate the probability of having a planned CS

The high rates of CS registered seem not to be completely justified and were the initial stimulus to investigate which factors may explain such practice.

We used a logit regression to model the probability of the event "planned CS" (*ces_el)* as a function of individual characteristics, clinical, social and economic factors.

The characteristics and factors considered are the following:

- Referring age at delivery (*age_rif*) calculated as the difference between the observed age and the average minimum age at delivery registered in the sample and at national level;
- Being foreigner (*foreigner*): woman not Italian; or being Italian (*Italian*);
- Having a previous CS (*ces_preg*);
- Number of pregnancy weeks over term (*gestaz*), calculated as the difference between the weeks of pregnancy observed and the 40th week;
- The expressed preference of the woman for a CS (*pref_ces*);
- The expressed preference of the woman for epidural analgesia (*epid_pref*);
- Presence of disease that may require a CS (*patol*);
- Attendance at delivery preparation courses (*corsi_prep*);
- Being catholic (*cattolica*);
- Being graduated (*laurea*) or having a diploma (*diploma*);
- Have a high degree of education (*titolo_stu*);
- Being unemployed (*no_job*);
- Being rich (*rich*): if woman gross income is equal or more than € 50.000 for year
- Have an autonomous job (*autonoma*);
- Being home keeper (*homekeeper*);
- Being not married (*no_married*).

The results of the model (Tab A.1 Appendix) show that the probability of having a planned CS increases with age: older women are more exposed to risks and complications that might require a CS. Moreover, getting pregnant in later age can be very difficult and expensive for older women that may require an assisted procreation: in these cases the baby is considered "precious" and planned CS is necessary to avoid complications.

The probability of having a planned CS increases if women have had a previous CS (to avoid complications), and if women express the desire of having a CS.

Even if CS should be practiced only for clinical reasons and not for mother request, in many cases an implicit agreement between the clinician and the patient is possible (especially if the doctor practices both in private sector and in the same hospital where the woman will deliver[8]).

The probability of a planned CS decreases before the 40th week of pregnancy.

An interesting result shows that being foreigner and unmarried decreases the probability of planned CS. The first result might be due to cultural reasons: some ethnic groups assign more value to pain during delivery and consider women more strength if they are able to manage this experience. In the second case, unmarried woman are more likely to be young and are probably not incurred in a previous CS before.

The presence of diseases or bad health conditions that may require CS are positively related with the probability of a planned CS, but are not significant.

The results seem to confirm the results of another study done in different Italian hospitals and that show that, apart from few medical indications, CS is practiced for non clinical reasons (Osborn JF., Signorelli C., 1995).

3. Cost analysis

The cost analysis aims at evaluating the full cost of each alternative delivery method. We consider both the direct health costs (for delivery, surgical intervention, hospitalisation and in-stay) and from a broader perspective also the indirect costs (medications after delivery, complication costs, time lost, caregivers assistance). For each delivery method (vaginal with and without epidural analgesia and CS) we identify and evaluate the direct health costs due to the specific procedure (items, materials, pharmaceuticals, human resources and times, in-stay costs, diagnostic and laboratory tests, treatments and interventions), the direct health costs for complications (CS for urgency, obstetrics procedures, postpartum complications).

The evaluation of the direct health costs is done through a *micro-costing analysis*, with the identification, measurement and evaluation of each single cost item involved in the assistance process.

[8] As explained in the previous chapter, doctors can have a real interest in practicing planned CS (financial incentives, logistic reasons, preventive practice, reduction of risks), but also woman can prefer CS because they think is painless.

This methodology, even if more laborious and less generalizible than a *gross-costing analysis*, gives a better and specific insight of the relation existing between the activities and the costs (Brouwer W., Rutten F., Koopmanschap M., 2001).

The individuation and measurement of each cost item has been done through direct measurement, with punctual collection of data from clinical record or through direct interview with physicians, nurses. We followed an *activity based costing* approach to evaluate all the activities done during the hospitalisation.

We used administrative data and regional tariffs only for the daily pension cost[9] and the laboratory analysis because a micro-costing analysis would have been too expensive for the aim of the study. In tab.7 we show a sample of the laboratory analysis with tariffs used to evaluate the diagnostic exams.

Tab. 7 Tariffs (Tariffs Nomenclator Veneto Region 2006) (euro)

Cod.	***Description***	***Tariff***
H 90.65.3	GRUPPO SANGUIGNO ABO e Rh (D).	€ 8,55
H 90.65.4	GRUPPO SANGUIGNO ABO/Rh II controllo.	€ 5,65
90.62.2	EMOCROMO: Hb, GR, GB, HCT, PLT, IND. DERIV	€ 5,15
90.04.5	ALANINA AMINOTRANSFERASI (ALT) (GPT) [S/U].	€ 2,85
91.09.4	TOXOPLASMA ANTICORPI (E.I.A.).	€ 12,10
90.72.4	PROTEINA S LIBERA [P].	€ 10,80
90.72.5	PROTEINA S TOTALE [P].	€ 10,80
90.66.2	Hb - EMOGLOBINA [Sg/La].	€ 1,90
90.75.4	TEMPO DI PROTROMBINA (PT).	€ 2,85

Source: Tariffs Nomenclator Veneto Region 2006

The costs of pharmaceuticals and items used during delivery and in-stay is an average cost (with IVA) referred to the specific unit where the item is used (delivery room, surgery or unit). In tab. 8 we show an example of the database that contains the hospital costs of a sample of drugs used in delivery room and in-stay.

Tab. 8 Database of the administrative costs of pharmaceuticals

Pharmaceutical Description	***Deliv. room***	***In-stay***
F15F110 METHERGIN IM IV 6F 1ML 0,2/MG/ML METILERGOMETRI	€ -	€ 0,22
F25A202 MIDAZOLAM IBI 5 MG/ ML F 1 ML	€ 0,34	€ 0,35
F15F420 MIOLENE FIALA 50 MG EV RITODRINA	€ 0,57	€ 0,57
F15F510 NALADOR FIALA 0,5 MG SULPROSTON	€ 11,14	€ 11,12
F24A520 NAROPINA 7,5 MG/ML POLYAMP DA 10 ML ROPIVA.	€ -	€ 11,81
F24A530 NAROPINA 10 MG/ML POLYAMP DA 10 ML ROPIVAC	€ -	€ 13,07
F02N430 NEO FURADANTIN 50 MG CPS NITROFURANTOINA	€ 0,05	€ 0,05

[9] The pension costs consider only the costs for food and in-stay and not the health costs, as they have been already evaluated through ABC.

Through direct interview and direct measurement we identified all the activities done by each professional figure from the arrival of the woman in hospital (in labour or to book a planned CS) till her exit. For each activity we identified all the human resources involved, the time spent and the items used (tab. 9).

Tab. 9 Plan of the activities done during in-stay

Activities	*Prof. figure*	*q.ty*	*Minutes*
Clinical Record opening	nurse	1	15
Haematological blood test	nurse	1	5
Test-tube delivery	nurse	1	20
Trichotomy	nurse	1	5
Intravenous catheter insertion	nurse	1	5
Transfer to delivery room	OSS operator	1	10
Clinical record check	nurse	1	15
Transfer to bed	nurse	1	20
Sanitary activities, make bed	OSS operator	1	15
Position ice on the belly	OSS operator	1	2
VAS check up	nurse	1	60
Therapy administration	nurse	1	5
Check up visit	physician	1	10
	nurse	1	10
	trained nurse	1	10

Source: our elaboration

The unit cost for hour (with the total amount of wage in the year) of the human resources has been supplied by the administrative unit of the hospital: we identified the professional figures (gynaecologists, surgery staff, nurses, technicians, administrative personal) for each unit referred to delivery room, surgery room and obstetric units. The average cost for hour of each figure has been calculated as ratio between the wage and the number of hours worked in the year. The cost contains the basic wage and the extra time worked. In tab.10 we summarize the cost of human resources[10].

Tab. 10 Average cost for hour (a.c.h.) of human resources in delivery room and obstetric unit

Obstétrical unit	**clinic**	**division**	**a.c.h**
Health manager	75,92	71,86	***€ 73,89***
Health staff	26,17	26,22	***€ 26,19***
Non-health staff	21,48	21,26	***€ 21,37***

Surgery- delivery room	**clinic**	**division**	***a.c.h***
Health staff	26,22	26,19	***€ 26,20***
Non-health staff	20,79	20,87	***€ 20,83***

Source: our elaboration

[10] In the hospital there are two units that use the delivery and surgery room: the so called Clinic and the Division of Asl. All the physicians and nurses are often used in common, especially in the surgery room where there is a lack of nurses. The delivery room and surgery room are common to both the unit, but each one has a different in-stay unit. Seldom, some patients from division are sent to the clinic if there are no beds.

The identification and evaluation of the direct health costs born from the women entrance in hospital till her discharge, has been done through a database. In the database, for each cost item we identify the consumption and the respective economic value to calculate the average cost for each delivery method. For each patient we collected in the clinical records all the data useful to determine the cost of hospitalisation, for the in-stay, the time spent in delivery room during labor, in surgery room for CS (in the report we can find the hour of intervention start and end and the human resources involved), the diagnostic tests and the pharmaceutical therapy (tab.11).

Tab. 11 Data collected from clinical records

Data collected from clinical records
Personal data
Hospitalisation data (admission data, type and length of in-stay)
Method of delivery and clinical indications
Delivery/intervention data (times, human resources involved)
Pharmacological therapy in delivery room/surgery
Pharmacological therapy during the in-stay
Diagnostic and laboratory tests
Barthel indexes

Source: our elaboration

The direct cost of human resources for each surgical intervention has been evaluated through clinical report data: in the report we find the figures involved and the time spent.

For each professional figure we identified the cost for hour and for minute to calculate the cost for each patient (tab.12).

Tab. 12 Costs of human resources for surgical intervention (euro)

Human resources	**Nr. persons**	**Cost/hour**	**cost_ min**
Obstetrician-midwife	1	26,20	€ 0,44
Gynaecologist	1	73,89	€ 1,23
Special. STRUTT	2	26,20	€ 0,87
Surg. instruments physician	1	26,20	€ 0,44
Surg. instruments assistant	1	20,83	€ 0,35
Obstetrician assistant	1	20,83	€ 0,35
Anaesthetist	1	73,89	€ 1,23
Anaesthetist assistant	1		€ -
Nurse of surgery room	1	26,20	€ 0,44
Total	**10**	**294,26**	**€ 5,34**

Source: our elaboration

The human cost in surgery room may vary with the intervention complexity from € 133,00 to € 534,00 but on average is € 287,00 (tab. 13).

Tab. 13 Cost of human resources during surgical intervention in surgery room (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
humanres_caesarean	63	287.6819	88.05121	133.5	534

Source: our elaboration

The cost of the diagnostic tests done before and after delivery has been evaluated using the regional tariffs. Some tests are done routinely, such as blood group and serologic tests (HiV, hepatitis) or control tests after delivery; in many cases some tests may be done to check women conditions due to particular diseases (diabetes or complications). The type and number of diagnostic tests have been collected from clinical report and evaluated with the correspondent tariff, to obtain a total cost for each patient.
The results show that there is no difference in costs due to the delivery method and the costs may vary between € 218,00 and € 291,00 (tab.14).

Tab. 14 Costs of diagnostic tests for each delivery method (euro)

Delivery method	Variable	Obs	Mean	Std. Dev.	Min	Max
Caesarean (all)	Cesarean	87	285.6437	79.83165	142	535
Planned CS	Ces_election	54	291.037	75.73862	142	535
Urgent CS	Ces_urg	33	276.8182	86.58791	142	473
CS after induction	Ces_induced	28	287.25	85.55294	142	473
CS after epidural	Ces_epidural	5	218.4	74.47684	142	312
Vaginal (all)	Vaginal	122	254.1721	87.27573	142	610
Spontaneous VD	Vag_spon	88	241.6818	75.5631	142	384
Induced VD	Vag_induced	34	286.5	106.6928	142	610
Epidural an. (all)	Epidural	41	280.6341	61.49421	142	430
Epid. followed by CS	Epid_ces	6	289.3333	35.75286	248	333
Epid. followed by VD	Epid_vag	37	280.1351	63.55145	142	430

Source: our elaboration

We calculated the costs for pharmaceuticals during labour, delivery and in-stay for each patient and we made an average for each delivery method (tab. 15).
The results show that the costs for drugs for a VD is on average € 33,00 (€ 31,00 in a natural delivery, € 33,00 with epidural and € 40,00 if induced).
The pharmaceutical cost for CS is on average € 44,00, but if we distinguish between elective and urgency CS, the second one costs on average € 65,00.

Tab. 15 Costs of pharmaceuticals for each method of delivery (euro)

Delivery method	Variable	Obs	Mean	Std. Dev.	Min	Max
Caesarean (all)	Cesarean	80	44.11413	67.5696	2.97	560.4
Planned CS	Ces_election	53	33.3917	31.71712	8.87	232.4
Urgent CS	Ces_urg	27	65.16185	105.6702	2.97	560.4
Vaginal (all)	Vaginal	91	33.07282	72.06698	1.91	441.22
Spontaneous VD	Vag_spon	64	31.19063	74.80935	1.91	441.22
Epid. followed by VD	Epid_vag	29	33.15104	65.58399	3.1	337.76
Epid. followed by CS	Epid_ces	6	38.77833	38.35647	7.15	98.18
Induced VD	Vag_induced	29	40.84748	65.11087	3.21	337.76
CS after induction	Ces_induced	15	84.372	136.5887	2.97	560.4

Source: our elaboration

If we consider the in-stay length for each delivery method a VD may require a minimum stay of three days up to ten days. The difference in length of stay between natural, induced and delivery with epidural is of one day, whereas CS requires a longer stay (tab.16).

Tab. 16 Average days of in-stay for each delivery method

Delivery method	Variable	Obs	Mean	Std. Dev.	Min	Max	AO_ Italy	AO_ Veneto
Vaginal (all)	Vaginal	88	5.170	1.655.514	3	11	4.41	4.33
Induced VD	Vag_induced	26	5.846	205.314	4	11	5.27	5.03
Spontaneous VD	Vag_spon	62	4.887	1.380.245	3	10	3.56	4.03
Epidural an. (all)	Epidural	38	5.684	1.645.719	4	10	.	.
Epid. followed by CS	Epid_ces	6	6.666	1.861.899	5	9	.	.
Epid. followed by VD	Epid_vag	32	5.05	1.565.763	4	10	.	.
Caesarean (all)	Cesarean	78	6.294	1.020.682	4	9	7.07	7.24
Planned CS	Ces_election	52	6.230	.6749113	5	9	6.20	6.20
Urgent CS	Ces_urg	26	6.423	1.501.282	4	9	7.55	8.28

Source: our elaboration

The length of stay has a relevant impact in term of cost that is expressed by the postpartum assistance.

The cost of the activities done by the human resources during the in-stay has been calculated through the identification of all the activities done during the hospitalisation: we made a distinction between the activities done only once (clinical report start, transfer from/to delivery room, checkout), and the activities done every day (food administration, check-up, drugs administration, controls). There are some activities that may vary with the number of diagnostic tests done (blood injections,

check of results), the pharmacological therapy, and the delivery method (for CS women must wear specific collants, or due particular therapy).
In tab.17 we show the costs for the in-stay for each delivery method, including the human resources costs and materials used.

Tab. 17 Costs of in-stay activities (euro)

Activities	Vaginal	Caesarean
Daily activities	€ 15,28	€ 60,70
Una tantum	€ 89,56	€ 197,26
Variable activities		
Blood tests	€ 4,16	
Inser/rem phlebo	€ 2,18	

Source: our elaboration

For each patient we calculate the in-stay costs taking into account the length of stay registered in the clinical report, the treatments done and other variable costs.
The results show that on average the cost for in-stay is quite high for CS: especially if practiced on urgency, a CS cost almost € 604,00, whereas the VD cost on average € 177,00 (tab.18). The in-stay for a woman who had epidural analgesia without complications costs € 183,00, but if after epidural an urgent CS is the in-stay costs can rise up to € 612,00.

Tab. 18 Average cost for in-stay (euro)

Delivery method	Variable	Obs	Mean	Std. Dev.	Min	Max
Caesarean (all)	Cesarean	79	592.8608	64.34876	457	760
Planned CS	Ces_election	53	587.2642	42.27254	510	756
Urgent CS	Ces_urg	26	604.2692	94.87109	457	760
Vaginal (all)	Vaginal	90	177.6333	32.29862	136	297
Spontaneous VD	Vag_spon	62	172.6129	27.14162	136	277
Induced VD	Vag_induced	28	188.7500	39.85402	151	297
Epidural an. (all)	Epidural	39	249.4872	164.0232	151	755
Epid. followed by CS	Epid_ces	6	612.1667	111.7666	513	755
Epid. followed by VD	Epid_vag	33	183.5455	29.13663	151	260

Source: our elaboration

To evaluate the cost of the surgical intervention in case of CS, we identified all the activities done during the intervention, the human resources involved, the health material used and the time spent. Some activities are done before and after the

intervention (room preparation and cleaning) and are standard, whereas other may vary with the length of the intervention.

The costs of human resources not depending by the time of intervention are € 50,91 where as the costs that depend by the length are almost € 5,34 for minute (tab.12).

In tab.19 we show the costs of activities and materials used for the different delivery methods. The material used during intervention is standard and do not requires particular variations, so the cost for resources consumption is almost € 480,00 for each patient.

Tab. 19 Costs of variable activities (euro)

Activities-Cost items	**Cost**
Activities in surgery room for CS	€ 50,91
Variable activities for CS (interv. time)	€ 5,34 / min
Standard activities for vaginal delivery	€ 26,19
Materials for vaginal delivery	€ 103,81
Material used for CS (standard)	€ 480,00
Pharmaceuticals-drugs costs	For patient
Episiotomy	€ 118,33
Epidural analgesia	€ 75,00
Surgery room utilization	€ 154,00
Delivery room utilization	€ 118,00

Source: our elaboration

The cost for human resources and the material used in delivery room has been evaluated in the same way and is respectively of € 26,19 and € 103,81.

The cost of the drugs used during CS (fentanest, bupivacain, electrolytic solution ecc.) is included in the pharmaceutical costs, as the consumption varies with the length of intervention and the type of patient (the quantities are reported in clinical report).

For the VD with episiotomy, the evaluation of the cost of human resources, drugs and pharmaceuticals has been done separately, with the identification of the persons involved, the activities and the consumption.

The episiotomy requires the presence of a physician and a nurse, it lasts on average 20-30 minutes and is done with local analgesia (lidocain). The full cost for episiotomy is almost € 118,33 and it is the same with or without analgesia.

Epidural analgesia, if required by the patients, is actually on charge of the hospital, so we must carefully analyse the costs involved. The human resources involved

(anaesthetists and nurse) cost about € 24,00, whereas the material (Thuoy, analgesia) costs € 51,35, for a total cost of € 75,00.

The anaesthesiology visit that the patient must do before epidural or in case of CS costs on average € 12,30.

The use of the surgery room and delivery room is almost € 154,00 for surgical intervention and € 118,00 for natural delivery[11].

The full cost including drugs, materials, diagnostic tests, in-stay, assistance during delivery and hospitalisation, epidural or episiotomies) has been charged of almost 20% to take into account the general indirect costs (structure costs, services, administrative costs)[12].

We show the average total cost of each delivery method, without considering the general costs and with the 20% of general costs (tab. 20-a-b).

Tab. 20-a Total costs on average for each delivery method, without general costs

Delivery method	***Variable***	***Obs***	***Mean***	***Std. Dev.***	***Min***	***Max***
Caesarean (all)	Cesarean	87	1858.69	225.5636	1073.18	2288.99
Planned CS	Ces_election	54	1884.243	151.9097	1244.57	2268.49
Urgent CS	Ces_urg	33	1816.876	309.2113	1073.18	2288.99
Vaginal (all)	Vaginal	114	856.7704	117.2811	651.16	1228.16
Spontaneous VD	Vag_spon	84	836.6865	102.5845	651.16	1217.45
Induced VD	Vag_induced	30	913.0056	137.9763	651.16	1228.16
Epidural an. (all)	Epidural	42	1076.11	339.8024	766.58	2149.415
Epid. followed by VD	Epid_vag	36	944.8581	77.44268	766.58	1098.81
Epid. followed by CS	Epid_ces	6	1863.622	191.2882	1562.159	2149.415

Source: our elaboration

Tab. 20-b Total cost on average without labour, with general costs (euro)

Delivery method	***Variable***	***Obs***	***Mean***	***Std. Dev.***	***Min***	***Max***
Caesarean (all)	Cesarean	87	2230.428	270.6763	1287.816	2746.788
Planned CS	Ces_election	54	2261.092	182.2916	1493.484	2722.188
Urgent CS	Ces_urg	33	2180.251	371.0535	1287.816	2746.788
Vaginal (all)	Vaginal	114	1028.125	140.7373	781.392	1473.792
Spontaneous VD	Vag_spon	84	1004.024	123.1015	781.392	1460.94
Induced VD	Vag_induced	30	1095.607	165.5716	781.392	1473.792
Epidural an. (all)	Epidural	42	1291.332	407.7629	919.896	2579.298
Epid. followed by VD	Epid_vag	36	1133.83	92.93121	919.896	1318.572
Epid. followed by CS	Epid_ces	6	2236.347	229.5459	1874.591	2579.298

Source: our elaboration

[11] Surgery room and delivery room are dedicated, so there are no other units using them, and the costs can be divided only for the interventions done in each one.

[12] The choice of this percentage is not casual, but has been suggested by the Administrative unit, even if a deep analysis of the Accounting report is required to calculate the data in a more accurate way.

