UNIVERSITY OF MODENA AND REGGIO EMILIA

Research Doctorate in
Clinical and Experimental Medicine (CEM)

Doctorate School in
Clinical and Experimental Medicine (CEM)

Cycle XXVIII

Building Health Care Value through the Culture of Clinical Outcome Evaluation

Candidate: Marta Rigoni

Advisor: Prof. Marco Vinceti
Advisor: Dr. Giandomenico Nollo

Doctorate School Coordinator: Prof. Giuseppe Biagini

Doctorate School Executive Director: Prof. Giuseppe Biagini

Riassunto

Costruire un sistema sanitario basato sul valore e sul continuo miglioramento delle cure e dei servizi erogati è uno scopo condiviso da molti Paesi e Organizzazioni. Inoltre la valutazione delle prestazioni cliniche è di cruciale importanza per l'accountability dei servizi sanitari pubblici e per la definizione delle politiche sanitarie. L'analisi degli outcome è fondamentale per prendere decisioni consapevoli, indirizzare e programmare cambiamenti clinici ed organizzativi migliorando la qualità delle cure e dei servizi, soprattutto in un momento storico di risorse limitate. A questo proposito tra gli strumenti ufficiali adottati nel Sistema Sanitario Nazionale italiano, il Programma Nazionale Esiti (PNE) nel corso degli ultimi anni è diventato lo strumento più riconosciuto per la misurazione, valutazione e confronto tra le attività ospedaliere e gli esiti clinici. In coerenza con tale quadro, nella Provincia Autonoma di Trento, sono state sviluppate delle iniziative rivolte a fornire una valutazione completa e basata sul contesto locale dei processi di cura. Tale valutazione si costruisce su dati provenienti da fonti cliniche ed amministrative.

Questo progetto di dottorato mira a disegnare, condurre e sperimentare una azione strutturata per sviluppare un programma locale di valutazione dei processi di cura. In particolare, la valutazione degli esiti si è focalizzata sulla analisi di percorsi clinici e modelli organizzativi attraverso lo studio di specifici casi d'uso di grande rilevanza clinica.

L'analisi sui casi specifici, ha implicato lo studio di più di 4.500 pazienti, ha consentito l'acquisizione di metodi statistici e delle competenze tecniche ora disponibili per una più ampia applicazione. Il lavoro ha coinvolto medici e professionisti sanitari e contribuito alla diffusione di una cultura della valutazione dei risultati aprendo la strada ad un programma provinciale per la valutazione degli esiti clinici.

In particolare il primo capitolo di questa tesi rappresenta la parte teorica e si focalizza sui nuovi indirizzi, strumenti organizzativi e di implementazione necessari per la costruzione di una sanità pubblica che miri al continuo miglioramento di se stessa e dei suoi servizi. Raggiungere questo scopo richiede l'acquisizione di competenze tecniche, un importante cambiamento culturale e la messa in pratica di nuovi paradigmi quali la centralità del paziente, la creazione di una leadership sanitaria efficiente e nuovi modelli organizzativi che armonizzino tutti gli attori coinvolti nei processi di cura.

Nel secondo capitolo vengono sintetizzati le metodologie della ricerca ed i metodi statistici utili per pianificare uno studio di valutazione degli esiti.

Il terzo capitolo fornisce una rapida panoramica internazionale, e utili referenze per chi fosse interessato ad approfondire l'argomento, dei sistemi valutativi in atto in alcuni Paesi; inoltre viene presentato il Programma Nazionale valutazione Esiti (PNE).

Nel quarto capitolo vengono esposti due casi di studio relativi ai percorsi clinici. Il primo si riferisce alla valutazione di due opzioni dialitiche per i pazienti affetti da malattia renale cronica in Trentino, il secondo alla valutazione degli outcome per pazienti anziani con frattura del collo femore nell'ospedale Santa Chiara di Treno, dopo l'introduzione di un percorso clinico di Ortogeriatria.

Nel quinto capitolo la valutazione si è focalizzata sui cambiamenti organizzativi avvenuti nel reparto di Medicina Interna dell'ospedale Santa Chiara di Trento, dove si è passati da una organizzazione standard ad una organizzazione per Intensità di cura.

Il sesto capitolo espone le conclusioni, i limiti e gli sviluppi futuri del lavoro.