From the analysis we can see that CS is more expensive if compared to VD, especially if practiced in urgency.

Nevertheless, if we consider the minimum and maximum values of each method we can see that the costs may vary a lot, and in some case they can have the same cost, or in some extreme cases the VD can be more resource consuming than CS (in the range between € 1.287,81 and € 1.473,79).

A vaginal delivery with epidural analgesia, where is possible and without complications, costs on average € 1133,83, a bit more than VD, but it can reach also costs € 2.579,29 if it ends up in urgent CS.

If we consider the assistance that patients receive from the entrance in hospital and during all the labour length, the costs may differ a lot (tab. 20-c,d).

From the woman entrance in hospital till the delivery many hours may pass, during which the nurses and physicians must give all the possible assistance.

From the data in the clinical reports we can see that during this time the obstetric, the gynaecologist and nurses assist the patient, administer drugs (oxitocyn, prepydil) and visit her at regular intervals.

Nurses and obstetrics are always present during labor and assist the patient at least for 20 minutes every hour, whereas the gynaecologists visit her at least for 5 minutes for a total costs of almost € 15,00 for hour.

For each patient we can calculate the cost of assistance during labour in delivery room collecting data from the clinical report (time of arrival, first visit, baby born hour). If we consider also this component of costs in the total cost of delivery the full cost of VD increases.

In tab 20-c we show that including the cost of assistance during labour the full cost of a CS in urgency increases on average of € 280,00 up to € 822,00, VD cost increases of € 138,00 and € 163,00 with induction, up to € 378,00 in the worst cases[13].

The cost of VD with epidural increases of almost € 200,00, from € 160,00 to € 300,00 for VD and up to € 555,00 if CS is required.

[13] Induction through prepydil may prolong the length of delivery and induce dystocia.

Tab. 20-c Total cost on average with labour assistance, without general costs (euro)

Delivery method	***Variable***	***Obs***	***Mean***	***Std. Dev.***	***Min***	***Max***
Caesarean (all)	Cesarean	87	1947.003	314.9965	1073.18	2974.014
Planned CS	Ces_election	54	1884.243	151.9097	1244.57	2268.49
Urgent CS	Ces_urg	33	2049.701	459.2576	1073.18	2974.014
Vaginal (all)	Vaginal	114	972.3639	147.362	689.04	1543.21
Spontaneous VD	Vag_spon	84	945.1707	126.9762	689.04	1343.61
Induced VD	Vag_induced	30	1048.505	174.1596	758.37	1543.21
Epidural an. (all)	Epidural	42	1242.382	427.2574	811.25	2612.425
Epid. followed by VD	Epid_vag	36	1077.627	102.1708	811.25	1343.61
Epid. followed by CS	Epid_ces	6	2230.909	236.1529	1966.63	2612.425

Source: our elaboration

Tab. 20-d Total cost on average with labour assistance and general costs (euro)

Delivery method	***Variable***	***Obs***	***Mean***	***Std. Dev.***	***Min***	***Max***
Caesarean (all)	Cesarean	87	2336.404	377.9958	1287.816	3568.817
Planned CS	Ces_election	54	2261.092	182.2916	1493.484	2722.188
Urgent CS	Ces_urg	33	2459.641	551.1092	1287.816	3568.817
Vaginal (all)	Vaginal	114	1166.837	176.8344	826.848	1851.852
Spontaneous VD	Vag_spon	84	1134.205	152.3714	826.848	1612.332
Induced VD	Vag_induced	30	1258.206	208.9916	910.044	1851.852
Epidural an. (all)	Epidural	42	1490.858	512.7089	973.5	3134.91
Epid. followed by VD	Epid_vag	36	1293.153	122.605	973.5	1612.332
Epid. followed by CS	Epid_ces	6	2677.091	283.3835	2359.956	3134.91

Source: our elaboration

3.1. The opportunity cost of an emergency equipe

The hospital considered for this study is characterised by the constant presence of human resources and anaesthetists that can assist the patients in every moment, both during night and, in the week-end and holidays[14].

Nevertheless we must consider the possibility that in some hospitals the presence of human resources is not constant, but limited during week with lack of assistance in the moment where is more required. The delivery event cannot be planned and for this reason the possibility to practice epidural is limited.

The possibility to have an equipe that can assist women 24 hours over 24 during VD and to practice epidural is an opportunity cost that must be take into account comparing the alternative methods of delivery.

The evaluation of the cost of an equipe has been done from the cost data already calculated and can be estimated in almost € 152,46 for hour and € 3.659,04 in the 24

[14] In the hospital there is a sufficient number of physicians, and medicine students that can substitute the structured personal.

hours. If we consider also the presence of an anaesthetist to practice epidural the cost rises to € 226,35 for hour and € 5.432,40 in the 24 hours.
These data are useful if compared with the cost of an equipe required for a planned CS, as they show the difference of cost between alternative procedures. As already reported the cost for the human resources during planned CS is very high and reaches € 294,26 for hour.

3.2. The indirect costs and the private costs

In the study we evaluate not only the direct health costs, but also the cost not directly linked to factors used during delivery.
In particular we consider the costs due to the possibility of breastfeeding, the costs to go back to hospital to remove the suture points (for episiotomies or for CS), the private costs for private assistance or the cost for caregivers assistance (husband, parents, relatives).
We considered also the costs for the examinations during pregnancy and the prenatal diagnostic tests (amniocentesis, ECG).
All the information to evaluate the private and indirect costs have been collected through questionnaires (tab.21). Some questions aimed at calculating the eventual indirect costs due to delivery, such as the cost for artificial milk, for assistance postpartum. We asked women to quantify the assistance of caregivers in terms of time: in the questionnaire they must say if they will need assistance (paying or for free), who will assist them, how many hours for day, if the caregivers will change their activities, if they will lose days of job and leisure time, and how many.

Tab. 21 Data collected through clinical records

Individual data:
age, origin place, citizen, social-civic status
Social and economic data:
religion, level of education, profession, income (individual, familiar)
Clinical data:
disease during pregnancy, previous deliveries, prenatal diagnosis, week of preg., weeks worked, delivery method, breastfeeding
Preference:
preferred delivery, willingness to pay
Indirect costs:
home assistance, caregivers assistance, time lost

Source: our elaboration

In tab.22 we show the frequencies of breastfeeding after delivery for each method. We can see that women that delivered with VD breastfeed in the 92% of cases, whereas women those have had CS only in the 75.6%: CS reduces the possibility to breastfeed of 20% with respect to VD. Moreover, CS practiced on urgency reduces the probability of breastfeeding more than planned CS, (71,88% instead of 78%), because the less organization that characterised the urgency intervention makes more difficult to attach the baby at the mother's breast in the next two hours.

Tab. 22 Breastfeeding frequencies

Delivery method	Variable	Freq. Patients breastfeeding	Total patients	Percentage of woman breastfeeding
	All	168	197	85.28
Caesarean (all)	Cesarean	62	82	75.61
Planned CS	Ces_election	39	50	78.00
Urgent CS	Ces_urg	23	32	71.88
Vaginal (all)	Vaginal	106	115	92.17
Epidural an. (all)	Epidural	34	35	97.14
Total respond.	Total	209		100.00

Source: our elaboration

The natural breastfeeding can be considered a benefit index, because it has lot of advantages both for the mother and the baby.

Numerous studies show the potential positive effects of breastfeeding for mother's health: it reduces the risk of breast and ovarian cancer, the risk of osteoporosis; it increases the possibility of physical recovery postpartum. Some epidemiological studies show that maternal milk contributes to a better grew and development of the baby and reduces the risk of a wide number of acute and chronic diseases[15].

Moreover, breastfeeding has not only individual benefits, but produces social and economic advantages for the society, reducing the costs for medical expenditure, the absence from work of parents due to babies' diseases.

The direct economic benefits for the family are significant too: considering the actual market prices of artificial milk, we estimate that feeding a baby in the first 6 months of life (exclusive period of breastfeeding suggested by the WHO) costs on average almost € 412,62 (it may vary between € 142,00 and € 690,00)[16]. The cost for artificial feeding

[15] American Academy of Pediatrics workgroup on breastfeeding. Breastfeeding and the use of human milk. Paediatrics 1997;100:1035.

[16] In Italy there are many brands of milk on the market and the prices vary a lot, so we considered a sample of 22 from the most used product in Italy (from Humana, Milupa, Miltina, Mellin, Beba Nestlè, Coop ecc.). For the

in the first year is on average € 907,00, but can reach also € 1.520,00 (tab. 23), confirming the results of a previous study conducted by Bonati (1998)[17].

Tab. 23 Costs for artificial feeding (euro)

Period	Mean	min	max
6 months	412.62	141.75	691.74
1 year	907.11	311.65	1520.73

Source: our elaboration

To evaluate the transport costs for the visit to the patient during the hospitalisation, from husband and relatives, we considered the data referred to the patient's place of residence to evaluate the distance in km from the hospital. The evaluation has been done considering the petrol cost born to travel every day of in-stay from home to hospitals (tab.24). In the same way we evaluated the transport costs to go to the hospital to remove the suture point after the demission (tab.25).

Tab. 24 Transport costs for visits (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
C_trasp_visits					
Total	201	15.50642	27.17254	0	180
Caesaren Section	83	24.54373	37.88223	0	180
Vaginal Delivery	118	9.149661	12.55659	0	65.5
Epidural Analgesia	36	11.64778	13.0009	0	65.5

Source: our elaboration

Tab. 25 Transport costs to remove suture points (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
C_trasp_rimo					
Caesarean Section	83	4.064458	6.025272	1	30
Vaginal Delivery	118	1.945085	2.671052	0	14.92

Source: our elaboration

The cost of the home assistance after delivery has been indicated in the questionnaire by the patient and corresponds to the monthly wage paid (tab. 26). In this case the data

evaluation we considered the daily dose of milk in grams that a baby must have in the different periods of life, as suggested by the pediatric association, and the total quantity for each period (first weeks, first month and next) has been evaluated using the price of the correspondent artificial milk for kg.

[17] The Italian study conducted in 1998 estimated that the financial cost for artificial feeding in the first year of life is almost €780. See Bonati M., Vivarelli P., Brunetti M. *Il costo economico del non allattamento al seno*. Quaderni ACP 1998;6:10.

must be normalized with respect to the individual and familiar income, as generally, women with higher economic capacity can pay more for assistance. The same can be said for the profession practiced, as it can have a different impact on the length of assistance: autonomous women are more time flexible if compared to employed women.

Tab. 26 Costs for assistance in the postpartum (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
C_assistance					
Tot	190	93.42105	213.9237	0	1000
Caesarean Section	76	124.3421	255.0155	0	1000
Ces_elec	46	139.1304	250.7573	0	800
Ces_urg	30	101.6667	264.0805	0	1000
Vaginal	114	72.80702	179.7417	0	1000
Vag_no alg	78	81.41026	188.1401	0	1000
Epidural	36	54.16667	160.9681	0	800

Source: our elaboration

In the postpartum the 28% of women will be assisted by the husband, 21% by parents and 5% by other people (tab.27). The 46% of women will not ask for assistance.
The costs for the days of job lost by caregivers have been quantified using the monthly wage, from which we determined the daily cost (tab. 28-a,b).

Tab. 27 Caregivers' assistance in the postpartum

Caregiver	Freq.	Percent.	Cum.
any	96	**45.93**	45.93
other	10	**4.78**	50.72
parent	44	**21.05**	71.77
Husband/partner	59	**28.23**	100.00
Total	209	100.00	

Tab. 28-a Average days of job lost by caregivers

Variable	Obs	Mean	Std. Dev.	Min	Max
Gg_persi					
Total	105	1.504762	2.981107	0	15
Caesarean (all)	44	1.590909	3.060006	0	10
Ces_elec	30	2.1	3.487416	0	10
Ces_urg	14	.5	1.400549	0	5
Vaginal	61	1.442623	2.946889	0	15
Vag_no alg	39	1.153846	2.18293	0	9
Epidural	22	1.954545	3.969854	0	15

Source: our elaboration

Tab. 28-b Costs of job lost by caregivers (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
C_Gglav_perso					
Tot	209	54.24097	203.3153	0	2045.45
Caesarean (all)	87	46.23824	150.5343	0	909.090
Ces_elec	54	66.91919	184.712	0	909.090
Ces_urg	33	12.39669	49.88717	0	227.272
Vaginal	122	59.94784	234.2522	0	2045.45
Vag_no alg	85	42.19251	151.6189	0	818.181
Epidural	37	100.7371	358.2517	0	2045.45

Source: our elaboration

In the questionnaires have been reported also the monthly hours of leisure time lost by the caregivers. In tab.29 we show the average amount of hours lost for each delivery method: CS requires more assistance if compared to VD.

Tab. 29 Average of monthly hours of leisure time lost by caregivers

Variable	Obs	Mean	Std. Dev.	Min	Max
Tl_lost					
Tot	206	27.23301	53.71664	0	240
Caesarean (all)	84	29.28571	58.16026	0	240
Ces_elec	51	34.11765	61.194	0	240
Ces_urg	33	21.81818	53.17745	0	240
Vaginal	122	25.81967	50.62976	0	240
Vag_no alg	85	22.94118	50.20964	0	240
Epidural	37	32.43243	51.66158	0	180

Source: our elaboration

For the evaluation of the leisure time we used as proxy the hour cost of wage for the marginal hours of job (extraordinary), assuming that leisure time could be spent at work. We increased of 35% the hour wage from salary and we multiplied it for the hour of time lost reported. We calculated it only for the first month for simplicity, but we could extend the analysis for the following months (tab.30).

Tab. 30 Average cost of the monthly time of leisure lost by caregivers (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
C tl_mese					
Tot	60	113.2528	168.2455	0	715.9091
Caesarean (all)	25	116.2159	203.6371	0	715.9091
Ces_elec	15	138.0114	215.8928	0	715.9091
Ces_urg	10	83.52272	189.9954	0	596.5909
Vaginal	35	111.1364	140.8458	0	477.2727
Vag_no alg	21	112.5	144.4475	0	477.2727
Epidural	14	109.0909	140.624	0	477.2727

The time lost by husband is not considered

In tab.31 we report the total private and indirect costs born by patients and their relatives due to the delivery event.

Tab. 31 Total indirect and private costs (euro)

Variable	Obs	Mean	Std. Dev.	Min	Max
Tot_costs	185	760.2428	842.2415	120.55	6565.63
Caesarean (all)	75	875.6392	909.6488	120.55	3905.197
Ces_elec	46	1006.736	997.1797	156.5	3905.197
Ces_urg	29	667.6926	718.1571	120.55	2669.306
Vaginal (all)	110	681.5634	787.5897	191.35	6565.63
Vag_spon	75	630.5672	571.146	191.35	2927.241
Epidural	35	790.841	1122.76	246	6565.63

Source: our elaboration

3.3. A model to estimate the delivery costs factors

To understand which factors may impact more on the delivery cost, we used a model to estimate the delivery cost as a function of women characteristics, such as age, origin, level of education, profession, health conditions, and as a function of interventions and procedures used during the hospitalisation.

To estimate the delivery cost we used a statistic regression that consider the dependent variable *tot_cdir* representing the total cost of delivery (only health costs), as a function of the following explicative variables:

- *age_rif*, the difference between the age observed and the minimum age at delivery in the sample and in Italy;
- *deg_ref*, the difference between the days of in-stay observed and the minimum length;
- *foreigner*, dummy with value one if the mother is not Italian;
- *laurea* and *diploma* dummy with value one if the women is graduated o has a diploma;
- *no_job* dummy with value one if the woman is not employed;
- *ces_preg* dummy with value one if the woman had a previous CS;
- *patol* dummy with value one if the woman has disease;
- *gestaz* is the difference between the observed week of pregnancy and the 40th week;
- *ces_urg* or *ces_el* dummy with value one if the woman had CS in urgency or planned CS;

- *indpil* dummy with value one if the woman has been induced during labour;
- *episio* dummy with value one if the woman has had episiotomy;
- *epid* dummy with value one if the woman has had epidural analgesia;

The results of the model show that the factors that impact more on the delivery cost are the "*deg_rif*", the incremental days of in-stay that the patient spends in hospital with respect to the minimum number of days (Tab. A2 in appendix).

The planned caesarean section and the urgency caesarean increases the costs of delivery of almost € 825,00 and € 998,00. Epidural analgesia and episiotomy, even if in a marginal way, can increase the average cost of delivery up to € 120,00.

The individual characteristics of the patients, especially the social and economic factors are not significant to determine the full cost of delivery.

4. Measures of mothers' satisfaction and effectiveness of delivery

4.1. If women could choose, which delivery method would they prefer?

In the questionnaire we asked patients to say which delivery method they would have preferred (between VD without analgesia, VD with epidural and planned CS), if they could have been free to choose, motivating the answer.

In tab. 32 we show a synthesis of the preference degree with respect to each delivery method. The results show that in general more than a half of the interviewed women would have a VD with epidural analgesia, the 27% would not have epidural and 12% would prefer CS.

Tab. 32 Preferred delivery method

delivery_pref	Freq.	Percent	Cum.
N.R.	14	6.70	6.70
Caesarean section	25	11.96	18.66
Epidural	112	**53.59**	72.25
Vaginal	58	27.75	100.00
Total	209	100.00	

Source: our elaboration

If we analyse the data taking into account the type of delivery that the woman have really had, the results seem to be more significant (tab. 33).

Women who had a VD, in the 36% of cases would have the same delivery, the 56,5% would have VD but with analgesia, and only 2,5% would have a CS.

Only one half of the women that did not have epidural would like to have it, but the other half has not been satisfied of delivery and would like to deliver without analgesia.

Women who had epidural followed by a natural delivery would repeat the same experience in the 78,39% of the cases, because they have been happy of the event, but the 9,3% of them would not have epidural because of the further complications occurred.

Women who had CS after epidural would have epidural again in the 66% of cases[18], or would prefer elective CS in the 16% of the cases, but any of them would have a VD without analgesia.

Women who had CS in general still prefer it in the 25,3% of cases, but the 49,4% would prefer a natural delivery with analgesia to feel less pain, and only the 16% of them would prefer a VD without analgesia.

Tab. 33 Preferred delivery method (with respect to the delivery experience had)

Delivery experience	***VAGINAL (all)***			***Vaginal without analgesia***		
Delivery_pref	Freq.	Percent	Cum.	Freq.	Percent	Cum.
N.R.	6	4.92	4.92	6	6.31	6.32
Caesarean section	3	2.46	7.38	1	1.05	7.37
Epidural analgesia	69	**56.56**	63.93	44	**46.32**	53.68
Vaginal analgesia (no ep)	44	**36.07**	100.0	44	**46.32**	100.0
Total	122	100.00		95	100.00	

Delivery experience	***EPIDURAL ANALGESIA***			***Epidural followed by VD***			***Epidural followed by CS***		
Delivery_pref	Freq.	Percent	Cum.	Freq.	Percent	Cum.	Freq.	Percen	Cum.
N.R.	2	4.65	4.65	1	2.70	2.70	1	16.67	16.67
Caesarean section	4	9.30	13.95	3	8.11	10.81	1	16.67	33.33
Epidural analgesia	33	**76.74**	90.70	29	**78.38**	89.19	4	**66.67**	100.0
Vaginal analgesia (no ep)	4	9.30	100.0	4	**10.81**	100.00			
Total	43	100.00		37	100.00		6	100.0	

Delivery experience	**CAESAREAN (all)**			**Urgent_CS**			**Planned_CS**		
Delivery_pref	Freq.	Percent	Cum.	Freq.	Percent	Cum.	Freq.	Percent	Cum.
N.R.	8	9.05	9.05	6	11.11	11.11	2	6.06	6.06
Caesarean section	22	25.29	34.48	19	35.19	46.30	3	9.09	15.15
Epidural analgesia	43	**49.43**	83.91	20	**37.04**	83.33	23	69.70	84.85
Vaginal analgesia (no ep)	14	16.09	100.00	9	16.67	100.00	5	15.15	100.00
Total	87	100.00		54	100.00		33	100.00	

Source: our elaboration

[18] The value is not much significant because the sample is very small.

If we distinguish the type of CS, women who had a urgent CS are more willing do it again with respect to women who had a planned CS (35% in the first case and only 9% in the second), because they know that the procedure was important to save their life or the baby's one.

The 16% of women who had a urgent CS would like to have a VD without analgesia: part of them are the same women who had complications after epidural.

Finally, women who had a planned CS would do it again in the 9% of cases, and would prefer VD in the 85%: they think VD is more natural way of having a baby and it allows a shorter recovery. The 69,7% of them would have epidural analgesia.

4.2. Patient wellbeing, pain, anxiety and childbirth perception

The delivery event differs from the other healthcare interventions (therapies and surgical operations) because it does not improve or worsen the quality of life of the patients and it is not direct to modify a pre-existent health status.

After delivery a woman can certainly have some repercussion in physical terms: if during CS is possible to remove fibro-adenomas or cysts she will benefit form the delivery, but if delivery have some complications her health status can get worse (such as depression, incontinence, uterine injuries, or hysterectomy in the worst cases).

Changes in the quality of life due to delivery are limited to the labor period, the delivery moment and the postpartum period. Nevertheless, these changes are temporal and can often be solved in few days, thus the classical instruments generally used in the economic evaluations used (such as QALYs, EuroQol (EQ-5D) and the questionnaires SF_36 o SF_12 (Jomeen J., Colin T., 2005) are not useful.

A first index of women clinical status before and after delivery is given by the Barthel index (Mahoney F, Barthel DW, 1965). The index consists of 10 dimensions and for each dimension it assigns points from 0 to 10 to physical conditions, such as the ability to walk, eat, dress. The final scores can vary from 0 to 100 (where 0 is the higher disability and 100 is the perfect health status).

We collected the Barthel index of the women involved in the study from clinical reports and we show the results in tab. 34.

From the analysis of the sample we can see that the patients entering in hospital with labor (spontaneous VD) have a Barthel index on average quite low if compared to

other women, and this is due to the physic pain that they are feeling, but they register better results when they exit the hospital.

Women asking for epidural analgesia enter with a low index and this seems to justify the need to reduce the pain through analgesia. Vaginal delivery with operative procedure has low index at entrance, but the higher index at the exit. The same good results at the exit can be reached by the induced VD, that presents good indexes also at the entrance, because the woman will start to suffer only after induction. The CS has high Barthel indexes at entrance if the intervention is planned, and low indexes if practice in urgency. In both the cases the indexes at the exit are the lowest in the Barthel scheme.

Tab. 34 Barthel index at entrance and exit for each delivery method

Delivery method	*Entrance*	*Exit*
Vaginal with epidural	66	95
Vaginal _induced	77	98
Vaginal_spontan	62	94
Planned caesarean	96	88
Urgent caesaren	78	89

Source: our elaboration

According to the main literature, the instrument used to evaluate the impact of delivery on woman's well being must be clinical and psychological instruments.

The psychological determinants that may give information about the maternal status may be synthesized by the following variables: anxiety, pain perception, maternal satisfaction of the delivery event. The level of psychological and social stress, associated to anxiety, can cause risks on the obstetric condition of the mother and the wealth of the baby.

Anxiety is linked in the mother to a higher perception of the labor and the delivery (Waldenstrom V., 1999) and to an increasing probability or postpartum depressive humor (Mckee MD, 2001; Da Costa, Larouche, Dritsa, & Brender, 2000).

In the woman perception of the pain during labor there is a qualitative difference between pain in a sufferance context, with lack of help, and the pain in a comfortable context, with aims and strategies direct to contrast the pain, as epidural.

For the delivery event the evaluation of the patient's well being must be done through anonymous questionnaires that can value the clinical and psychological dimension, and the changes of such dimension due to the delivery.

The instruments used to this aim are: S.T.A.I. (state-trait anxiety inventory) Form Y (Scale A-B) (Spielberger C., Gorusch, 1970) and Italian Questionnaire of Pain-Q.U.I.D. (Questionario Italiano del Dolore) before delivery (to estimate psychological aspects of anxiety and pain not confounded by the fear and the concern for the next delivery), S.T.A.I. and C.P.Q. (Childbirth Perception Questionnaire) two days after delivery to understand the maternal satisfaction due to the delivery method.

The questionnaires, administered by specialized personnel, have been analysed to calculate indexes of women well being for each delivery method.

The preliminary results of the analysis refer to the results of the postpartum C.P.Q. questionnaires, administered to almost 133 patients (66% of the sample)[19].

The questionnaire is divided into three parts and aims at evaluating the woman satisfaction with respect to three different dimensions: the satisfaction of the physical and sexual satisfaction during pregnancy, labour and delivery, the satisfaction of the childbirth experience and the satisfaction of the interaction with the partner[20].

In tab. 35 we show the results of the CPQ questionnaires for each delivery method.

The results show that the women that have had CS have index of physical satisfaction lower that the women that delivered naturally.

Probably, women that have CS may feel worst because of the abdominal injury and the suture points (the same can be said for women that have had episiotomies and have lower indexes).

Epidural analgesia seems not to have impacts on physical satisfaction, because the values are the same of the women that delivered without analgesia.

The satisfaction of the delivery event seems to be very low for woman that have had CS, because the indexes are 21 over 52, but comparing CS in urgency and election the first one has better results (probably the women that live the labour event felt to be more active and present for the delivery).

[19] The analysis is not completed because the sample of women has been selected in a limited temporal interval and too recent, to administer the questionnaire after two months. A new survey is taking place and the results will be published soon.

[20] The first section of the questionnaire refers to the physical and sexual dimension and consists of 5 questions to understand if women were embarrassed of her aspect during pregnancy, labor and delivery, if she thinks that it will have an impact in her future life and relationship. The second section of the questionnaire refers to the satisfaction of the delivery method and the behavior during delivery, the ability to control pain, the self-esteem. The third section consists of 9 questions in which we ask woman to give a value of the interaction she had with the partner during pregnancy, the labor time and the delivery, which impact delivery will have on the relationship and the impact that the baby will have on their relationship (see appendix).

Women that have had VD are on average more satisfied, especially if they could reduce the pain thanks to epidural (the index for VD is 29,2 without epidural and 31,7 with epidural).

The same results have been registered for the third dimension of satisfaction: women that have had epidural are more satisfied of the interaction with the partner (because for VD the partner can assist the woman during delivery, whereas this is not allowed during CS) and they are more faithful with respect to their future relationship and the impact that the baby will have on it.

Tab. 35 Maternal satisfaction of delivery event (CPQ) for each dimension

Delivery method	***Physical_sexual dimension sat.***	***Child_birth event dimension sat.***	***Parner_relat dimension sat.***	***Total satisfaction***
Caesarean (all)	7.596774	21.35484	12.04839	41.16129
Caesarean_elect	8	18.15385	11.23077	37.64103
Ces_urg	6.913043	26.78261	13.43478	47.13043
Vaginal	9.169014	29.25352	15.85915	54.09859
episiotomy	8.725806	29.79032	16.22581	54.53226
Epidural	8.916667	31.70833	16.91667	56.70833
TOTAL	8.43609	25.57143	14.08271	48.06767

Source: our elaboration

In the whole, the possibility to deliver with less pain during labour seems to grant better indexes of satisfaction with respect to other delivery methods, both for the physical and sexual dimensions, both for the delivery event and the relationship with the partner (tab.36).

Tab. 36 Total satisfaction

Total satisfaction	***Obs***	***Mean***	***Std. Dev.***	***Min***	***Max***
Caesarean section	62	21.35484	17.57345	1	80
Caesarean_elect	39	18.15385	17.98755	1	80
Caesarean_urg	23	26.78261	15.43404	26	77
Vaginal	71	29.25352	15.2729	22	93
episiotomy	62	29.79032	14.0581	28	88
Epidural	24	31.70833	14.44172	32	93

Source: our elaboration

The Q.U.I.D. and S.T.A.I. questionnaires have been administered to a sample of more than 100 patients, but we just provide some preliminary results, as the data collection is still going on. The selection criterion for these two tests are very strictly and they must be repeated at least after two months to evaluate the changes, so the study need of a significant sample of participants to get the first significant results [21].

However, preliminary results show that there are no significant differences in the pain dimensions after delivery among the alternative delivery methods.

Before delivery there is no significant difference in pain perception among women having alternative methods of delivery, even if those delivering with epidural analgesia have the highest scores (this would justify the demand of analgesia).

Two days after delivery the pain perception increase in all the patients: those who had epidural have the lowest scores, followed by those who had CS (because they are still treated with an antalgic bolus to limit the pain of the surgery intervention), whereas those who had vaginal delivery without epidural are those suffering more.

The results two months after delivery show that the difference in pain among vaginal, epidural and caesarean are not significant.

No significant results are found also for the anxiety dimension, measured with the STAI Y-form questionnaire.

The only dimension that varies significantly is the state-A anxiety: women having vaginal delivery without epidural analgesia have the lowest anxiety score both before and after delivery; those having epidural have the highest anxiety before delivery; anxiety decreases after vaginal delivery both with and without epidural, but it increases after CS.

[21] For these instruments the sample must be composed only by Italian patients, with an age of 22-42 years old, at first delivery and with a natural prognosis of pregnancy. The questionnaires must be administered before delivery after two days and at least after two months after delivery. The sample selection principles and the administration methods can be a limit, because they can give problems both for the patients recruitment and compliance (many patients decide to leave the study after so many months), both for the collection of data (it requires a long time) and the elaboration of the results (the first results are available after months).

5. Cost-effectiveness analysis

For each delivery method we can build cost-effectiveness ratios and make a comparative analysis using the costs and the effectiveness data obtained so far (tab.37).
A first index of cost-effectiveness (*COST/CPQ*) has been calculated comparing the total costs (*Mean T_Cost*) of each delivery method with the total average score from the *Childbirth Perception Questionnaire* (*CPQ_tot*).
A second index of effectiveness is represented by the possibility to breastfeed after delivery: we compare the total average cost and the probability to breastfeed (*%br_feed*) to calculate a second index of cost-effectiveness (*Cost/breast*).
The results of cost-effectiveness analysis in each case show that VD is preferred to CS, because it allows better indexes of effectiveness and less costs. VD with epidural analgesia is still preferred to CS, but the indexes of cost-effectiveness on average are not so good as for VD without analgesia because epidural can have complications and end up in urgent CS, with worst results both in terms of costs and benefits for women.

Tab. 37 Cost-effectiveness indexes for each delivery method

Delivery	***COST/CPQ***	***MeanT_cost***	***CPQ_tot***	***% br_feed***	***COST/brest***
Caesar_tot	54,84	2.257,40	41.16129	75,61	€ 29,86
Caes_el	**59,60**	**2.228,00**	**37.38462**	**78,00**	**€ 28,56**
Caes_urg	48,90	2.304,89	47.13043	71,88	€ 32,07
Vaginal_tot	21,61	1.170,01	54.17	92,56	€ 12,64
Vag_no epid	**21,13**	**1.107,85**	**52,42**	**90,59**	**€ 12,22**
Epidural	22,90	1.321,07	56.70833	95,24	€ 13,87
Epid_vag	**22,59**	**1.302,97**	**57,69**	**97,22**	**€ 13,40**
Epidur_no epis	18,40	1.149,69	62,50	97,14	€ 11,84
Vaginal_no epis	18,72	905,56	48,37	97,17	€ 9,32

Source: our elaboration

6. Results and conclusions

Despite the debates few studies have paid attention to the real cost of alternative delivery methods, vaginal delivery with and without analgesia and caesarean section.

This study allows for a better knowledge of the real costs of alternative delivery methods and their differences in the Italian framework.

The results show that in general CS is more expensive if compared to VD, but the difference is marginal in case of complications or if we consider the opportunity cost of time during labour.

On a hand this is useful to highlight the differences in terms of costs between the alternative procedures, and on the other hand to compare the real costs of the intervention to the correspondent DRGs tariffs.

The results of the study show that in general the real costs of delivery are rather similar to the tariffs (tab.38). Comparing the costs of each intervention with the correspondent DRGs tariff we can see if tariffs cover the real costs and if eventual differences are justified: the costs seem to be aligned with the regional tariffs, but in many cases planned CS can give positive profit margins and induce opportunistic behaviours (according to Fabbri, Monfardini, 2000).

In fact, if we consider the labour assistance and we compare the total costs of CS and VD with the correspondent tariffs the difference is marginal. On average, when the tariff is higher than the cost, the CS has a positive margin of almost € 223,00 that can reach € 1.124,00 and lost of no more than € 776,00 in the worst cases. The vaginal delivery, in the best situation can have a positive margin of almost € 234,00, but on average the cost is not covered by the tariff for almost € 49,42, reaching huge lost of € 620,00 in the most complex cases.

Tab. 38 Full costs and DRGs tariffs (taking into account assistance during labor)

	Without general costs			***With general costs***		
	min	***max***	***average***	***min***	***max***	***average***
Caesarean	1073,18	2974,01	1974,00	1.287,81	3.586,81	2.336,40
DRG 371	2197,78	2197,78	2197,78	2.197,78	2.197,78	2.197,78
Difference	1124,60	-776,23	223,78	909,97	-1.389,03	-138,62
Vaginal	689,04	1543,21	972,36	826,84	1.851,85	1.166,83
DRG 373	922,94	922,94	922,94	922,94	922,94	922,94
Difference	233,90	-620,27	-49,42	96,10	-928,91	-243,89

If we consider the general costs (20% of total), the average cost of each type of delivery are not covered by tariffs, for € 138,00 the CS and € 244,00 the VD.

In general CS may give higher positive margin with respect to VD and lower costs: these results are quite astonishing if we consider that CS is a surgical procedure and for this reason should be more resource consuming.

Despite this, we must keep in mind that VD, even if it is a natural event, consumes lot of resources too, especially human resources assistance during labour.

This aspect should be carefully investigated, especially if we think at the lack of nurses in many hospitals.

The elective CS allows for a more efficient organization of human resources, materials and spaces, avoiding congestion. Moreover CS can be practiced in the most appropriate moments, avoiding week end, night hours and holidays, where there is less personal.

The measurement of the real costs of each delivery method is useful to estimate the potential saving that a reduction in the inappropriate CS rates would cause.

In tab.39 we show the savings in cost terms that we could obtain reducing the rate of CS to the rate registered in the same type of hospital in Italy (31,34%) and Veneto Region (26,95%)[22].

We chose to consider this rate instead of the 20% suggested by the WHO, to take into account the higher complexity that characterises the hospital of our study.

If we consider the deliveries practiced last year in the A.O., over a total of 3.994 deliveries, almost 34% have been done with CS, and in clinic the rates reaches the 42%.

If we assume that the inappropriate CS can be done vaginally with epidural, and we reduce the rates of CS to 31.34% e 26.95% we could save respectively € 186.327,00 or € 258.922,00 (tab. 39).

Moreover, if we consider the case in which the more expensive CS are replaced by VD that cost less, in the best hypothesis we could save between € 336.622,44 and € 467.774,04 (tab. 40). If we consider the worst hypothesis, in which the less expensive CSs are substituted with the most expensive VD with epidural, we would increment the costs from € 22.878 to € 31.791.

[22] The percentage of the CS delivery rates are available at the Minister of Health website: http://ministerosalute.it/datisis.jsp

Tab. 39 Potential savings from CS rates reduction (euro)

	Taking into account labor assistance costs			**Without labor assistance costs**		
	min	max	average	min	max	Average
Caesarean	*1.244,57*	*2.268,49*	*1.884,24*	*1.244,57*	*2.268,49*	*1.884,24*
31%	287.495,67	524.021,19	435.259,44	287.495,67	524.021,19	435.259,44
27%	399.506,97	728.185,29	604.841,04	399.506,97	728.185,29	604.841,04
Epidural	*811,25*	*1.343,61*	*1.077,63*	*766,58*	*1.098,81*	*944,85*
31%	187.398,75	310.373,91	248.931,84	177.079,98	253.825,11	218.260,35
27%	260.411,25	431.298,81	345.918,27	246.072,18	352.718,01	303.296,85
Diff 31%	**- 100.096,92**	**- 213.647,28**	**- 186.327,60**	**- 110.415,69**	**- 270.196,08**	**- 216.999,09**
Diff 27%	**- 139.095,72**	**- 296.886,48**	**- 258.922,77**	**- 153.434,79**	**- 375.467,28**	**- 301.544,19**

Source: our elaboration

Tab. 40 Savings hypothesis (euro)

	Taking into account labor costs		**Without labor costs**	
	31%	27%	31%	27%
Worst hypothesis	22.878,24	31.791,84	-33.670,56	-46.788,96
Best hypothesis	-336.622,44	-467.774,04	-346.941,21	-482.113,11
On average	-186.327,60	-258.922,77	-216.999,09	-301.544,19

Source: our elaboration

The results show that the introduction of epidural analgesia among LEA would certainly have a strong impact in economic terms, but the final effect is not clear. Epidural analgesia may reduce the number of inappropriate CSs, but it may also prolong labour and increase the number of CS practiced on urgency, increasing the costs due to complications.

From a societal perspective we consider also the implicit indirect costs due to the delivery event (transport costs, medications, cost for artificial milk, time lost by caregivers) and the impact in terms of benefits that each delivery method can have on patients.

Epidural analgesia reducing pain during labour seems to allow a better perception of the childbirth event and a higher ability to manage this experience.

The possibility to deliver with less pain gives higher results in terms of women satisfaction, both for the physical and sexual dimensions, both for the delivery event and the relationship with the partner. The cost-effectiveness analysis shows that in general VD with analgesia is preferred both in terms of costs and benefits, but in many cases epidural analgesia can end up in CS, with worst results.

In conclusion we think that the preliminary results presented in the study must be considered, especially with refer to the last law proposals that are addressed towards a higher attention for pain during labour.

Despite the implementation of the study has been complex and required the collaboration of many professional figures, we think that its extension and validation can give useful data, actually not available, on the real costs of medical practice in Italy.

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Appendix – The models results

Tab. A.1 Logit model results for the probability of a CS in election

	(1)	(3)	(4)	(5)	(6)	(7)	(9)
COEFFIC.	ces_el	ces_el	ces_el	ces_el	ces_el	ces_el	ces_el
age_rif	**0.139****	**0.128****	**0.112***	**0.124****	**0.115***	**0.115***	**0.116***
	(0.0558)	(0.0569)	(0.0600)	(0.0565)	(0.0610)	(0.0605)	(0.0613)
foreigner	-1.214	-1.191	**-1.651***	**-1.340***	**-1.633***	**-1.670****	**-1.637***
	(0.749)	(0.751)	(0.844)	(0.765)	(0.845)	(0.848)	(0.846)
diploma	-0.322	-0.346	-0.958	-0.222	-1.006	-0.951	-0.974
	(0.661)	(0.667)	(0.712)	(0.681)	(0.727)	(0.711)	(0.728)
no_job	0.170	0.120	0.0401	0.184	0.0328	0.0425	0.0160
	(0.514)	(0.519)	(0.563)	(0.523)	(0.562)	(0.562)	(0.561)
ces_pregr	**3.540*****	**3.595*****	**3.413*****	**3.459*****	**3.426*****	**3.385*****	**3.393*****
	(0.611)	(0.624)	(0.626)	(0.607)	(0.629)	(0.633)	(0.636)
patol	0.373	0.359	0.604	0.459	0.590	0.595	0.564
	(0.536)	(0.538)	(0.581)	(0.542)	(0.583)	(0.582)	(0.583)
gestaz	**-0.395*****	**-0.397*****	**-0.324****	**-0.382*****	**-0.323****	**-0.323****	**-0.323****
	(0.120)	(0.120)	(0.132)	(0.120)	(0.132)	(0.133)	(0.133)
laurea	-0.592	-0.737	-0.933	-0.408	-0.986	-0.893	-0.953
	(0.687)	(0.715)	(0.705)	(0.704)	(0.726)	(0.717)	(0.738)
no_married	**-1.321***	**-1.358***	**-1.398***	**-1.289***	**-1.403***	**-1.382***	**-1.384***
	(0.754)	(0.754)	(0.812)	(0.775)	(0.808)	(0.816)	(0.813)
homekeeper	-0.872	-0.906	-0.142	-0.692	-0.160	-0.128	-0.167
	(0.835)	(0.835)	(0.896)	(0.866)	(0.895)	(0.898)	(0.895)
rich		0.511				-0.179	-0.0901
		(0.594)				(0.668)	(0.681)
ces_pref			**2.563*****		**2.668*****	**2.607*****	**2.649*****
			(0.671)		(0.758)	(0.694)	(0.783)
epid_pref				-0.703	0.166		0.148
				(0.449)	(0.544)		(0.546)
Constant	-3.643***	-3.490***	-3.165***	-3.202***	-3.265***	-3.188***	-3.246***
	(1.101)	(1.104)	(1.126)	(1.139)	(1.175)	(1.127)	(1.173)
Observ.	207	204	207	207	207	207	204
R-squared	.	.	.	.	.	.	.

Standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1
STATA 10 version results

- *age_rif*: Referring age at delivery calculated as the difference between the observed age and the average minimum age at delivery registered in the sample and at national level;
- *foreigner:* women not Italian
- *diploma*, *laurea* : if woman has a diploma/laurea
- *no_job :* if woman does not work
- *ces_preg*: if woman has had previous CS
- *patol*: Presence of disease that may require a CS
- *gestaz*: number of pregnancy weeks over term as the difference between the weeks of pregnancy observed and the 40th week;
- *no_coniug*: if woman is not married
- *homekeeper*: if woman is homekeeper (dummy)
- *rich:* if woman income >= 50.000 euros
- *ces_pref:* if woman expressed preference for a CS
- *epid_pref:* if woman expressed preference for epidural
- *no_married:* Being not married (dummy)

Tab. A.2 Regression model results

reg tot_cdir deg_rif age_rif laurea ces_pregr patol gestaz ces_urg ces_el epid foreigner no_job epsio

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
COEFFICIENT	tot_cdir	tot_cdir	tot_cdir	tot_cdir	tot_cdir	tot_cdir	tot_cdir	tot_cdir
deg_rif	69.93***	70.35***	66.96***	64.72***	64.35***	63.91***	63.33***	61.71***
	(10.55)	(10.63)	(10.86)	(10.92)	(10.89)	(11.02)	(11.02)	(11.02)
ces_urg	999.8***	1004***	1002***	1111***	1121***	1123***	1123***	1115***
	(42.86)	(43.36)	(43.35)	(65.43)	(65.62)	(65.95)	(65.91)	(65.81)
ces_el	844.1***	854.2***	840.4***	948.8***	961.2***	962.3***	961.3***	924.2***
	(39.89)	(41.35)	(42.62)	(64.84)	(65.24)	(65.51)	(65.47)	(69.26)
epid	103.4***	103.4***	110.1***	106.2***	115.2***	115.4***	111.1***	112.8***
	(38.23)	(38.44)	(38.60)	(38.58)	(38.99)	(39.10)	(39.27)	(39.12)
age_rif		-1.971	-1.527	-0.597	1.240	1.318	1.021	0.960
		(2.935)	(2.994)	(3.081)	(3.332)	(3.350)	(3.358)	(3.345)
patol			54.77	58.04	63.22	62.92	64.51	69.46*
			(38.53)	(39.03)	(39.09)	(39.20)	(39.20)	(39.17)
gestaz			-8.763	-7.439	-7.975	-8.029	-9.416	-9.983
			(9.653)	(9.675)	(9.656)	(9.681)	(9.755)	(9.721)
episio				127.9**	135.9**	137.7**	132.1**	129.2**
				(56.83)	(56.95)	(57.40)	(57.57)	(57.36)
foreigner					56.28	54.94	67.59	62.68
					(39.46)	(39.81)	(41.37)	(41.32)
laurea						-8.926	-16.35	-20.59
						(29.95)	(30.66)	(30.65)
no_lavora							-36.82	-42.93
							(33.02)	(33.11)
ces_pregr								73.95
								(46.69)
Constant	821.3***	841.8***	826.2***	712.7***	666.1***	669.0***	692.2***	700.2***
	(26.79)	(43.41)	(44.63)	(69.03)	(76.21)	(77.02)	(79.73)	(79.56)
Observations	199	197	196	193	193	193	193	193
R-squared	0.863	0.864	0.865	0.867	0.868	0.868	0.869	0.871

Standard errors in parentheses *** p<0.01, ** p<0.05, * p<0.1
STATA 10 version results

- *age_rif*, the difference between the age observed and the minimum age at delivery in the sample and in Italy
- *deg_ref*, the difference between the days of in-stay observed and the minimum length
- *foreigner*, dummy with value one if the mother is not Italian
- *laurea* and *diploma* dummy with value one if the women is graduated o has a diploma
- *no_job* dummy with value one if the woman is not employed
- *ces_preg* dummy with value one if the woman had a previous CS
- *patol* dummy with value one if the woman has disease
- *gestaz* is the difference between the observed week of pregnancy and the 40th week
- *ces_urg* or *ces_elez* dummy with value one if the woman had CS in urgency or planned
- *epid* dummy with value one if the woman has had epidural analgesia
- *age_rif*, the difference between the age observed and the minimum age at delivery in the sample and in Italy

Appendix – The questionnaires (Italian Version)

N.CART _____ data somm. |__| __|__| Nome_____(opzionale)
Età |____| Cittadinanza _____ Paese d'origine _____
Comune di residenza _____ Religione_____

Titolo di studio:
Laurea o titoli superiori ..... |__| 1.
Diploma universitario o laurea breve.....|__| 2.
Diploma di scuola media superiore ..... |__| 3.
Diploma di scuola media inferiore .....|__| 4.
Licenza elementare ..... |__| 5.
Altro……..……|__|6.

Condizione professionale/non professionale
Occupata..... |__| 1.
Disoccupata .....|__| 2.
In cerca di prima occupazione ..... |__| 3.
Studentessa .....|__| 4.
Casalinga ..... |__| 5.
Altra condizione (ritirata dal lavoro, inabile, ecc) .....|__| 6.

Se occupata, **posizione nella professione (SPECIFICARE A LATO SE OPPORTUNO)**
Imprenditrice o libera professionista|……..|__| 1. _____
Altro lavoro autonomo……..|__| 2. _____
Lavoratrice dipendente: dirigente o direttivo……|__| 3. _____
Lavoratrice dipendente: impiegata……|__| 4. _____
Lavoratrice dipendente: operaia……..|__| 5. _____
Altro lavoro dipendente (apprendista, lavoro a domicilio, ecc)…… |__| 6. _____

Livello di **reddito personale** annuo in €:		Livello di **reddito familiare** annuo in €:	
0-15.000	|__|	0-15.000	|__|
15.000-30.000	|__|	15.000-30.000	|__|
30.000-50.000	|__|	30.000-50.000	|__|
> 50.000	|__|	> 50.000	|__|

Ha lavorato durante la gravidanza? Si |__|1. **numero settimane** |____| no |__| 2.
Stato civile:
Nubile…….|__| 1.
Coniugata…….|__| 2.
Separata…….|__| 3.
Divorziata……|__| 4.
Vedova……..|__| 5.

Precedenti concepimenti/parti (numero): |__|__| Num. **tagli cesarei precedenti** |__|__|

Visite di controllo in gravidanza:
Nessuna……|__| 1.
Fino a 4 (minori o uguali a 4)…….|__| 2.
Più di 4……..|__| 3. Indichi il **numero** di visite di controllo|__|__|
Prima visita di controllo in gravidanza a settimane |__|__|
Numero di **ecografie** |__|

Indagini prenatali: (indicare se le ha effettuate oppure no)
Amniocentesi: si |__| 1. no |__| 2.
Villi coriali: si |__| 1. no |__| 2.
Fetoscopia/funicolo centesi: si |__| 1. no |__| 2.
Ecografia > 22 settimane: si |__| 1. no |__| 2.

Decorso della gravidanza: Fisiologico |__| 1. Patologico |__| 2.
(importante) Se patologico specificare il tipo di **condizione** morbosa insorta durante la gravidanza: (es. diabete, ipertensione, gestosi ecc)
_____

Concepimento con tecniche di **procreazione medico assistita**: si |__| 1. no |__| 2.
Se si, indicare il metodo di procreazione medico assistita utilizzato (es. FIVET):
……
Età gestazionale (settimane compiute) al momento del parto nr: |__|__|
Frequenza a **corsi di psicoprofilassi** (preparazione) al parto: si |__| 1. no |__| 2.

Modalità del parto:
Parto spontaneo |__| Parto Indotto |__| Parto Pilotato |__| Parto Operativo |__|
Vaginale senza analgesia……..…|__|1.
Vaginale con analgesia…….…..|__| 2.
Taglio cesareo d'elezione (programmato)……..|__| 3.
Taglio cesareo in urgenza……|__|4.
Tempo di travaglio (in ospedale) ore |___|
Episiotomia/ Episioraffia (punti di sutura vaginale): si |__|
Data del parto |__|__| |__|__| |__|__|__|__| (giorno/mese/anno) |__|__| |__|__| (ora/minuti)
Genere del parto: Semplice(singolo)|__| 1.
Plurimo(gemellare)|__| 2. Nr. maschi |__| Nr. femmine |__|

Se avesse potuto scegliere una tipologia di parto, quale tra queste avrebbe preferito?
Vaginale senza analgesia……|__| 1.
Vaginale con analgesia(epidurale)……..|__|2.
Taglio cesareo d'elezione…….…..|__| 3. _____
Per quale motivo? _____

Quanto sarebbe stata disposta a pagare per il parto indicato come preferito se non fosse stato gratuito?
< 200 € |__|
200-400 € |__|
400-600 € |__|
600-800 € |__|
800-1000 € |__|
>1000 € |__|

Sta allattando? Si |__| 1. No |__| 2. Se no per quale motivo? _____

A seguito del parto, **avrà bisogno di impiegare una persona** che le presti assistenza pagandola, (es. baby sitter, domestica) ?
Si |__| 1. No |__| 2. Indicare l'importo mensile €_____

A seguito del parto, **avrà bisogno di una persona che si prenda cura di lei** o che la aiuti nello svolgimento delle normali attività? (si escluda dalla valutazione il ricorso a supporto esterno dovuto al carico di lavoro in più che un neonato comporta in ogni caso).
Si |__| 1. No |__| 2.

Se si **indicare chi**: coniuge |__| genitore |__| altro parente |__| non familiare |__| altro |__|

Se si, questa persona (coniuge, genitore, parente ecc..) quanto tempo le dedicherà **ogni giorno**?
2 ore |__| 4 ore|__| 6 ore|__| 8 ore|__| 10 ore|__|
12 ore |__|14 ore|__| 16 ore |__| 18 ore|__| 20 ore|__|

La persona che la assisterà (o che già l'ha assistita) (es. il coniuge, genitore, familiare) lavora?
Si |__| 1. No |__| 2.

Se si, dovrà (o ha già dovuto) modificare la sua attività lavorativa per assisterla?
Si |__| 1. No |__| 2.
Se si come? (es. passando al part time, cambiando lavoro)_____

La persona che la assisterà (ha assistita) ha già perso giorni di lavoro?
Si |__| 1. Quanti in media?_____ No |__| 2.

Qual è la retribuzione media mensile in € della persona (coniuge, genitore,ecc) che si è occupata di lei?
< 600 € |__|
600-1000 € |__|
1000-2000 € |__|
2000-2500 € |__|
>2500€ |__|

La persona che la assiste ha già perso/perderà del proprio tempo libero?
Si |__| 1. Quanto in media al giorno?_____ Per quanto tempo?_____ gg
No |__| 2.

Appendix – The questionnaires (English Version)

N.CART _____ data admin. |__| __|__| Name_____(opt)
Age |____| Citizen _____ Origin Place _____
Residence place _____ Religion_____

Level of education:
Laurea o higher degrees (PhD) ..... |__| 1.
University diploma or short laurea….....|__| 2.
High school diploma ……..... |__| 3.
Secondary school diploma……. .....|__| 4.
Primary school ..... |__| 5.
Other ……|__|6.

Professional condition
Employed..... |__| 1.
Unemployed .....|__| 2.
Looking for a first job ……..... |__| 3.
Student…. .....|__| 4.
Home keeper..... |__| 5.
Other (retired, disable, ecc) .....|__| 6.

If employed, **type of profession (add details if necessary)**
Entrepreneur of professionist ……..|__| 1. _____
Other autonomous job……..|__| 2. _____
Dependent worker: manager……|__| 3. _____
Dependent worker: employee……|__| 4. _____
Dependent worker: workman.……..|__| 5. _____
Other dependent worker (trainer, work at home, ecc)……. |__| 6. _____

Personal gross income in € (for year):
0-15.000 |__|
15.000-30.000 |__|
30.000-50.000 |__|
> 50.000 |__|

Familiar gross income in € (for year):
0-15.000 |__|
15.000-30.000 |__|
30.000-50.000 |__|
> 50.000 |__|

Did you work during pregnancy? Yes |__|1. **number of weeks** |____| No |__| 2.
Marital status**:**
Unmarried…….|__| 1.
Married……|__| 2.
Separated…….|__| 3.
Divorced……|__| 4.
Widow……..…..|__| 5.

Previous deliveries (number): |__|__| Previous Caesarean Sections (number): |__|__|

Check up during pregnancy:
No visit……|__| 1.
Less than 4 ……..…|__| 2.
More than 4……..|__| 3. Number of visits: |__|__|
First check-up during pregnancy at week nr |__|__|
Number of ecographies |__|

Prenatal investigations:
Amniocentesis: yes |__| 1. no |__| 2.
Villography: yes |__| 1. no |__| 2
Foetusscopy/funicolocentesis: yes |__| 1. no |__| 2
Ecography after 22 gest.weeks: yes |__| 1. no |__| 2

Course of pregnancy: Physiologic |__| 1. Pathologic |__| 2.
(important) Specify any problem or complication had during pregnancy: (es. diabetes, hypertension)
_____

Did you use any medical procreation device? yes |__| 1. no |__| 2.
If yes, indicate the type of assisted procreation method (i.e. FIVET):
……

Pregnancy week at delivery: |__|__|
Attendance to delivery preparation courses: yes |__| 1. no |__| 2.

Delivery method:
Spontaneous delivery |__| Induced delivery |__| Pilotated delivery |__| Operative delivery |__|
Vaginal without epidural analgesia……..…|__|1.
Vaginal with epidural analgesia…….…..|__| 2.
Planned Caesarean Section……..…..|__| 3.
Urgent Caesarean Section……..……|__|4.
Labour hours (in hospital) |___|
Episiotomy/(suture points): yes |__|
Data of delivery |__|__| |__|__| |__|__|__|__| (day/month/year) |__|__| |__|__| (hour/minutes)
Type of delivery: Single delivery|__| 1.
Plurim delivery (twins)|__| 2. Nr. males |__| Nr. females |__|

If left free to decide, which of the following delivery method would you have preferred?
Vaginal without analgesia……|__| 1.
Vaginal with analgesia(epidural)……..……..|__|2.
Planned caesarean section…….,,,,,,,.……..…..|__| 3. _____
Why? _____

If you could pay for the preferred delivery method, which would be your willingness to pay for it? (or, if the preferred delivery method was not free, and you must pay for it, how much would you pay for it?)
< 200 € |__|
200-400 € |__|
400-600 € |__|
600-800 € |__|
800-1000 € |__|
>1000 € |__|

Are you breastfeeding? Yes |__| 1. No |__| 2. If no, why? _____

After delivery, when you will be back home, would you employ a person to help you with the baby or the home works? (i.e. baby sitter, home keeper) ?
Yes|__| 1. No |__| 2. Gross monthly payment €_____

After delivery, when you will be back home, will you ask anyone to assist you or help you in the normal domestic activities? (the help must be due to you physical conditions, not for the presence of the baby)
Yes |__| 1. No |__| 2.

If yes, who will help you: partner |__| parent |__| relative |__| friend |__| other |__|

If yes, how many hours a day will he/she spend to help/assist you?
2 hours |__| 4 hours |__| 6 hours |__| 8 hours |__| 10 hours |__|
12 hours |__|14 hours |__| 16 hours |__| 18 hours |__| 20 hours |__|

Does the person who will help/assist you (i.e. partner, parent, relative, friend) work?
Yes |__| 1. No |__| 2.

If yes, will he/she change his/job job activities/conditions to assist you? Yes |__| 1 No |__| 2.
If yes, how? (ex. asking for a part time job, changing work, retiring)_____

Did the person who will assist you already loose days of job?
Yes |__| 1. How much on average?_____ No |__| 2.

Which is the average monthly income of the person assisting you?
< 600 € |__|
600-1000 € |__|
1000-2000 € |__|
2000-2500 € |__|
>2500€ |__|

Will he/she loose her leisure time to help you (or did he/she loose leisure time to assist you)?
Yes |__| 1. How many hours a day?_____ For how long?_____ days/months
No |__| 2.

Appendix – The Childbirth Perception Questionnaire

Nome……(opzionale) Età…… Data……

ISTRUZIONI: Legga ciascuna frase e poi esprima il suo accordo o disaccordo barrando con una crocetta il numero corrispondente alla sua risposta.

SODDISFAZIONE DELLA PROPRIA PRESENZA FISICA E SESSUALE

- Mi sono sentita imbarazzata del mio aspetto fisico durante la gravidanza.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Mi sono convinta del fatto che non sarò attraente come ero prima della gravidanza.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Il desiderio o l'attività sessuale sono diminuiti durante la gravidanza: sono preoccupata su come questo influenzerà l'andamento nei prossimi mesi.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Mi sono sentita imbarazzata del mio aspetto fisico durante il travaglio ed il parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Il desiderio o l'attività sessuale sono diminuiti durante la gravidanza: sono preoccupata di come questo possa influenzare il mio matrimonio/la mia relazione.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

SODDISFAZIONE DELLA CONDOTTA DURANTE TRAVAGLIO E PARTO

- Sono soddisfatta del mio comportamento durante il travaglio ed il parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Ho perso il controllo emotivo di me stessa durante il travaglio.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sento di non avere affrontato il dolore fisico durante il travaglio così come le altre donne.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sono soddisfatta della modalità con cui ho partorito.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- In seguito all'esperienza della nascita del mio bambino, la mia autostima è cresciuta.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Ho provato delusione per la mia condotta durante il travaglio ed il parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sono soddisfatta di quanto controllo io abbia avuto sulle decisioni prese durante l'esperienza della nascita del mio bambino.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sono soddisfatta della dose di medicine/quantità di medicazioni che mi sono state offerte durante il travaglio ed il parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Mi sento delusa riguardo l' esperienza della nascita del mio bambino.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- In seguito all'esperienza del travaglio e del parto, sento di non aver affrontato molto bene il dolore.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Pensavo che il travaglio ed il parto sarebbero stati più semplici per me di quello che invece sono stati.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Ho fatto cose durante il travaglio ed il parto di cui ora mi sento imbarazzata.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- In seguito all'esperienza della nascita del mio bambino, mi sento molto meno fiduciosa in me stessa.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

SODDISFAZIONE DELL'INTERAZIONE CON IL COMPAGNO DURANTE IL PARTO

- Ho sentito che il mio compagno era consapevole dei miei bisogni durante l'esperienza di parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Ho sentito il mio compagno emozionalmente vicino durante il travaglio.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Penso che l'esperienza della gravidanza abbia rafforzato la relazione con il mio compagno**.**
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sono preoccupata che il bambino possa avere in qualche modo un cattivo effetto sulla relazione con il mio compagno.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Penso che l'esperienza del travaglio abbia rovinato la relazione con il mio compagno.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Sento che il mio compagno è stato collaborativo/aiutante così come avrebbe dovuto essere durante l'esperienza di parto.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Mi sento soddisfatta di come il mio compagno ed io abbiamo comunicato durante il travaglio.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Penso che il bambino avrà un buon effetto sul mio matrimonio/relazione.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

- Il mio compagno sta spendendo tutto il tempo a sua disposizione per farmi visita in ospedale.
  [1] Completamente
  [2] Moltissimo
  [3] Molto
  [4] Un po'
  [5] Molto poco
  [6] Per nulla

Appendix- The Childbirth Perception Questionnaire (English)

Name…….(optional) Age…… Data……

Instructions: Read each sentence and cross your agreement or disagreement.

Satisfaction with Physical Appearance/Sexuality

- I felt embarrassed about my physical appearance during pregnancy(*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- I am concerned that I will not be as physically attractive as I was before I had a baby(*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- Sexual activities or desire frequently decreases for the first 6-8 weeks after delivery: I worry about how this will affect the next few months(*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- I felt embarrassed about my physical appearance during labor and delivery (*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- Sexual activity or desire frequently decreases for the first 6-8 weeks after delivery: I worry about how this will affect our marriage in the long run (*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all

Satisfaction with Delivery and Conduct During Labor/Delivery

- I feel satisfied about my conduct during labor and delivery
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- I lost control of myself emotionally during labor (*)
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all

- I feel that I did not deal with the physical pain during labor as well as other women do (*)
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I am satisfied with the way I delivered (vaginal or caesarean)
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- As a result of my childbirth experience, my self-respect has gone up
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I feel disappointed about my conduct during labor and delivery(*)
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I was satisfied with how much control I had over decisions made during my childbirth
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I am satisfied with the amount of drugs/medications I used during labor and delivery
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I am disappointed by my childbirth experience (*)
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- As a result of the labor and delivery experience. I feel I do not cope very well with pain (*)
    [1] Completely
    [2] Very much
    [3] Much
    [4] Little
    [5] Very little
    [6] Not at all
- I thought that the labor and delivery would be easier for me than they were (*)
    [1] Completely
    [2] Very much
    [3] Much

[4] Little
[5] Very little
[6] Not at all

- I did things during labor and delivery that I am now embarrassed by (*)
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- As a result of my childbirth experience I feel less self-confident (*)
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all

Satisfaction with Interaction with Spouse During Childbirth

- I felt my husband was aware of my needs during the childbirth experience
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- I felt emotionally close to my husband during labor
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- I think the experience of pregnancy has strengthened my relationship with my husband
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- I am worried that the baby will in some ways have a bad effect on my relationship with my husband (*)
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- I think the experience of labor has hurt my relationship with my husband (*)
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little
  [6] Not at all
- I feel that my husband was as helpful as he could have been during the childbirth experience
  [1] Completely
  [2] Very much
  [3] Much
  [4] Little
  [5] Very little

[6] Not at all

- I am satisfied with how my husband and I communicated during labor
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- I think the baby will have a good effect on our marriage
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all
- My husband is spending as much time as possibly can visiting me in the hospital
  - [1] Completely
  - [2] Very much
  - [3] Much
  - [4] Little
  - [5] Very little
  - [6] Not at all

(*) asterisked items were reverse-scored.

CHAPTER 5

THE ECONOMIC EVALUATION OF A COLORECTAL CANCER SCREENING PROGRAM IN THE PROVINCE OF FERRARA

Abstract[†]

Colorectal cancer (CRC) is one of the most common forms of cancer in western countries, and represents the second leading cause of cancer mortality in Europe (AIRT, 1998-2000). Early detection and removal of cancerous lesions can reduce the incidence of CRC, its mortality (Sonnenberg, 2000; Lieberman, 1995) and improve patients' quality of life (Taupin et al., 2006; Miles et al., 2006).

Aim of this work is to propose the results of a cost-effectiveness analysis of a screening program for the colorectal cancer prevention in Italy. We use as case-study the experience of a CRC screening program started in 2005 in the Province of Ferrara to determine the full cost of the screening program, compare the costs and the effectiveness of the adopted techniques (FOBT and colonoscopy).

A micro-costing analysis is used to identify and evaluate all the costs involved in each phase of the screening program, following an activity-based costing approach to consider all the activities done in the assistance process.

The effectiveness of the diagnostic instrument used, FOBT (faecal occult blood test) combined with colonoscopy, is valued in terms of early detected lesions and years of life gained.

The preliminary results show that, after the screening implementation, a huge number of new cases of hyperplasic polyps, dysplastic adenomas and carcinomas have been detected. Moreover, the early diagnosis allows the diagnosis of colorectal cancer at the earliest Dukes' stages.

Finally, we use the cost and effectiveness data collected to estimate the costs for year of life gained, using a Miscan Model.

[†] This chapter has been developed in collaboration with the Department of Economics, University of Ferrara, the University Hospital S.Anna in Ferrara and the Erasmus University in Rotterdam. It was partially supported by a research collaboration contract with the Department of Economics, University of Ferrara.

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1. Introduction

The economic evaluation of public healthcare programs and interventions is assuming an increasing role in the decision making process of public administrators. The healthcare context is becoming complex: the health care demand is increasing both in quantitative and qualitative terms and the public resources are scarcer. For this reason the policies adopted and the following decisional choices must be legitimated also from an economic perspective.