Contents

List of abbreviations

ALOS = Average Length of Stay

CI = Confidence Interval

DRGs = Diagnosis Related Groups

EMUR = Sistema informativo per il Monitoraggio dell'assistenza in Emergenza-Urgenza

HD = Haemodialysis

HIS = Hospital Information System

HR = Hazard Ratio

HTA = Health Technology Assessment

IC = Intensity of Medical Care

ICA = Intermediate Care Area

ICP = Integrated Care Pathway

ICU = Intensive Care Unit

IM = Internal Medicine ward

IQR = Interquartile range

MCA = Medium Care Area

NEWS = National Early Warning Score

NHS = National Healthcare System

OR = Odds Ratio

PACA = Post-Acute Care Area

PD = Peritoneal dialysis

PNE = Programma Nazionale Esiti

RCTs = Randomized Controlled Trials

RR = Risk Ratio

SC = Standard of Medical Care

SD= Standard Deviation

SDO = Scheda di Dimissione Ospedaliera

TQM = Total Quality Management

WHO = World Health Organization

Executive summary

This PhD project aimed to build solid foundations for the creation of a provincial program for the evaluation of healthcare outcomes in the Autonomous Province of Trento.

The evaluation of health care interventions assumes a central importance in a healthcare system, because it represents a pillar for the continuous improvement in the quality of care and health services. We strongly believe that a value-based Healthcare is a “data-driven” approach and for this reason, in this project, we stressed on the importance of clinical outcomes evaluation. Outcome evaluation goes beyond the limits of self-reference and leads to a health care system able to steadily validate or change decisions based on quantitative comparison of outcomes. A famous statement attributed to Florence Nightingale that appropriately captures the performance–quality–management relationship is “The ultimate goal is to manage quality. But you cannot manage it until you have a way to measure it, and you cannot measure it until you can monitor it” (1) (2).

In order to achieve our scope, we worked on different case studies of major clinical relevance, which helped us to practically deal with the matter and to acquire and develop the methodological and statistical skills necessary for the evaluation of healthcare performances.

The diffusion of outcome evaluation is a cultural process that can lead to a value-based healthcare. Its value lies in the multidisciplinary of the approach necessary for a multi-dimensional assessment. Indeed, the critical approach of outcome evaluation is based on the combination of research methodology and data analysis with clinical experience. The involvement and collaboration of various professional figures, such as physicians, nurses, researchers, health managers, helps to achieve a more extensive and complete assessment. In addition, the approach favours team working, positive climate and organizational attitude.

The creation of a value-based health care system able to ameliorate itself and the quality of its services is not an easy task. The process is mainly cultural and involves many actors, each with his own rights, duties, specific prospects, requests, and skills. This means to deal with the multidimensionality, multidisciplinary, and new academic and managerial concepts of public health.

The complexity of the healthcare system can create variance among patients care and in the provision of services, defects in appropriateness and continuity, and poor integration in care. The successful management of such complex situation requires the definition of new organization design and models. Care pathways and organizational models approaches could be successfully implemented, because, in addition to other positive aspects, they are based on the centrality of the patient and aim to coordinate and harmonize organizational and operational aspects.

For the purpose of this thesis, we chose to focus on the evaluation of care pathways and organizational models implemented in Trentino health system as practical case studies. Each study was conducted in close collaboration with the professionals of the specific medical area increasing the awareness of health professionals towards the outcome evaluation. This was a first important step to tackle the cultural shift required in the value-based healthcare system perspective.

The first part of this thesis introduced the theoretical basis of the work. In the first chapter, we presented a speculative introduction on the principal trends, topics, and implementation tools related to the management of the healthcare system. The scope is to create a value-based healthcare, which must be centred on the patient, by creating an effective healthcare leadership. Leadership behaviours are the most influential factors shaping organizational culture, empowering relationships with co-workers, and encouraging changes to deliver high-quality care (3). In the chapter, we provided the definitions of clinical governance and evaluation, we dealt with the concepts of accountability and appropriateness of care services and, finally, we showed the importance of the introduction of organizational models in the clinical practice.

In the second chapter, we reported the main methodological issues and described the statistical instruments used for outcomes evaluation.

The third chapter presented a rapid overview of the assessment of International Systems performance and useful references to deepen the topic. In addition, we introduced the institutionalized Italian National Program Outcomes – PNE – Programma Nazionale Esiti, developed by the National Agency for Regional Healthcare Services - Agenas - Agenzia Nazionale per i Servizi Sanitari Regionali for the Ministry of Italian Health.

The practical and applicative aspects were described in the second part of the thesis.