Economic evaluations of healthcare are considered a normal practice in many economic and political frameworks, but in the Italian context their diffusion is still limited. This aspect is reflected in the scientific literature, where the main studies are conducted in the American and English frameworks.

Aim of this work is to propose the results of a cost-effectiveness analysis of a screening program for the colorectal cancer prevention in Italy.

In particular we expose the case study of a screening program adopted in the Province of Ferrara, in Emilia Romagna Region.

After a short description of the colorectal cancer (CCR) characteristics, we describe the screening program implemented in the Province of Ferrara to prevent CCR and the methodology of data collection and analysis. In the second part we present some preliminary results of effectiveness in terms of incidence reduction and number of lesions detected. Finally, after a short description of the MISCAN (Microsimulation SCreening Analysis) model used to estimate the number of saved years of life with the screening program, we show the results of the cost-effectiveness analysis[1].

The results presented in this analysis required almost three years of research and can be considered complete and reliable for the cost analysis, whereas are still preliminary for the effectiveness analysis (the screening program is divided in more waves and we analyse only the first one, completed in 2007).

2. Colorectal cancer

Colorectal cancer (CCR) is one of the most common forms of cancer in Western Countries, representing the 11,3% of all men's cancer and 11,5% of all women's

[1]The Miscan Model simulation has been conducted by the Department of Public Health, at the Erasmus University Rotterdam by J.A. Wilshut.

cancer[2]. CCR represents the second cause of morbidity and mortality in each gender after breast and lung cancer, both in Europe and United States[3].

In European Countries almost 130.000 new cases of CCR and 90.000 deaths are registered every year; in Italy 37.600 new cases of CCR are diagnosed and 20.000 persons die for it every year[4].

More than 90% of cases are diagnosed in people over fifties, with a highest prevalence in male; in absence of risk factors, the probability of developing CCR after 50 years of age is 6%, whereas the probability of death is 2,5%.

In Emilia Romagna Region CCR represents some 14% of all cancer cases, with a mortality rate of 10,5% and 12,1% in males and females respectively[5].

In Ferrara Province, referral place of the study, since 1998 to 2002 almost 1.897 cases of CCR (of which 1.036 males and 861 females) have been observed: an incidence rate of 124,4 and 94,8 cases every 100.000, for males and females respectively.

The cancer prevalence in Ferrara, as calculated in January 2003, is 299 cases in one year, 1.054 in the 5 years before and 1.669 in the 10 years before.

CCR survival (for cohort of incidence), in the period 1995-1999, is 80% and 78% in the first year for male and female, and it increases for women in the following years: 65% in three years and 61% in the following five years, versus 64% and 55% for men. The survival in the following ten years is 53% for women and 45% for men.

According to the data mentioned so far, CCR can be considered the second cause of death for cancer after the lung cancer, and one of the big national emergencies, both in terms of social and economic costs.

In the National Health Plan 1998-2000 CCR has been considered as a priority in terms of intervention and with the National Oncology Plan of the Minister of Health new guidelines have been defined in order to counteract the incidence of this disease through specific prevention plans.

Theoretically, screening may reduce mortality in two ways. First, detection of an asymptomatic cancer in an early stage may result in an improvement in prognosis. Second, evidence exists that most colorectal cancers develop from adenomas and that

[2] AIRT data referred to 1998-2002.
[3] According to AIRT data, CCR represents the 10,4% of cancer deaths in men and 12,4% in women.
[4] In 2002 10.526 deaths have been registered for men and 9.529 for women respectively.
[5] In 1997, 1.800 new cases of colorectal cancer have been registered in men and 1.600 in women; an increment of 25,4% and 23,3% respectively compared to 1992; in 2002 the deaths from this disease have been 851 for men and 703 for women.

this process takes years. Detection and removal of adenomas may thus lead to prevention of cancer.

There are many risk factors to keep into account in the primary prevention and diagnosis: first, the fact of living in western countries, than the genetic and environmental factors, the alimentary behaviour, the life styles and the familiarity.

With refer to the last aspect, it has been estimated that the first degree relatives of patients with CCR, in absence of genetic alterations, have a risk of 2-3 times higher to develop the same cancer with respect to people without familiar history of the tumour[6]. The risk increases if more subjects of the same family have had the cancer, or if it developed before the fifties (Fletcher R., 2007).

Potentially useful screening test for colorectal cancer and its precursors are Faecal Occult Blood Test (FOBT), flexible sigmoidoscopy, barium enema (BE) and colonoscopy (CSCPY).

Randomised controlled trials of faecal occult blood testing have shown that screening can reduce CCR mortality (Mandel 1993, Hardcastle 1996, Kronborg 1996). Evidence on the effectiveness of screening test is well documented in literature.

FOBT reduces mortality of some 20% when executed annually (Ransohoff DF, 1997), flexible sigmoidoscopy reduces mortality of some 40% (Sonnenberg, 2000), while colonoscopy reduces mortality of some 75% (Sonnenberg et al., 2000, Winawer et al, 1993).

Evidence on the effectiveness of BE and endoscopic-based screening strategies, however is still limited, and the size of health benefits and costs is uncertain.

In few national contexts, such as the US, some studies were conducted to evaluate not only the effectiveness, but also the economic implications associated with the screening test. Sonnenberg et al. highlight the cost-effectiveness results among some alternative tests: the FOBT result is of almost $9.705 per year saved and some $11.382 per year saved for the colonoscopy.

Tappenden et al. (2007) refer that the use of flexible sigmoidoscopy, with or without FOBT, may generate a cost-effectiveness ratio close to £3.000 per year saved compared with a no-screening option. However, these studies are designed in specific national contexts, such as USA, thus are not comparable with the Italian one.

[6] A neoplasic familiarity for CCR is present in almost 20% of patients with intestine tumors.

In Italy, differently from other European Countries, the diffusion of this type of studies is limited, especially because of the lack of efficient informative systems in the local health organisations, which are not sufficiently developed for cost-analysis.
For this reason we need studies, applied to the National framework, to give a valid contribution to the knowledge of the cost-effectiveness of the screening programs.

2.1. The colorectal cancer screening program of the Health care Service of Emilia Romagna Region and the Province of Ferrara

2.1.1. Screening policy

The colorectal screening program presented in this study started in Emilia Romagna Region at the end of 2004[7]. In 2005 the program has been adopted by Local Health Organizations of the Province of Ferrara and it is still active.
Residents in Ferrara with an age of 50-69 years old, males and females, without a diagnosis for CCR, are invited every two years to have Faecal Occult Blood Test (unique sample) for free. The material used for the test (the kit) and the instruction to do the test are collected and delivered in a place defined by the LHO (pharmacies, district and local ambulatories).
If the test is negative (in absence of blood) the person receives the response at home by mail service and he/she is invited to repeat the test after two years.
If the test is positive (presence of blood) the person is called by phone to have a consultation with a clinician and invited for a colonoscopy.
Persons with an age between 70-74 years and those who have at least one relative of first degree affected by CCR are directly invited for a colonoscopy (without a previous FOBT) (Fletcher, 2005).
If the colonoscopy is negative, or if removed adenomas result negative after biopsy, patients are invited to repeat a FOBT after 5 years.
If preclinical invasive sections (polyps) or cancer in site are completely removed without residuals during colonoscopy, patient is invited to repeat colonoscopy every 3-5 years (it depends by the size and number of lesions).

[7] The target population of Emilia Romagna Region is almost one million people, residing in the Local Health Organizations (LHOs) of the Region.
The LOHs are Piacenza, Parma, Reggio Emilia, Modena, Bologna, Imola, Ferrara, Ravenna, Forlì, Cesena and Rimini.

If the colonoscopy is not sufficient to remove the neoplasic area, the patient is sent for a surgical operation. If the polyps or sections removed are positive for CCR, the patient is sent to chemotherapy.
The person is followed during all the diagnostic process and also during surgical and oncologic treatments and in the follow-up (Declan-Fleming RY., 1998).

2.2. Screening activities and compliance data

The screening program developed in Ferrara Province has been organized in more waves of invitations: this study refers to the first wave, started in 2005 and concluded in 2007.
The adoption of the Regional Plan in Ferrara required the constitution of a scientific and technical committee representative of all the professional figures involved in the program in the Local Health Organization and in the University Hospital. The committee has been defined in order to efficiently organise and manage the entire early diagnosis process and all the diagnostic and treatment activities of the program.
After the committee constitution, a population target has been defined and an operative protocol of the screening and monitoring activities has been set up.
In the meantime advertising activities have been implemented to encourage the population to participate to the program and to involve the general practitioners and the local media.
After this initial planning phase, a first operative phase began to invite the population to do a FOBT and to send the responses and the solicitations to non-responding persons.
The second level activity consists in the invasive diagnostic colonoscopy for persons with a positive FOBT, whereas the third level consists in the surgery activity to remove possible neoplasia and the oncologic treatments to treat the cancer.
A follow-up activity is reserved both for persons with a negative FOBT, and for persons that after colonoscopy have been diagnosed for preclinical cancer or CCR.
In Ferrara Province the person involved in the program are 99.207, 51.444 females and 44.763 males.

From the 21st March 2005, start day of the screening, to the 31st March 2007, in Ferrara Province more than 99.200 people (51.444 women and 47.763 men) have been invited to do a simple FOBT for free.

The compliance have been 49% and the almost 50.500 people have been invited again (tab.1). If we consider the persons invited but dead, emigrated, transferred or the persons excluded because they have had a recent test or diagnosis, the compliance percentage reaches the 52%.

Tab. 1 Screening program scenario: compliance at the first level

(1) Target population	**98.866**
* people of 50-69 years	
(3) Inesitated invitations	**3.183**
Anagrafic errors	30
Dead persons	1.732
Not documented diagnosis of CCR	271
Documented diagnosis of CCR	48
Emigrated	1.051
Unknown adress	2
Transferred	26
Other	23
(5) Respondents	**48.596**

(2) Invitations	**99.207**
* also people of age 49-70	
(4) Exluded after the invitation	**2.461**
not documented colonos. in the 5 years	6
documented colonoscpy	34
exams not done	20
recent FOBT not documented	383
definitive exclusion	786
FOBT in 5 years	495
Unknown adress	734
other reasons	3
(6) Compliance	
compliance percentage (5)/(2)	49,0%
adjusted compliance percentage (5)/(2-3)	50,6%
adjusted compliance percentage (5)/(2-3-4)	51,9%

Source: our elaboration

Almost 45.549 persons had a negative FOBT and have been invited to repeat the test after 2 years, whereas 3.045 tests were positive, almost the 6,3% of total (tab.2).

Tab. 2 Positive FOBTs

FIRST LEVEL DIAGNOSTIC INVESTIGATION	
(7) Number of persons examined	**48596**
(8) Number of persons with negative FOBT	45549
(9) Number of persons with positive FOBT	3045
(10) Number of inadequate FOBT	2
(11) Percentage of positives at the first level (9)/(7)	**6,27%**

Source: our elaboration of screening centre data

Patients with a positive test are invited to have a speech with a physician in order to evaluate the possibility to do a colonoscopy. The presence of faecal occult blood, in the most part of cases does not mean the presence of polyps or cancer lesions.

At the end of the first wave, in March 2007, almost the 76,5% of person with a positive FOBT have had a colonoscopy (tab 3). Individuals refusing a second level investigation are 21% of those with a positive FOBT, but part of them have already had a colonoscopy or a second FOBT, or are waiting for a check-up (tab. 3).

Tab. 3 Second level diagnostic investigations: compliance

SECOND LEVEL DIAGNOSTIC INVESTIGATIONS	
(12) Number of persons who did the second level exams	**2326**
(13) Number of persons who did not do the second level exams	**102**
exams not executed for..	1
definitive exclusion	5
waiting for a colonoscopy	68
refuse the visit	28
(14) Number of persons refusing further investigations	**646**
clisma with double contrast	1
documented colonoscopy	94
not indicated-possible side effects	6
exit from the program for CCR	8
FOBT in 2 years	72
FOBT in 5 years	9
check up in 12 months	4
check up in 36 months	2
check up in 60months	1
refuse further investigations	4
refuse of second level investigations	445
(15) Number of positives without a second level control	**7**
(16) Number of persons with an open report for second level inv.	**2967**
ENDOSCOPIC EXAMS	
(17) Number of persons with a first completed colonoscopy (reach ca	**1.990**
(18) Number of persons with an incomplete first colonoscopy	**305**
(19) that complete with a 2nd colonoscopy	54
(20) that complete with a BE-RX	85
(21) that completed with a BE-RX and a 2nd colonoscopy	13
(22) no completing	153
(23) Number of persons having only a BE-RX	**33**
Second Level compliance	
(24) Number of persons having at least a further investigation (17)+(18)+(23)	**2.328**
(25) Percentage of compliance in the second level (24)/(9)	**76,5%**

Source: our elaboration of screening centre data

The second level diagnostic tests are done in 5 different structures of the Ferrara Province health district: the endoscopic centre of the University Hospital of Ferrara, the hospitals of Argenta, Cento, Comacchio and Delta.

In tab. 4 we summarise the total number of colonoscopies done in Ferrara and Province, for each type of exam. The total number of exam differs from the number of

persons attending the second level diagnostic phase, because in some cases the first colonoscopy must be repeated and a patient can have more than one exam.

Tab. 4 Colonoscopies done in Ferrara and Province

COLONOSCOPIES	FERRARA CITY	PROVINCE	TOTAL
SIMPLE COMPLETE COLONOSCOPY (EXPLORATIVE)	318	420	738
COMPLETE COLONOSCOPY WITH BIOPSY	157	207	364
COMPLETE COLONOSCOPY WITH POLYPECTOMY	411	543	954
SIMPLE PARTIAL COLONOSCOPY (EXPLORATIVE)	70	130	200
PARTIAL COLONOSCOPY WITH BIOPSY	29	54	83
PARTIAL COLONOSCOPY WITH POLYPECTOMY	8	15	23
(26) ALL COLONOSCOPIES DONE	**993**	**1.369**	**2.362**

Source: our elaboration of screening centre data

Persons with negative colonoscopy are invited to repeat a FOBT after 5 years, otherwise the treatment differs with respect to the type of lesion.

The 10% of the patients which attended a second level diagnostic investigation have been invited to surgery, and the 83% of them have been operated (tab 5).

The surgical treatment for the resection of the neoplasic area, have been done in almost 186 patients, of which the 16,7% to the descending colon, 17,2% to the ascending colon, the 4,8% to transverse colon, 27% to sigmoid-rectum and the 29% had a sigmoidectomy.

Tab. 5 Third level compliance and type of surgical interventions

THIRD LEVEL	
(27) Persons invited for a surgical intervention	225
(28) Persons having the intervention	186
(29) Compliance (28)/(27)	82,7%

TYPE OF SURGICAL INTERVENTION	FERRARA CITY	PROVINCE	TOTAL	%
a. total colectomy	1	0	1	*0,5%*
b. transverse colectomy	3	6	9	*4,8%*
c. right emicoloectomy (ascendent colon)	13	19	32	*17,2%*
d. left emicolectmy (descending colon)	9	22	31	*16,7%*
e. segmentary resection	1	2	3	*1,6%*
f. sigma anterior resection	25	25	50	*26,9%*
g. sigmoidectomy	26	28	54	*29,0%*
h. intervention done, unknown type	1	5	6	*3,2%*
(30) TOTAL SURGICAL INTERVENTIONS	**79**	**107**	**186**	
i. persons not having intervention	26		54	
l. not known if the person did an intervention	0		2	
TREATED PATIENTS	**105**	**137**	**242**	

Source: our elaboration of screening centre data

With the second level investigations, colonoscopies and surgery, 204 cancers were detected, 533 low risk adenomas, 552 advanced adenomas and 66 cancerized adenomas (tab.6).

Tab. 6 Lesions detected with the second level diagnostic investigation and surgery

LESIONS	*centro screening center data*	*surgically treated*
cancer	*204*	*117*
low risk adenomas	*533*	
advanced adenomas	*552*	*31*
cancerised adenomas	*66*	*33*
unknown		
TIS (tumor in situ)		
TOTAL	***1355***	***181***

Source: our elaboration of screening centre data

According to the Dukes' stages (Dukes, 1932), 116 CCR were in stage A, 34 in stage B, 42 in stage C and 6 in the most advanced stage D. Cancer in stage zero were 41 and 3 were not identified (tab. 7).

Tab. 7 Dukes' stages of lesions and cancer detected

DUKES STAGES	**RECTUS**	**COLON**	**TOTAL**
STAGE 0	2	**39**	**41**
STAGE A-B not at risk	4	**112**	**116**
STAGE B at risk	1	**33**	**34**
STAGE C	0	**42**	**42**
STAGE D		**6**	**6**
UNKNOWN		**3**	**3**
TOTAL	**7**	**235**	**242**

Source: our elaboration of screening centre data

All the patients with CCR in Duke's stage B at risk, stage C and stage D have been treated with chemotherapy.

3. Methods

3.1. Cost analysis

The cost evaluation of the screening program have been done using a *micro-costing analysis,* with the identification, measurement and detailed evaluation of the single cost elements involved in the process. This methodology, although laborious and less generalizible if compared to a *gross-costing analysis*, gives a higher and specific insight of the relation between the characteristics of each activity and its cost (Brouwer W., Rutten F., Koopmanschap M., 2001).

To this aim, the screening program process has been divided in macro-activities (fig. 1):

1. activities of first level:
    a. adoption of the Regional program, organization and coordination of the province program;
    b. advertising and promotion of the program among the population to increase the compliance;
    c. management of the invitations;
    d. distribution, collection and laboratory analysis of FOBTs;
2. activities of second level:
    a. colonoscopy and RX exams for the positive FOBT;
3. activities of third level, therapeutic activities:
    a. endoscopic therapy;
    b. surgery;
    c. chemo-radio therapy;
4. follow-up process:
    a. follow up for the patients with negative FOBT, or colonoscopy;
    b. follow up for patients treated with chemo-therapy.

For each macro activity we identified all the single activities done and the resources involved. The individuation and measurement of each single cost item has been done through direct measurement and/or interviews with the hospital staff.

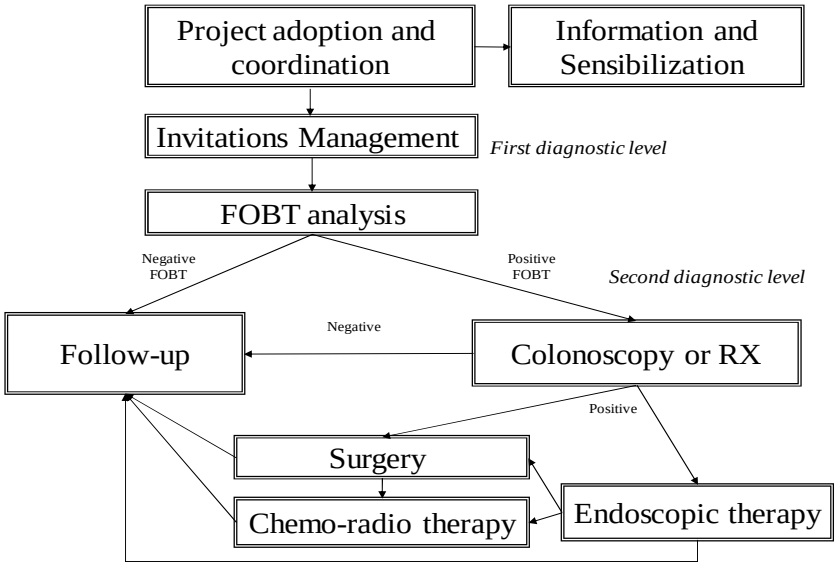
The only cost element for which we decided to use the value provided by the Planning and Control Unit of the hospital is the daily cost of hospitalisation, for which the

micro-costing analysis would have been too expensive in term of time and effort with refer to the study aim.

For the same reason we used the regional tariffs for the evaluation of the laboratory analysis, because the informative system of the hospital is not sufficiently developed to provide significant data of the costs born in the laboratory units for each type of test.

For each macro activity we highlight the *variable costs*, which vary with the volume of compliance to the screening program, and the *rising costs*, born only after the program implementation and that would not be born in absence of screening program.

Fig. 1 Macro-activities of the CCR cancer screening program



Source: our elaboration

3.2. Methods of evaluation of each cost item

3.2.1. Human resources

The human resources cost have been valued considering the effective time spent by each professional figure in all the activities involved in the screening program.

For all the macro-activities mentioned before, we identified the professional figures involved and their effort in term of work hours[8].

The measurement of the time spent in each activity was done directly or through interviews, as physician and nurses are involved in different ways in the activities of endoscopic diagnosis, surgery and hospitalisation.

[8] In some cases, for specific activities we were able to identify the exact name of the person involved and thus use his/her salary cost for the economic evaluation.

The technician and administrative staff were more involved in the management and coordination activities, whereas the physicians were dedicated to the diagnostic and treatment activities. Part of the clinician was also involved in professional training and development, so part of their time have also be dedicated to periodical meetings of the management phase of the program.

The evaluation of the human resources has been done using the average cost for hour[9] of each professional category (senior doctors, manager doctors of complex or simple units, physicians, manager or professional nurses, technicians).

With respect to the study aim and according to the main literature (Amaduzzi, 1973, Matz A., Curry O.J., Franck G.W. 1978, Selleri, 1984, Santesso E., 1987), we considered an average cost for hour that considers the part of fix salary, the social expenses, and the variable items referred to extraordinary work or managerial responsibility charge.

3.2.2. Health materials and pharmaceuticals

The health material consists in health items and drugs used during the diagnostic tests, the surgical interventions and the oncologic treatments.

The economic evaluation of pharmaceuticals and health materials has been done through the individuation of the average consumption for each patient using the purchasing cost of the hospital pharmacy for the costing evaluation.

3.2.3. Health instruments

The cost of instruments has been evaluated using the purchasing cost of each item, calculating the utilization for the screening program. Some instruments have been appositely purchased for the screening program and they are exclusively used for the screening activities, so their cost can be entirely spread over the volume of patients examined. For all the instruments already used in the hospital before the screening implementation, the costs have been calculated using the amortization quotes.

[9] The cost is the average cost for single professional figure, provided by the human resources unit of the hospital, referred to 2005-2007; the cost considers both the national collective work contracts in different areas, and the integrative collective work contracts in the specific organization.

4. Cost analysis results for each macro-activity of the screening program

4.1. First level activities

4.1.1. Adoption, implementation and organization of the screening program

The adoption of the Regional screening program in Ferrara required the constitution of a scientific interdisciplinary committee to represent all the professional figures involved in the program, both with the Local health organization and the University Hospital. The committee was responsible of the efficient management and organization of all the screening process.

In this phase almost 18 persons (doctors, nurses, statisticians, epidemiologists, and hospital directors) were involved to detect the target population to be invited, and to set up a protocol for planning and monitoring the screening activities. Informative and advertising activities have been implemented during this phase to publish the plan and to involve the general practitioners and the local media.

Some of the activities were repeated monthly, others were done only once for the first two years of screening.

Data concerning the activities done, i.e. the meetings and training, the person involved and the time spent by each person, were provided by the screening centre[10].

The total cost of this phase was € 122.729,00 (tab.8).

4.1.2. Informative and sensibilization activities

During this phase the scientific committee was involved in clinical meetings, professional training courses, Regional and Provincial meetings, and conferences, informative and advertising activities through journals, media and telecommunication networks. The economic evaluation of these activities has been done using the information provided by the screening centre.

For the first years, the total cost of these activities was almost € 38.362,00 for human resources and materials (tab.8).

[10] The screening centre record all the activities done, the meetings, the person involved and the times.

4.1.3. Organization and management activities

This phase consists of all the activities done to manage the target population: acquisition and maintenance of specific software to select the persons to be invited for the FOBT and to send the recalls for those not participating at the first call.

The cost of the software for the first two years was almost € 36.650,00.

The cost for the invitation letters, recall letters and telephonic calls for the first wave was almost € 196.000,00.

In the two years the organization and management activities absorbed human and material resources for almost € 233.000,00 (tab.8).

4.1.4. Faecal Occult Blood Tests

For this first diagnostic phase a full-time biologist has been appositely recruited to analyse the tests of the program for €19.200,99 (tab.8). A part-time delivery man was recruited to collect the tests samples every day for € 18.763,20. The total cost for human resources in this phase is almost € 38.000,00 for the first two years.

For the FOBT analysis are used two instruments OC sensor of the Alfa Wasserman Society, on loan, a reagents furniture and a control kit, for a total cost € 209.181,00 in the two years. The material cost for the FOBT results to be sent at home by mail was almost € 25.000,00. On average a single FOBT costs € 5,00 per person.

Tab. 8 Total cost for the first level of activities

Project planning and implementation	€	122.729,30
Information activities-Advertising	€	38.362,20
Management activities	€	232.548,12
FOBT		
(1) fixed costs (kit reagent)	€	209.181,60
(2) byologist cost	€	19.200,00
(3) transport costs	€	18.763,20
(4) refert. POSITIVES	€	23.231,01
(5) refert. NEGATIVES	€	60,90
(6) telephonic calls	€	1.218,00
TOTAL	**€**	**271.654,71**
TOTAL COSTS FOR THE FIRST LEVEL OF ACTIVITIES	**€**	**665.294,33**

Source: our elaboration

4.2. Second level diagnostic activities

Individuals with a positive FOBT result are invited for a consultation with a physician, to evaluate the possibility to have a second level diagnostic exam. An endoscopist have a talk with the eligible patient for almost 10-15 minutes, during which he must explain the potential benefits and risks of a colonoscopy and try to reassure the person. The cost of the visit, almost €11,00 for patient, is entirely represented by the time spent by the doctor to see the patient, as any other material is involved. At the end of the first two years almost € 34.081,00 have been spent during this phase (tab. 10).

4.2.1. The endoscopic activity

The second level diagnosis is generally done with an endoscopic exam. For the study we did the economic evaluation of different type of endoscopic exams: a simple colonoscopy (when the investigation does not require biopsy or therapy), a colonoscopy with biopsy when a section of the damaged area is selected and removed to be sent for further investigation, a polypectomy if one or more polyps are detected and removed. All these examinations are "complete", if the colonoscopy reaches the caecum, or "partial" (incomplete) otherwise.

The endoscopic exams require different professional figures: an endoscopist, a nurse, a technician, a managerial nurse and an administrative person. Complete and partial colonoscopies have a different length, thus the cost of human resources can vary for each type of colonoscopy as the time required can differ with refer to the type of exam.

The colonoscopy requires a preparation therapy to clean the colon: the oral assumption of 8 bags of Isocolan costs less of € 2,00 per person. The colonoscopy is an invasive endoscopic exam that can often cause pain, therefore some sedative drugs are used during the investigation (Atrophine, Morphine, Midazolan and Ultiva), for a total cost of € 3,52 for person.

During the endoscopic exams different instruments are used, such as flexible endoscopes, borescopes, monitors, those total annual cost (almost € 100.000,00) can be amortized over almost 6.500 endoscopic exams, for a unitary cost of € 15,39.

The materials used during the endoscopic exam (endoscopic equipment, flexible tubes, pliers, lubricant gel, linen, towels) cost almost € 38,26 for a simple colonoscopy, € 46,79 for a colonoscopy with biopsy and € 69,36 for a polypectomy.

On average a simple complete colonoscopy costs € 171,00 (€ 140,00 if partial), a complete colonoscopy with biopsy costs € 179,00 (€ 171,00 for a partial one), a colonoscopy with polypectomy costs up to € 232,00 (€ 149 if partial) (tab.9)[11].
The costs for endoscopic exams done in the first wave are almost € 465.000,00 (tab.10).

Tab. 9 Costs of each colonoscopy

Type of colonoscopy	Cost
Complete colonoscopy (only explorative)	€ 171,00
Complete colonoscopy with biopsy	€ 179,53
Complete colonoscopy with polypectomy	€ 232,10
Partial colonoscopy (only explorative)	€ 140,54
Partial colonoscopy with biopsy	€ 171,64
Partial colonoscopy with polypectomy	€ 149,07

Source: our elaboration

Tab. 10 Costs for the second level activities

SECOND LEVEL ACTIVITIES		
TEL.SPEECH AND FIRST VISIT	**€**	**34.081,16**
Endoscopic Investigations		
colonoscopy preparation	€	4.166,57
colonoscopy total (a)	€	458.754,05
emost. & tatoos	€	92,20
refert and results+call of NEGATIVES	€	1.630,43
TOTAL	**€**	**464.643,25**
TOTAL COSTS FOR THE SECOND LEVEL	**€**	**498.724,41**

Source: our elaboration

4.2.2. Complications of endoscopic exams

The endoscopic exam is an invasive investigation and sometimes it can have some complications. During the screening some immediate and latest complications have been registered, such as blooding or perforations.
As shown in the table 11, the most frequent cases of complication are represented by immediate blooding or vago-vagals, but generally complications are rare.

[11] The costs calculated in our study confirm the results of an Italian study conducted to evaluate the cost of endoscopic investigations. Rossi G, Battaglia G., Brunati S et al (2004) "Determination of the costs of digestive and endoscopic investigations" (in Italian), Gestione.

The costs of these complications have been evaluated in the second level diagnostic investigations and are included in the cost of the endoscopic exams (se the voice emostasi & tattoos in tab.10).

Tab. 11 Immediate and latest complications of colonoscopy

Immediate complications	Latest complications	Number of persons examined	Percentage %
1 - Vago-vagals	9 - Any complication	15	0,65%
2 - Blooding	9 - Any complication	20	0,87%
3 - Perforation	2 - Perforation	1	0,04%
5 - Other	4 - To be valued	1	0,04%
	9 -Any	3	0,13%
9- Any complication	1 - Blooding	2	0,09%
	4 - to be valued	5	0,22%
	9 - Any complication	2247	97,95%

Source: our elaboration

4.3. Third level activities

4.3.1. Surgery

Surgical treatments to remove the neoplasic area, have been done in almost 186 patients, of which the 16,7% to the descending colon, 17,2% to the ascending colon, the 4,8% to transversal colon, 27% to sigma-rectus and the 29% had a sigmoidectomy.
The activities of preparation for the surgical intervention, the operation, and the post-surgery activities require an anaesthetist, two surgeons, two specialized doctors, two nurses, two surgery technicians, a unit nurse manager and a technician, for a total average cost of € 860,90 for patient.
During the surgical operation anaesthetics and curars are used, for a total average cost of € 153,00 for patient.
The material used during the intervention consists in anaesthetic material (syringes, catheters, tubes and pumps) and surgical material (scalpels, surgical kit, sterilizers, suture kit). The cost for the suture threads differs with refer to the part of colon involved in the operation: the surgical intervention to the descending colon is more expensive if compared to the same intervention practiced to the ascending colon and it costs almost € 547,82 more.

The material for a surgical intervention costs almost € 1.086,00 for patient. For the 186 patients surgically treated the hospital spent almost € 1.523.000,00.
On average, the total cost for a surgical intervention is € 2.334,00 for each patient, but it can vary from € 2.060,00 to operate the ascending of colon, and € 2.608,00 for the descending colon (tab.12)[12].

4.3.2. Hospitalisation for surgical intervention

The surgical intervention is usually done in ordinary regime of hospitalisation and the patients stay in hospital for about 7 days. During the hospitalisation the patient is assisted by clinicians and nurses of the unit with different frequencies. On average the health care assistance in terms of human resources is € 71,95 every day. The pharmacological therapy (antibiotics, antiemetics, vitamins, fans, inhibitors, rehidratant solutions) has an average cost of almost € 164,00 for the entire period.
For each treated patient a week of hospitalisation costs on average €2.097,00 (tab. 12).
For the first two years of screening, the total cost for the surgical treatment of all the 186 patients, including the hospitalisation costs, was almost € 823.000,00.

Tab. 12 Surgery costs

THIRD LEVEL ACTIVITIES		
SURGICAL TREATMENT (unit patient)		
surgical intervention (human resources and material)	€	1.989,04
anestesia	€	231,06
general costs	€	114,51
TOTAL	**€**	**2.334,61**
TOTAL COST of SURGICAL INTERVENTIONS	**€**	**433.142,56**
IN-STAY (average of 7 days)	**€**	**2.096,69**
TOTAL IN STAY for all patients	**€**	**389.984,95**
SURGERY (intervention + in stay) (one patient)	**€**	**4.431,31**
SURGERY (intervention + in stay)	**€**	**823.127,52**

Source: our elaboration

[12] These results are quite similar to the Regional DRGs tariffs used to reimburse hospitals for the same intervention, but the tariffs do not distinguish the costs of the surgical operation for the ascending or descending colon.

4.3.3. Anatomo-pathology investigations

After an endoscopic exam or a surgical operation part of the area detected during the investigation can be sent to the anatomo-pathologic laboratory for a morphologic-byoptic analysis.

As the evaluation of the real cost of single exam of anatomy was too expensive for the aim of the study, we decided to use the costs provided by the anatomo-pathologic unit, that represent the material costs weighted by the effective number of hours worked (units of professional figures involved).

In tab.13 we synthesize the costs of each anatomo-pathological investigation, reporting the number of person involved.

Tab. 13 Costs of anatomo-pahological exams

Anatomo-pathological exams	***unit***	***costs***
Endoscopic biopsy of colon (unique site)	1	€ 21,00
Endoscopic biopsy of colon (multiple sites)	3	€ 70,00
Total colon colectomy	3	€ 240,15
Colon hemicolectomy with linfoadenectomy	5	€ 240,15
Colon polypectomy (multiple sites)	1	€ 21,00
Colon polypectomy (unique site)	3	€ 70,00
Segmental resection of colon	4	€ 171,22

Source: anatomopathologic unit data

Considering the frequencies of each type of investigation done, and applying the single costs to the total number of exams, the total cost of the anatomopathologic exams for the first wave is € 27.000,00.

4.3.4. Oncologic treatments

After the surgical intervention, patients with lesions or cancer have an oncologic visit to define the most appropriate therapy with respect to the cancer localization (if colon or rectus) the cancer stage and their general health conditions.

In table 14 we describe the type of treatments practiced for CCR for each type of cancer stage.

Patients with polyps (or patients who had a polypectomy) but without cancer, do not require an oncologic therapy, but are sent for a visit to the gastroenterologist.

Patients with a colon cancer in Dukes' stage A or B, but not at risk of further cancer development, are not treated but invited for a follow-up.

Patients with colon cancer in Dukes' stage B (not at risk) or stage C are treated with oxaliplatin, levofolinate and fluorouracil (Folfox therapy) in 12 administrations for at least 3-6 months if there are no co-morbidities, otherwise they are treated with capacitabine (Cap), administered in 8 cycles, for 6 months.

Tab. 14 Oncologic treatments for the CCR

DUKES STAGE	**COLON CANCER**
Polyps	Sent to gastroentoerologis without therapy
A and B not at risk	No therapy- Follow up
B at risk and C, without comorbidities	Folfox (6 cycles)
B at risk and C, with comorbidities	Capecitabina (8 cycles)
D I line	Folfiri+Bevaciz. (3 months)
D II line	Folfiri+Cetuximab (3 months) CPT-CET (3 months) Folfox (3 months)
D III line	Fumit-Mitomicina (3 months)
D with comorbidities	Capox (3 months) Fufaset (3 months)

DUKES STAGE	**RECTUS CANCER**
A and B not at risk	No therapy- Follow up
not surgically operated, no comorbidities not surgically operated, with comorbidities (or refuses infusor)	Fluorororacil + RT (35 days) Capecitabine + RT (5 weeks)
B surgically operated	DeGramont(2months)+5FU+RT+ DeGramont (2 months)
C	Folfox (2 months)+FU-IC+ RT+ Folfox (2 months)

Source: our elaboration of oncological guidelines data and information provided by the hospital oncologist (Dr. Marzola)

Patients with a colon cancer in the most advanced stages, Dukes'stage D, but still in good health status and without co-morbidities, are treated with different type of therapies till the most effective is found.

The first line treatment consists in a combination therapy of irinotecan, levofolinate, fluorouracil and bevacizumab (Folfiri+Bevacizumab) administred for at least 3 months, after which diagnostic exams are done to verify if the treatment is effective or not. If the patient reacts positively and there is evidence of a cancer regression, the therapy is administered for other 3 months, till the new exams.

If the first line treatment doesn't seem to be effective, the patient is treated with a second line treatment of Irinotecan and Cetuximab (Cpt-Cet), or with Folfox. If also this therapy is not effective, the patient is treated for other 3 months with a third line therapy of mitomycin and fluorouracil (Fumit). Old patients with cancer in Dukes's stage D and patients with comorbidity in the same stage are treated with capacitabine and oxaliplatin (Capox) for three months, or with folinic acid and fluorouracil (Fufaset).

For the rectum cancer the oncologic therapy can be done before the surgical intervention to conserve the sphincter. The therapy consists of continuous infusion of fluorouracil and radiotherapy for 35 days for patients without comorbidities, whereas patients with comorbidities or refusing the infuser are treated with Capacetabine and radiotherapy for 5 days a week for 5 weeks.

Patients with rectum cancer in Dukes'stage B are treated for 2 months with DeGramont therapy for 4 cycles, followed by a cycle of fluorouracil (5-FU) and other 2 months of DeGramont therapy.

Some oncologic therapies must be administered through a Groshong or Port central venous catheter, whose placement is done in surgery regime with the aim of local anaesthesia.

After the oncologic treatment patients enter in a specific follow-up scheme, with periodical check up every six month for the next three years.

Patients treated for colorectal cancer must have blood analysis and an abdominal ecography every six months and a colonoscopy every three years, and if treated for rectus cancer they also have a proctologic visit every 4-6 months and an optional thoracic Rx one a year for 2 years.

4.3.4.1 Cost evaluation of oncologic treatments

We analysed the cost of each oncologic therapy through the individuation and evaluation of all the activities done, the human resourced employed, the time required by each in every single activity, the therapeutical principles required (type and quantity) and the material used.[13]

[13] The identification of each therapy has been done with the aim of an oncologist. The cost data were provided by the hospital pharmacy.

During the oncologic therapy an oncologist is involved for the first visits, the follow-up and the therapy prescription, a nurse is involved for the preparation and the administration of the drugs and an administrative person is involved in the clinical record opening.

The human resources cost can vary between € 24,00 for a simple visit and check up to € 300,00 for the oncologic treatment of a person with CCR in Duke stage D.

The costs of materials and pharmaceuticals for the oncologic treatment differ with the type of adopted therapy. Each therapy consists in specific drugs utilization those quantities vary with the patient's characteristics (age, weight and height) and the treatment length. This cost can vary from a minimum of € 290,00 for a Fumit therapy, up to more than € 13.400,00 for a Cpt-Cet therapy.

Some oncologic therapies must be administered through a Groshong or Port central venous catheter, whose placement is done in surgery regime with the aim of local anaesthesia.

The economic evaluation of Groshong and Port catheters has been done separately because of the different material cost (the Groshong kit costs almost double) and the different placement procedures: the Port one must be removed in surgery room in the same times and with the same materials used during the placement, whereas the Groshong can be removed by a physician in ambulatory room and in less time.

On average the placement and removal of a Port catheter cost € 270,00, whereas the Groshong cost more than € 300,00.

Unitary costs of the oncologic therapies and total costs.

In tab 15 we summarize the costs of each therapy for the oncologic treatment of a single patient with an average body mass of 70 kilos of weight and 170 cms of height.

Almost € 311.263,00 have been born for the oncologic treatment of all the patients with colorectal cancer (tab.15).

4.3.5. Radiotherapy

Some chemotherapy treatments must be combined with radiotherapy.

Usually, a patient does 25 cycles or radiotherapy, in which a radiotherapist, a nurse, two technicians, an administrative and a physics are involved for an average total cost of € 788,00 for patient. The material used consists in radiographic films and papers for € 1,18 for patients. During the therapy florouracil is used for € 57,00.

The total cost to treat a patient is almost € 875,00. At present, only one patient has been treated with radio-therapy.

Tab. 15 Costs of oncologic treatments for each Dukes' stage of CCR

COLON TREATMENTS	NUMBER OF PATIENTS	COST FOR PATIENT	TOTAL COSTS
Polyps		€ 23,62	
A and B not at risk	112	€ 23,62	€ 2.644,97
B at risk and C, without comorbidities			
Folfox (6 cycles)	33	€ 4.496,42	€ 148.381,87
B at risk and C, with comorbidities			
Capecitabina (8 cycles)	42	€ 3.383,16	€ 142.092,84
D I line			
Folfiri+Bevaciz. (3 months)	6	€ 2.882,81	€ 17.296,83
D II line			
Folfiri+Cetuximab (3 months)		€ 11.082,03	
CPT-CET (3 months)		€ 13.949,69	
Folfox (3 months)		€ 4.496,42	
D III line			
Fumit-Mitomicina (3 months)		€ 772,95	
D with comorbidities			
Capox (3 months)		€ 5.023,81	
Fufaset (3 months)		€ 863,92	
RECTUM TREATMENTS	**NUMBER OF PATIENTS**	**COST FOR PATIENT**	**TOTAL COSTS**
A and B not at risk	4	€ 23,62	€ 94,46
not surgically operated, no comorbidities			
Fluoruroracil + RT (35 days)	1	€ 752,84	€ 752,84
not surgically operated, with comorbidites (refuses infusor)			
Capecitabine + RT (5 weeks)		€ 864,46	
B surgically operated			
DeGramont+5FU+RT+DeGramont			
C stage			
Folfox+FU-IC+RT+Folfox		€ 4.496,42	

Source: our elaboration

4.3.6. Nutritional therapy

In rare cases patients require a nutritional therapy of support if they have had an abdominal failure at the peritoneum: in case of metastasis the intestine can be blocked and the patient is not able to feed anymore.

An oncologist sees these patients and, if necessary, a nutritional doctor can be consulted to make a more precise evaluation. The visit takes for 30 to 45 minutes and can be followed by other diagnostic exams.

The nutritional therapy can be done for parental way (intravenously) or enteral way (through the gastrointestinal tract, nasogastric).

Specific guidelines establish in which cases the nutritional therapy must be practice and which patients are the most eligible: patients should have at least a residual expected life time of 2-3 months; patients with less than 2 month of life are just rehydrated with electrolytic solution.

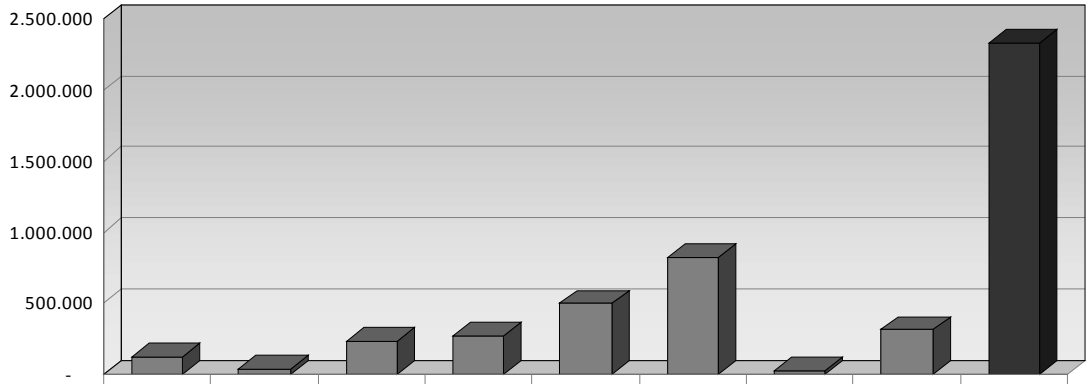
The nutritional therapy requires the insertion of a central venous catheter[14] and a minimum period of hospitalisation is required to monitor their health conditions.

At present any of the patients of the first wave have been treated with a nutritional therapy. The cost for the treatment of a single patient with an average expected life of 3 months is almost € 1.636,70.

5. Total costs, rising costs and variable costs for each activity

In figure 2 we show the total costs for each macro-activity at the end of the two years: the screening program has absorbed resources for almost € 2.326.000.

Fig. 2 Total cost of each level of activity



Source: our elaboration

[14] The catheters mainly used are:

- Central venous catheter (short term) in polyurethane, as the Arrow catheter: used for patients with a short expected life and embedded. It can be applied with local anesthesia by a doctor in ambulatory, or in surgery room. It requires the hospitalization in ordinary regime and a Rx. The support nutrition is done with specific nutrient solutions sacks: one sack is administered every day till death.
- Central venous catheter (long term): Groshong or Port, already inserted for the chemotherapy.

For each activity we also highlight the volume of activity (number of invitations, number of exams, number of patients treated) and the unitary cost for each activity (tab.16)

Tab. 16 Cost for each activity, volumes and unitary cost for patient

Activity	Total Cost	Overall activity	Unitary costs*
Adoption and coordination	€ 122.729,30	99.207 invited	€ 2,53
Information activity	€ 38.362,20	99.207 invited	€ 0,79
Management	€ 232.548,12	99.207 invited	€ 4,79
FOBT	€ 271.654,71	48.596 tests	€ 5,59
Second Level-Colonoscopy	€ 498.724,41	2.362 exams	€ 211,14
Surgery	€ 823.127,52	186 patients	€ 4.425,42
Anatomo pathology	€ 26.787,61		
Chemo-radio therapy	€ 312.138,94	198 patients	€ 1.576,46

*the unitary cost has been calculated over the total number of patients entering the screening
Source: our elaboration

We also consider the rising costs born after the project implementation and that would not have been spent otherwise (tab 17). For example, the recruitment of a dedicated person for the activities involved in the screening program can be considered a rising cost, whereas the cost of the staff already employed for the same activities is not a rising cost because included in the ordinary activities of the organization.

The cost of the management activities is rising for the 98%, because the software to manage the target population has been purchased appositely for the screening activity and the human resource implied have been recruited to do only this specific job.

In the rising costs are also included the costs for the materials and the delivery of the invitation letters and responses.

All the activity of first level, the FOBT tests, are rising costs, because the laboratory materials have been purchased for the screening program and the laboratory technician has been recruited exclusively for this activity.

The second level activities of endoscopic diagnosis lead to rising costs only for the 28%, represented for the main part by materials, as the health personal involved is already employed in this activities, independently from the screening project. For the same reason the cost of surgery is rising only for the 50%, for the materials and pharmaceuticals consumption.

The costs for the oncologic treatments are rising costs for almost the 94%, as the human resources are marginally involved, whereas the main part of the cost is represented by the therapies, the drugs and the diagnostic tests linked to the therapies.

We also consider the variable component of the costs related to the number of person who participate to the screening program. For example, the costs for the management of the population, the invitations and referrals delivery, the FOBT costs (but not the biologist cost), the first visits are all variable costs because they depend by the number of patients involved. The costs for endoscopic investigations and surgery interventions are variable only for the human resources, the materials and pharmaceuticals involved, but not for the cost of instruments and rooms used, because these costs do not depend by the volume of patients.

The total cost of the screening program is represented by the 69% by rising costs and by the 51% by variable costs.

Tab. 17 Total costs for the first two years of program, rising costs and variable costs

MACRO ACTIVITIES	Total costs	Rising costs	Variable costs
Program adoption and coordination	€ 122.729,30	€ 26.133,10	€ -
Information activities	€ 38.362,20	€ 36.441,00	€ -
Management activities	€ 232.548,12	€ 227.401,20	€ 74.539,36
Test FOBT (RSO)	€ 271.654,71	€ 271.654,71	€ 24.509,91
Speech and first visit for positives	€ 34.081,16	€ 34.081,16	€ 34.081,16
Second level exams (colonoscopies)	€ 464.643,25	€ 80.018,17	€ 186.805,35
Surgical intervention and hospitalisation	€ 823.127,52	€ 823.127,52	€ 823.127,52
Anatomopathology	€ 26.787,61	€ 26.787,61	€ 26.787,61
Oncologic Treatment	€ 311.263,81	€ 295.235,83	€ 311.263,81
TOTAL COSTS	**€ 2.326.072,80**	**€ 1.282.528,77**	**€ 1.455.202,24**

Source: our elaboration

6. Effectiveness analysis

In the cost-effectiveness analysis is extremely important to define the term "effectiveness", as the ability to positively change the natural history of the disease.

Measure of effectiveness can be represented by the number of early detective cases, by the incidence reduction, the prevention of malignant neoplasia through early treatment, the percentage of avoided deaths, the number of lives saved, the number of life years saved, the improvement of the quality of life after early diagnosis and treatment.

The effectiveness analysis can be referred to the following measures:

- Measurement of the expected and observed mortality;
- Analysis of the incidence, and the reduction of frequency of the disease;

- Analysis of the reduction in mortality rates or reduction of the side lethal effects deriving by the appearance of the disease.

The effectiveness of a screening can be valued through experimental and non experimental methods, as observational studies.

The most reliable experimental studies are the randomised and controlled clinical studies, where two populations are compared, one included in the screening program and the other, not included, used as control, in order to evaluate the incidence and mortality reduction through a cancer register. These studies are generally very expensive both in terms of economic resources and time, but they allow for a higher effectiveness measure as they are free from statistic confounding factors.

Other experimental studies, such as cohort studies, case control studies or correlation studies, are less expensive but more subjected to distortions due to confounding factors, and for this reason they do not provide reliable effectiveness results.

In this study we provide only preliminary results of the screening effectiveness, as the effects of the program in terms of incidence and mortality reduction will be available in the long term. It will take at least a couple of years to collect all the definitive outcome data to get significant effectiveness results. These results will contribute to compare the results in terms of cost-effectiveness of the screening program with the situation pre-screening in absence of program. The results will also contribute to confirm the literature data and to increase the knowledge of this subject in the Italian framework.

6.1. Evidence of FOBT effectiveness

The effectiveness of the FOBT in terms of incidence and mortality reduction are highly documented.

In 1993, a randomised controlled trial in Minnesota showed, after 13 years of follow-up, that annual faecal occult blood testing was effective in reducing colorectal cancer mortality by at least 33% (tab. 18). Biennial screening (i.e., every 2 years) resulted in only a 6% mortality reduction (Mandel, 1993). Two European trials (in England and in Denmark) subsequently showed statistically significant 15% and 18% mortality reductions with biennial screening(Kronborg, 1996; Hardcastel, 1996).

In 1999, Mandel et al provided updated results —through 18 years of follow-up— from the Minnesota trial that address the apparent inconsistent findings among the trials regarding biennial screening. The results from this study, together with the other two published randomised trials of faecal occult blood screening, are consistent in demonstrating a substantial, statistically significant reduction of 21% in colorectal cancer mortality from biennial screening (Mandel, 1999).

Tab. 18 Randomized clinical data of FOBT effectiveness in mortality reduction

RANDOMIZED CLINICAL DATA OF FOBT EFFECTIVENESS				
Author, country, year	Rehydration	Interval	Compliance	Mortality reduction %
Mandel, USA 1993	yes(83%)	Annual	90%	33%
Mandel, USA 1999	yes (83%)	Biennal	90%	21%
Kronborg, DK 1996	No	Biennal	67%	18%
Hardcastle, UK 1996	No	Biennal	59,6%	15%

Source: our elaboration

Non-randomised studies or case-control studies show the effects of FOBT on mortality reduction from colorectal cancer between 8% and 57% (tab. 19).

Tab. 19 Case-control studies of FOBT effectiveness in mortality reduction

CASE CONTROL STUDIES OF FOBT EFFECTIVENESS		
Author, year	Country	Mortality reduction %
Selby et al., 1993	USA	31%
Wahrendolf et al., 1993	Germany	Male 8% Female 47%
Lazovich et al., 1995	USA	28%
Salto et al., 1995	Japan	47%
Zappa e altri 1997	Italy	39%

Source: our elaboration

The effectiveness of FOBT has been object of numerous criticisms because the sensitivity and specificity[15] of the test can vary in presence of rehydration (Wells, 1977). Rehydration results in increased sensitivity from 50% to 92% (Mandel, 1989), but in decreased specificity.

[15]Sensitivity and specificity are the most widely used statistics used to describe a diagnostic test. The sensitivity is the ability of the test to identify the real positives and can be defined as P(T+|D+): the probability (P) of a positive test (T+) among patients with disease (D+). Tests with high sensitivity should be preferred when the risk of positive lost can have serious consequences, so for dangerous diseases, highly contagious or with fatal exit, and when the following diagnostic tests are not risky or expensive. The specificity is the ability of the test to identify the real negatives and can be defined as P(T-|D-): the probability (P) of a negative test (T-) among patients without disease (D-). Tests with high specificity should be preferred when the diagnostic tests following the first one are very expensive or risky.

A high sensitivity of the FOBT on one hand reduces the false negatives (negative results in presence of disease), but on the other sends a high number of patients to do a colonoscopy.

In this case there is a risk that part of diagnosed lesions is detected because of the great number of second level diagnostic tests done, and not because of the test ability to detect high risk individuals.

The ratio between the CCR detected by the screening at a given time (prevalence) and the expected CCR in the population (incidence), suggests an average early diagnosis not inferior to two years.

On the bases of the incidence registered in 2001 in the Province of Ferrara, almost 190 new cases of CCR were expected.

The screening program was able to detect 204 cancers, the 7% of the 3.045 patients with a positive FOBT (tab.20). We should also take into consideration the fact that the person with a positive FOBT are almost 6,3% of the complying population, but only 76,5% of these have had a second level diagnostic test, so the number of new cases of CCR could be underestimated.

In tab. 20 we describe in details the effectiveness data of the screening program in terms of compliance and diagnosis.

Tab. 20 Effectiveness data of the screening program

DESCRIPTIVE DATA OF COMPLIANCE AND EFFECTIVENESS			
	number	percentage	
Invited population at the end of first wave	99.207		
Persons who did the FOBT	48.596	49,0%	of compliance
Persons with positive FOBT	3.045	6,3%	of adherent
Persons who did a 2nd level examination (colonoscopy or RX)	2.344	77,0%	of positives at FOBT
Persons invited to surgery	225		
Numer of persons surgically operated	186	82,7%	of the invited person
Type of lesions			
Cancers	204	8,7%	of colonoscopies
Low risk adenomas	533	22,7%	of colonoscopies
Advanced adenomas	552	23,5%	of colonoscopies
Cancerized adenomas	66	2,8%	of colonoscopies
Other lesions	3	0,1%	of colonoscopies
Tumors in situ (TIS)	41	1,7%	of colonoscopies

Source: our elaboration using Screening Centre data and Provincial Tumours Register data

In order to measure the effectiveness of the screening program we must analyse separately the two types of diagnostic exams involved, the FOBT and the colonoscopy.

Numerous studies in literature show that the effectiveness of the two tests depends by the compliance rate and that a minimum level of compliance is required to reduce the mortality from CCR with both the tests (Lieberman D., 1995).
With compliance rate of 100% the FOBT can prevent the 47% of deaths from CCR, whereas a compliance rate of 50% reduces the mortality only to 23%.
In the same way, colonoscopy allows for a reduction of 80% in mortality from CCR in case of total compliance and only 40% if the compliance is just 50%.
These aspects have not only an impact in terms of effectiveness, but also in terms of efficiency, as part of the fix costs of the program cannot be spread over the total volume of diagnostic tests and the unitary cost for each patient increases, with a consequent increment of the cost-effectiveness ratio of the intervention.

6.2. Effectiveness of the screening program in the Province of Ferrara

The first effectiveness data referred to the screening program have been provided by the Tumours Register of the Province. The data show that since 2005, year in which the program started, the incidence of all lesions is increased. In particular, hyperplastic polyps are increased from 368 new cases in 2005 to 451 in 2006 (versus the 230 of the previous years), adenomas are increased from 1.043 new cases in 2005 and 1.242 in 2006 (versus the almost 800 in the previous years), but especially adenomas with dysplasia are increased from 300 before the 2005 to 444 and 655 in 2005 and 2006 respectively. Finally, in 2006 have been detected 492 new cases of cancer versus the 455 new cases in 2005.
An important result of the screening program concerns the stadiation of the detected tumours: since 2005 the cases of cancer in Dukes'stage A are increased from 10% to 14% with respect to 2004, whereas the cases of cancer in the worst stages are decreased, from 9,4% to 8,1% in stage B, from 53,2% to 50,6% in stage C and form 17,1% to 16,5% in stage D.
In the biennium 2005-2007 the incidence was of 12,6% for polyps, 47,6% for adenomas, 29% for dysplastic adenomas and 10,8% for cancers. Comparing these data with the incidence percentage registered before the screening program implementation (13,1% of polyps, 46% of adenomas, 18,2% of dysplastic adenomas and 22% of

cancers) we can see how an early diagnosis of dysplastic adenomas can reduce the incidence of colorectal cancer in the future.

Adenomas, if early detected and removed can increase the possibility of a total eradication without metastasis diffusion. This confirms the importance of the screening program, which not only can reduce the incidence of cancer and save human lives, but also can save future costs due to avoided surgical and oncologic treatments for the most advanced disease stages.

7. The adoption of the MISCAN model to evaluate the effectiveness of the screening program

7.1. The MISCAN-COLON model (Loeve F., 1999; van Ballegooijen, 1992)

The evaluation of the colorectal cancer screening has been done employing the micro-simulation program MISCAN-COLON[16].

The Model is an adapted version of the MISCAN, a micro-simulation screening analysis (Habbema, 1984), which is being used for breast cancer and cervical cancer screening evaluation. The model is based on a Markov model, but it allows for less simplification and therefore more flexibility in exploring various assumptions and can be used to simulate all candidate screening tests.

The program can be divided into two parts: a natural history part and a screening part.

In the first one, life histories are generated in absence of screening, assuming that in this period colorectal polyps, adenomas and cancer may develop and cause death.

The second part of the program simulates the presence of a screening for colorectal cancer that will change some life histories.

The stochastic model underlying the simulation is specified in the input of the program. The input relates to demographic characteristics, the epidemiology and the natural history of the disease, and the characteristics of the screening.

Natural history without screening

The first part of the program simulates a population of individuals that may develop several colorectal lesions. For each person the program simulates a life history that

[16] See Appendix for further details.

consists of the age and stage at diagnosis and age and cause of death; individual's life history is based on lesions histories.

The progression of lesions can be divided into three phases: a preclinical non-invasive polyp phase, a preclinical invasive cancer phase, and a clinical cancer phase. In each individual more than one lesion can emerge and to each lesion an anatomical site in the bowel is assigned. Each lesion can develop into cancer, and it is possible that a person has more than one cancer.

The history of a lesion consists of its successive stages and the ages of the individual at which transitions between stages occur. For each lesion in a person the program generates a lesion history that sometimes can result in death from colorectal cancer. Individuals may die from other causes if the lesions are not fatal, or if they emerge late in life time.

An example of life history of a person who develops three lesions in his life is described in fig. 3-a.

First, from the life table the program generates an age at death from other causes that is not affected by colorectal cancer. Then, the lesion histories are generated.

In general, the first stage after onset - the moment at which a lesion can be detected by screening – is a preclinical non-invasive (polyp) stage. Then, a lesion can develop from a preclinical polyp stage to a preclinical cancer stage, in which lesion is already invasive, but not yet diagnosed.

As shown in fig.3 we can distinguish at least three types of lesions:

- lesion 1 is still in the polyp phase when the person dies from other causes;
- lesion 2 is invasive from the beginning and can lead to death if not detected;
- lesion 3 is a preclinical polyp appeared late in life or after clinical diagnosis of cancer, and may not cause death because the individual dies for other causes.

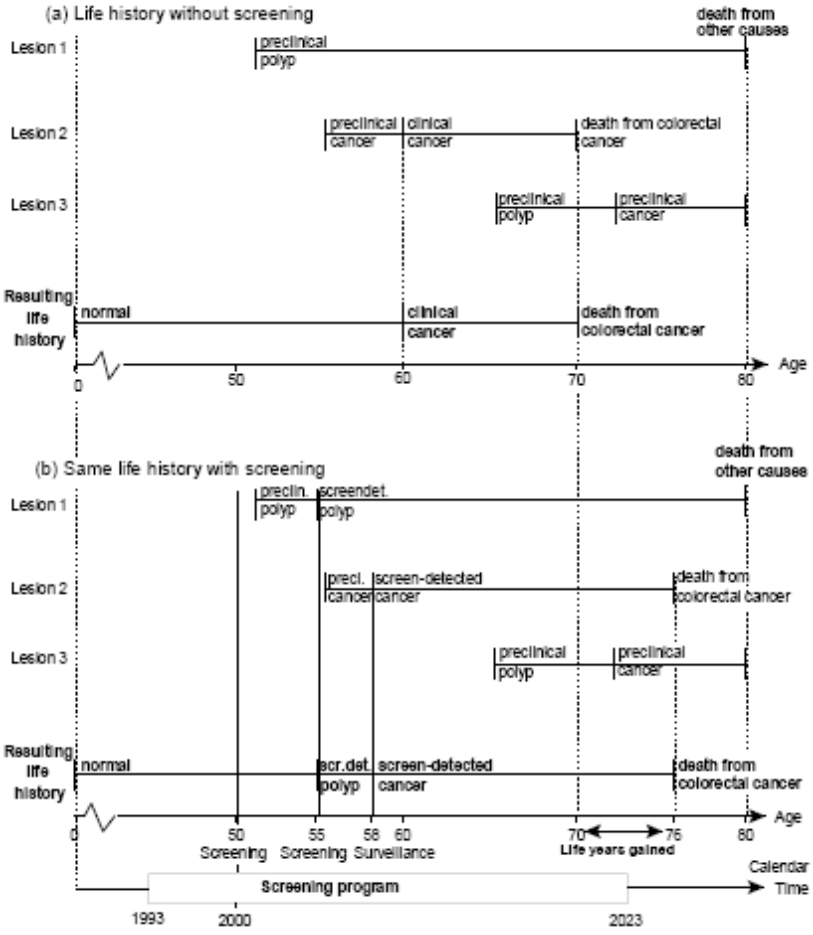
Fig. 3-a shows the life history of an individual in absence of screening. The diagnosis of cancer is made when the first evident signs and symptoms occur, the lesion enters the corresponding clinical cancer stage and a survival time is generated. The survival time depends on the stage of the cancer at the moment of diagnosis.

In case of a lesion 1, or a lesion 3 the person dies from other causes at age 80.

A lesion 2 is diagnosed at age 60 and has a survival time of 10 years, leading to death from disease at age 70.

The life history begins in a stage without disease, then the person enters in a clinical stage at the age at which lesion 2 is diagnosed (age 60). During the diagnostic process all cancers will be found, thus the person the person transits to the clinical stage of the most developed cancer at the time of diagnosis. The age of death of a person with clinical cancer is the age at death from colorectal cancer or the age at death from other causes, whichever comes first. The example shows that a person with colorectal cancer that would have died at age 80 for other causes, dies at 70 from the disease, and thus loses 10 life-years due to colorectal cancer.

Fig. 3 (a) An example of a life history for a person who develops three lesions over his life in a situation without screening; (b) The life history of (a) in presence of screening



Source: Loeve,van Ballegoijen, 1997

Screening

In the second part of the program a screening policy for colorectal cancer is simulated. A screening policy must define the target population, the ages at which screening

examinations are scheduled, the period of screening, the diagnostic tests to be used, and the diagnostic follow-up.

The sensitivity and specificity of diagnostic tests vary for type of test and for lesions in different disease stages. A screening test with low sensitivity results in a high probability of false-negative results, in which a lesion in a preclinical detectable stage is missed. And if the lesion is missed because of a difficult localization it is likely that the tumour will be missed again at the next screening. This can be modelled as a systematic negative test result for the lesion.

With the screening a lesion in a preclinical phase transits to the screen-detected phase. A person enters the screen-detected stage of the furthest progressed lesion that was found during screening and diagnostic follow-up.

Screen-detected lesions are removed and the patient enters in a surveillance period.

If only non-invasive stages are found, it is assumed that all screen-detected lesions are removed, that their development stops, and that they will not lead to colorectal cancer death. When a cancer is detected, the person is treated and enters in the follow-up.

The age at death from colorectal cancer can be affected in different ways by screen detection: screening can prevent the death from disease, it can delay the age at death, the person can die at the same age as in absence of screening, or for complications after detection, or a new survival can be generated independent of the age at death from cancer without screening.

The life history described in fig. 3-a is represented in fig. 3-b in a situation with screening. The example assumes that screening is performed for 30 years, from 1993 to 2023. At age 50 the individual is screened when no lesions are developed yet. Five years later the person have a second screening and a lesion 1 is detected as a polyp. The lesion is removed, and the person transits to the screen-detected polyp stage and is kept under surveillance. At age 58 a third screening test detects a lesion 2 in a cancer stage and the person transits to the screen-detected cancer stage. The early diagnosis allows the treatment of cancer and increases survival: colorectal cancer death is delayed from 70 to 76 years of age.

The person dies from the disease due to lesion 2 at the age of 76, losing 4 life-years because of death from colon cancer, instead of dying at 80 for other causes. In absence of screening this person would have died at 70, therefore the screening results in a gain of 6 life-years.

7.2. Formal description of the model

The input for the simulation relates to demography, the epidemiology and the natural history of the disease, and the characteristics of the screening.

In this section we present a formal description of the model whereas parameters details are summarized in Tables 21 and 22.

Demography

The model simulates an age-structured population, or a birth cohort, generating the date of births and of death from other causes for each person. A distribution of births over calendar years and from a life table is used for the simulation. The model can use population strata (for gender, age) with its own distribution of births and its own life table, thus potential differences in cancer risk and other characteristics in the population can be modelled.

Epidemiology and natural history

Development of lesions. The progression of lesions can be divided into three phases: a preclinical non-invasive polyp phase, a preclinical invasive cancer phase, and a clinical cancer phase. In each individual more than one lesion can emerge and to each lesion an anatomical site in the bowel is assigned. Each lesion can develop into cancer, and it is possible that a person has more than one cancer. In the situation with screening, screen-detected phases are added.

Preclinical incidence. In the model we can define up to three different type of lesions each of which is defined by a unique initial stage.

Lesions can develop and the subsequent stages may be more than one: a lesion could start as adenoma and develop into cancer or being invasive from the beginning.

It is assumed that lesions of different types develop independently in a person. Colorectal lesions may be randomly distributed among the population and each individual should have the same risk of develop new lesions, but differences in genetic and environmental factors result in heterogeneity in preclinical incidence. Therefore risk differences between individuals are modelled by the introduction of a risk index for each individual: a high risk index indicates a relatively high probability to develop lesions[17].

[17] For each person a risk value is determined by a random drawing from a gamma distribution, which is a continuous probability distribution ranging between 0 and infinity (Law, 1982). The mean and variance of this gamma distribution can be specified for every stratum and each type of lesion. A high-risk group can be modelled

Anatomical site. Each lesion is located at a specific anatomical site and a distribution of sites can be specified. It is assumed that the anatomical site of a new lesion is independent of the anatomical site of previous lesions. The sensitivity of screening tests can but need not depend on anatomical site, as well as transitions and durations.

Transitions and durations of lesions. The history of a lesion consists of its transitions for a stage to another and the duration in each stage. Each possible transition between two stages has a probability distribution of the dwelling time in the present stage[18]. In the model transition probabilities are specified.

Screening

Screening policy and compliance. Screening policies consists of the ages at which persons are invited to screening, the period and the screening tests at each age and examinations. The screening can use up to three tests. Individuals without clinical colorectal cancer are invited to attend a screening test. Attendance probabilities may differ for population strata and age.

Characteristics of screening test.

The probabilities on positive or negative screening on the absence or presence of lesions and on the sensitivity and specificity of the test.

The test specificity –the probability of a negative result in absence of lesions- can be defined for each test. In persons with lesions, test results are generated for each lesion independently.

The anatomical site of a lesion can influence the sensitivity of the screening, therefore a site-specific sensitivity can be specified in the model. The probability to reach the caecum can specified too.

When more than one screening test is used the model assumes that the results are independent (the probability of a positive test result does not depend of the results of

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by a stratum with a high mean of the risk index. The risk to develop lesions of a type is proportional to the risk index for that type and the age-specific preclinical incidence rate for that type.

The gamma distribution for risk in the population results in a negative binomial distribution of colorectal lesions at a given age in the population (Mood, 1974). This distribution is widely used in the conceptually similar field of modelling parasite burden in the population (de Vlas, 1993). If the variance of the gamma distribution for risk indices is small, the distribution of colorectal lesions at a certain age will approach a Poisson distribution.

[18] Four types of dwelling time distribution functions are currently implemented in the model: a constant duration (parameter: mean), an exponential distribution (parameter: mean), a Weibull distribution (parameters: shape, mean), and a piecewise uniform distribution (parameters: (*ai, bi*), *i* = 1, .., *n*, where *ai* is a dwelling time and *bi* = *P*(dwelling time _ *ai*)). The mean of exponentially or Weibull distributed dwelling times can depend on age and anatomical site. Simple model specifications will assume independence between the dwelling time in a stage and a dwelling time in a previous stage. However, it is possible to specify that durations in successive stages are correlated. This correlation is characterized by a parameter with values between -1 and 1. Independence of dwelling times is indicated by a value of 0; deterministic dependency on the previous dwelling time is indicated by ± 1.

the same test in previous screenings), even if this assumption is realistic only if false test results occur randomly. The program considers also the possibility of systematic errors. Both systematic negative and systematic positive test results may occur[19].

Prognosis after screening. If screening is positive, it is assumed that all screen detected polyps are removed, that their development stops and they will not lead to cancer death. The possible prognostic consequences after cancer screen detection are:

- the person is cured and won't die of the detected cancer;
- the moment of death is delayed;
- the moment of death does not change;
- the person may die after screening (complications);
- a new survival can be generated independent of death in absence of screening.

Follow-up after screening. Possible follow-up strategies are the following:

- the person is invited to the next screening round (for small adenomas);
- the person returns to the screening after several years (for false positive FOBT);
- the person will be kept under surveillance until no lesions are found (for large or villous adenomas).

7.3. Application of the Miscan Model for the screening program in Ferrara

The Miscan-colon model is used to simulate two alternative strategies in the Emilia Romagna population from 2004 to 2008. One strategy is the screening program with the FOBT between ages 50-69; the other strategy is the absence of screening.

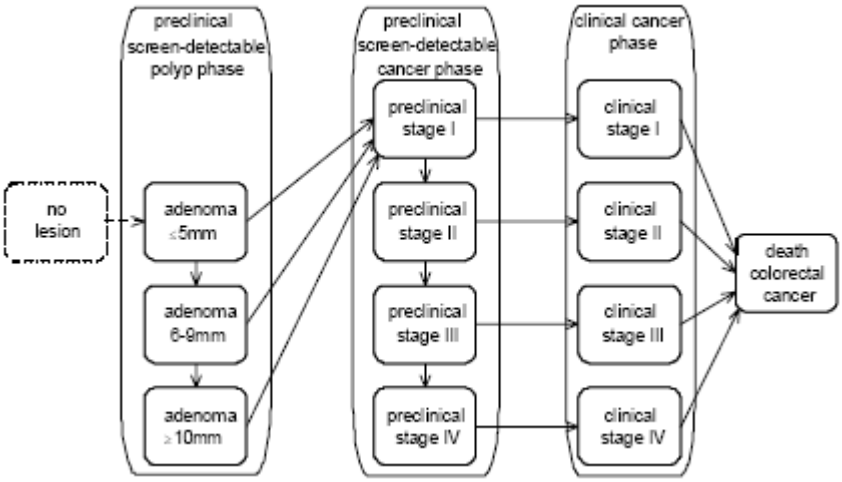
Preliminary assumptions about the natural history and screening characteristics were implemented, using the information provided by the screening centre and the Provincial Cancer Register .

Parameter values are based on literature and expert opinion. Some aspects, such as the clinical incidence in the situation without screening and survival after clinical detection, are based on Cancer Registers data of Emilia Romagna and Ferrara Province. A summary of the assumptions is given in tables 21 and 22.

[19] Systematic test results can occur for:
• person (for example, it is possible that an FOBT is always positive in a person);
• test examination (for example, it is possible that all small polyps within reach are missed at sigmoidoscopy because of bad bowel preparation);
• lesion (for example, a lesion can be missed systematically because of a difficult localization in the bowel).

In figure 4. the assumed natural history of colorectal cancer is presented. The adenoma stages are subdivided according to size, while the cancer stages are based on the Dukes classification and the Italian ICD-10, C-18,20 classification.

Fig. 4 Natural history of colorectal cancer



Source: Loeve, van Ballegoijen, 1997

Tab. 21 Summary of demographic and natural history parameters and assumptions used in the model

Parameter	**Model specification**
Population size Ferrara Province	347.582 in 2004; 350.000 in 2005
Life tables of death from other causes	Based on age-specific mortality rates in Ferrara population
Types of lesions	Initial stage adenoma < 5mm Adenoma > 10mm
Stages	Dukes stages: Stage I, stage II, stage III, stage IV
Sensitivity of the diagnostic test	100% in all preclinical stages
Parameters of the distribution of the risk index	Average risk
Age-specific preclinical incidences rates	Based on clinical incidence stage distribution data in 2004 and a prevalence of adenomas
Site distribution	Site distribution of clinical cancers in Cancer Register data in 2004
Transition for each stage	Based on clinical stage distribution in Cancer Register data in 2004 and size distribution of adenomas in literature studies
Duration in stages	*Dwelling time distributions in preclinical stages:* exponential *Mean total duration of preclinical stage of lesions that grow into cancer:* 20 years *Mean duration of preclinical cancer stage*: 3.6 years *Survival in clinical stages*: Cancer Register data
Correlation between durations	100% between durations in preclinical stages.

Source: our elaboration with program data and assumption

Tab. 22 Summary of screening parameters and assumptions used: biannual FOBT test (if negative); followed by a colonoscopy (if positive) and FOBT every five years (if negative colonoscopy).

Parameter	**Model specification**
Screening policy	First and last year of screening: 2005-2007 Screening ages: 50-69 Screening test: FOBT test Second diagnostic test: Colonoscopy
Specificity and sensitivity of the test FOBT	Specificity: 98% Sensitivity for adenoma < 5 mm: 0% Sensitivity for adenoma 5-9 mm: 5,4% Sensitivity for adenoma >9 mm: 17,9% Sensitivity for cancer: 70%
Specificity and sensitivity of colonoscopy	Specificity: 100% Sensitivity for adenoma < 5 mm: 75% Sensitivity for adenoma 5-9 mm: 85% Sensitivity for adenoma >9 mm: 95% Sensitivity for cancer: 95%
Reach of each screening test	FOBT: sensitive for lesions in whole colon Colonoscopy: 97% reached caecum; 3% need a second colonoscopy; 1% need BE-RX
Sensitivity of the diagnostic test	100% in all preclinical stages
Diagnostic follow up after a positive result for each test and preclinical stage	Yes
Treatment	After someone is diagnosed with CRC. An individual is assumed to receive initial therapy, continuous therapy an terminal treatment, depending on how long someone lives after diagnosis. If someone dies within a year, the whole period is assumed terminal If someone lives longer than a year, but dies within 2 years after diagnosis, 1 year is assumed terminal, and what is left is assumed initial If someone survives more than 2 years, 1 year is terminal, 1 year is initial and what is left is continuous
Prognosis after screening	After screen-detection of a polyp: 100% cure After screen-detection of a cancer: new survival based on stage-specific survival of clinical cancer
Follow-up after screen detection of each non invasive stage	*After a positive screening test or surveillance test without lesions detected or only adenomas < 5mm detected*: Number of years without screening (surveillance interval): 5 Next test after surveillance interval: screening test *After a positive screening test or surveillance test with adenomas 6-9mm and/or >10mm detected:* Number of years without screening (surveillance interval): 3 Next test after surveillance interval: screening test
Mean life expectancy at diagnosis of cancer after a screening test	19,15
Attendance to screening	50% for FOBT 67,5% of positive FOBTs have a colonoscopy

Source: our elaboration with program data and assumption

7.4. Miscan model results

The simulation program provides two outputs: a file containing all the outcomes for the evaluation of the screening policy (postproceeding file) and a standard output file.
The contents of the model outputs are described in details in tab.23.
Results are reported per year and aggregated over time.
The file specifies the age groups into which the output is divided, the reference year for discounting and the discount percentages.
The annual number of entries and the number life-years are reported for each clinical stage.

Tab. 23 Contents of model output

– Number of first and repeat invitations and screenings, and the number of surveillance tests
– Number of prevented and detected cancers by screening and surveillance and number of prevented deaths from colorectal cancer
– Number of life-years gained by the screening program
– Number of positive and negative results of screening and surveillance examinations in each preclinical stage (by age group)
– Number of entries to each stage (by age group)
– Number of life-years and number of life-years lost by the disease (by age group)
– Number of disease-specific deaths and the number of non specific deaths (by age group)
– Totals over the whole simulated time period, for the situation with and without screening discounted by three percentages
– Number of first and repeat invitations, number of screening examinations, and number of surveillance tests
– Number of positive and negative diagnostic follow-up tests after a positive screening test
– Number of entries and life-years in clinical and screen-detected stages
– Number of disease-specific deaths
– Number of life-years lived
– Number of life-years lost by disease

The discounted totals over time contained in the postprocessing output file are used to calculate the costs and effects of the screening program.
Costs are assigned to screening tests, diagnostic tests, cancer treatment and follow-up. Costs per life-year gained and costs per prevented death are calculated using three discount percentages, 1,5%, 3% and 4%.
In Table 24, the simulated undiscounted totals, for the a million persons over the whole simulated time period of 30 years, are shown for biennial FOBT screening, and no screening.

Tab. 24 Predicted undiscounted totals per 1.000.000 persons in 30 years

Number of invitations and screening's effects

Discount rate	0,00		
	screening	no screening	difference
Nr. first inv.	574.760	0	574.760
Nr. rep inv.	3.158.965	0	3.158.965
Total inv.	3.733.725	0	3.733.725
Nr. first scr.	287.519	0	287.519
Nr. rep. scr.	1.578.510	0	1.578.510
Nr. pos. scr	88.229	0	88.229
Nr. neg. scr.	1.777.800	0	1.777.800
Total screenings	1.866.029	0	1.866.029
EFFECTS			
Deaths from disease	39.203	41.392	-2.189
Life years lost by disease	483.955	515.928	-31.973

Source: our elaboration of model results

The results show that the screening allows a reduction of more than 2.100 deaths from CCR and a reduction of almost 32.000 life years lost.

In Table 25, the correspondent simulated total costs of the screening are shown for biennial FOBT screening and the situation in absence of screening; the results are reported also for the 3% discount factor (this discount rate is the most used in literature), and show an incremental cost of almost € 67.721.000.

Tab. 25 Predicted costs of the screening for each discount factor

COSTS

Discount rate	0,00			0,03		
	screening	no screening	difference	screening	no screening	difference
Screenings	74.666.165	0	74.666.165	49.541.929	0	49.541.929
Surveillance tests	0	0	0	0	0	0
Diagnostics screening	25.109.200	0	25.109.200	16.874.129	0	16.874.129
Clinical diagnostics	27.869.200	30.123.600	-2.254.400	10.863.920	12.138.240	-1.274.320
Complications screent.	0	0	0	0	0	0
Complications surv.	0	0	0	0	0	0
Compl. diag. in scr. pr	202.953	0	202.953	136.225	0	136.225
Compl. at clin. diag.	209.019	225.927	-16.908	81.479	91.037	-9.557
Total treatment	2.233.929.400	2.244.116.500	-10.187.100	881.508.600	879.055.800	2.452.800
Total	2.361.985.937	2.274.466.027	87.519.910	959.006.282	891.285.077	67.721.205

Source: our elaboration of model results

The cost effectiveness of the screening program is given by the ratio between the total screening costs and the prevented deaths or life-years gained.

The incremental cost effectiveness ratio (ICER) of the screening program compared to the situation in absence of screening is given by the ratio between the incremental costs of the program and its incremental effects:

$$ICER = \frac{COSTS_{SCREENING} - COSTS_{NO\_SCREENING}}{EFFECTS_{SCREENING} - EFFECTS_{NO\_SCREENING}}$$

The final results (tab. 26) show that the ICER (Incremental Cost Effectiveness Ratio) of the program, compared with no screening, for a 3% discount rate, is € 5.315,00 for life year gained and € 61.492,00 for prevented death.

Tab. 26 Cost-effectiveness results of CCR screening program

Discount rate	0,00	0,03	0,015	0,04
Costs				
Screen costs	74.666.165	49.541.929	60.231.808	43.937.426
Surveillance costs	0	0	0	0
Diag screen costs	25.109.200	16.874.129	20.379.925	15.034.220
Clin diag costs	-2.254.400	-1.274.320	-1.670.480	-1.079.760
Complications costs	186.045	126.667	152.101	113.222
treatment costs	-10.187.100	2.452.800	-2.187.500	4.402.850
Total costs	**87.519.910**	**67.721.205**	**76.905.854**	**62.407.958**
Effectiveness results				
deaths gained	2.189	1.101	1.528	900
lifeyears gained	**31.973**	**12.741**	**19.792**	**9.695**
Cost effectiveness results				
Per prevented death	39.982	61.492	50.331	69.334
Per lifeyear gained	**2.737**	**5.315**	**3.886**	**6.437**

Source: our elaboration of model results

8. Conclusions

The results presented in this work show that a colorectal cancer screening program has certainly a great impact in terms of costs born by the local health organization and the society. In particular, with the screening new cases of lesions and cancers can be detected, increasing the cost for the following treatments that would not have been born in absence of screening. Nevertheless the effectiveness of the screening program cannot be valued only in clinical terms (number of lesions diagnosed, number of lives saved) but also in economic terms: the screening allows an early detection of adenomas and lesions at the first stages, with consequent savings of money due to avoided future treatments.

From an economic point of view, also compliance has a strong impact in the program effects, as the fixed costs born to adopt and implement the program can be highly spread, reducing the unitary cost of the screening for single patient. A high compliance can increase the costs due to further diagnostic exams and treatments for the people found positives, but can also avoid the future costs of treatments, especially for the latest and worst stages of the disease.

The preliminary results of the MISCAN-COLON Model simulation show that the screening program will prevent almost 1.100 deaths, with 12.741 years of life gained in a period of time of 30 years (at a discount rate of 3%).

Comparing the costs born in the first wave of the screening with the number of years potentially saved, the model show that the incremental cost effectiveness ratio of the program is almost € 5.315 for life year gained.

The results of this study confirm the results of similar studies conducted in other countries (Sonnenberg 2000, 2002), and highlight the importance of implementing a screening program not only for the importance that prevention can have in clinical terms, but also for the economic impact of such a policy to save future avoidable expenses.

From a societal perspective it would be extremely interesting to evaluate the non medical costs of the screening program, such as the time off work for the subjects and their caregivers, travel costs, production losses, out of pocket expenses and intangible costs (Heitman S. et al, 2008). In particular, we would like to measure the psychosocial consequences of the screening in terms of quality of life for the patients (Brodersen J. et al, 2007; Whynes DK, 1994) and mental health (Taupin D., 2006). Participation in screening programs for malignant disease may have psychological health effects that could outweigh the beneficial effects of the screening itself (Wardle J, 2006) and increase the anxiety in case of positive results (Miles A., 2005).

Attendance to screening program may results from individual risk aversion, patients' preferences (Pignone N., 1999) and psychosocial impacts (Ling BS., 2001; Tymstra, 1987).

To this aim, during the next waves of the screening program a questionnaire will be administered to patients entering the program in order to measure the impacts of the screening in terms of quality of life.

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Appendix- The MISCAN-COLON model

The MISCAN model is a micro-simulation screening analysis (Habbema, 1984) based on a Markov model, but it allows for less simplification and therefore more flexibility in exploring various assumptions and can be used to simulate all candidate screening tests.

A version of the MISCAN model has been used to predict the impact of breast cancer screening on clinical medicine (de Koning, 1990) and the impact of breast cancer screening on quality-adjusted life-years (de Haes, 1991).

The MISCAN model has also been used to estimate cost-effectiveness of cervical cancer screening in The Netherlands (Koopmanschap, 1990, van Ballegooijen 1992).

The MISCAN-COLON model is an adapted version of the MISCAN model, used to predict the impact and cost-effectiveness of colon cancer (Loeve F., 1999).

A first application has been done in Minnesota to study the impact of FOBT screening, and then in California to evaluate the impact of the sigmoidoscopy screening.

The total MISCAN-COLON program is divided in two parts: a simulation program and a post-processing program for output.

The programs require Windows 1995 and are written in Delphi. It takes about 60s on a 133-MHz Pentium to simulate the results over 100.000 individuals screened for six times. Simulations use a random number generator, the Ecuyer 1992, composed of two disjoint random number sequences and with two initial seeds. The variance between simulation runs is reduced assigning to a life history the same random number sequence.

The model uses a gamma distribution to extract a risk index R_i –the risk to develop a lesion of type i for each type of lesion and for each individual life history. The distribution is based on two parameters α and β with mean $\alpha\beta$ and variance $\alpha\beta^2$.

The gamma distribution has a density function:

$$f(x) = \begin{cases} \dfrac{\beta^{-\alpha} x^{\alpha-1} e^{-x/\beta}}{\Gamma(\alpha)} & \text{if} \quad x > 0 \\ 0 & \text{otherwise} \end{cases}$$

Where a_0 denotes age 0 or the age at which the last lesion of type i developed. The probability to develop lesions of type i at age a in a person in which the risk index equals 1 is the onset rate $h_i(a)$. It is assumed that the onset rates are constant over age intervals denoted by (b_u, b_{u+1}), $u = 1, 2, ...$

The corresponding accumulated preclinical incidence between age a_0 and a in a person with risk index R_i equals:

$$H_i(a, a_0) = R_i \int_{a_0}^{a} h_i(y)d$$

The probability distribution for the age a_i at which a new lesion of type i develops is:

$$\Pr(a_i \leq a) = 1 - \exp[-H_i(a, a_0)]$$

The age at which a new lesion of type i develops is calculated by solving this equation, replacing the probability with a random number u, uniformly distributed between 0 and 1.

The program provides two output files: a file for postprocessing and a standard output file. The postprocessing program calculates costs per life-year gained and costs per prevented death using three discount percentages.

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