In particular, in chapter four, we focused on the assessment of clinical pathways by analysing specifics case studies of major clinical relevance. The evaluation of clinical pathways was exemplified in two case studies: the assessment of two different therapeutic options for chronic kidney disease patients cared in the whole Province of Trento, and the assessment of an orthogeriatric care pathway for elderly patients with hip fracture implemented at the S. Chiara hospital of Trento.

A representative example of organizational models evaluation was provided in chapter five by the outcome assessment of a new approach of inpatient management, carried out in the Internal Medicine ward of the S. Chiara Hospital in Trento, and based on Intensive medical care.

Finally, chapter six of the thesis included the conclusions and future developments of this work.

1 Importance of performance evaluation in clinical processes

1.1 Trends in Healthcare

1.1.1 Value and value-based Healthcare

Value-based health care is becoming the focus of many health care reorganization efforts around the world. Value-based health care promises, indeed, to be a more effective and more sustainable approach for limiting the increase of care costs than traditional approaches such as consumption examinations or cost controls, improving quality and outcomes (4). According to the Boston Consulting Group, a virtuous improvement cycle that enhance value is shown in Figure 1.

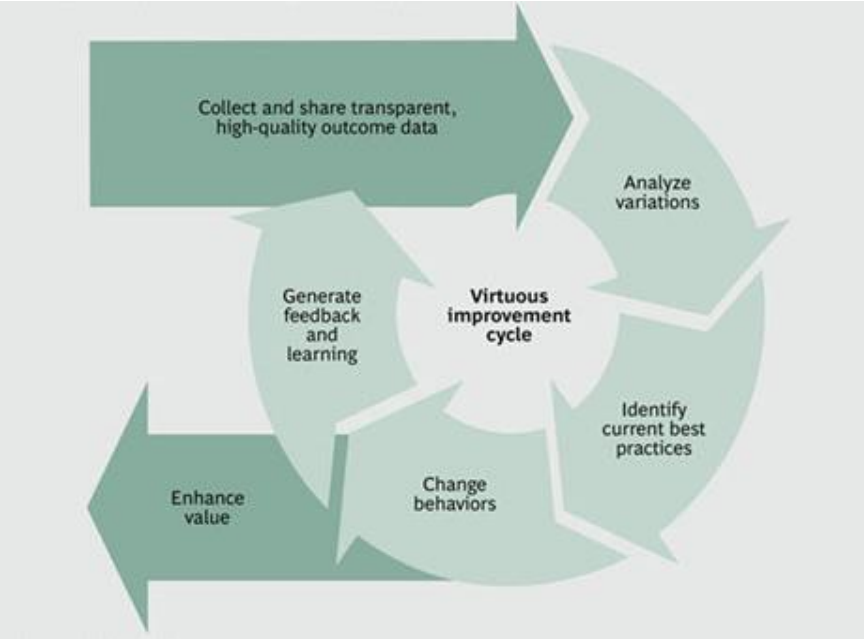


Figure 1. *Value-based Health care delivers improved health outcomes (4).*

The first step is to collect and to share transparent, high-quality outcome data. This point implies very important aspects: first, there is the necessity to have a solid and efficient information system to collect data, that means having infrastructure, common standards, a limited number of Information Technology platforms, and common legal rules in order to regulate the use of patients' data. The data itself must be of high quality that means having datasets compiled correctly and completely. The engagement of clinicians must be broad and active to achieve this point. To improve the quality of care, value-based health care have to be a data-driven approach. The most effective way to collect relevant data is

through disease registries that track selected health outcomes in a population of patients with the same diagnosis or who have undergone the same medical practice. We also have to share the results in a transparent manner, then to have accountability and communication among the involved stakeholders. Value-based health care requires the active dissemination and use of outcome data.

The second step is to analyse variations. This includes an honest outcomes analysis. If there are differences from what was thought to be the expected result, we must take it into account.

The process continue with the identification of the current best practice. Value-based health care is a data-driven approach also for the identification of the new and evidenced best practices.

Change behaviours is the next very crucial step. Changing behaviour can be a difficult task, which takes time to come materialized. Some resistances to change may occur because it is easier to do as we have always done, and it is more difficult to change the routine and practice because it requires effort and determination. In addition, other many fundamental aspects such as communication is important. Some of them are: distribution of educational materials which covers the strengths of the new change, educational meetings, local consensus processes, thus the inclusion of participating providers in discussion to ensure that they agreed that the chosen clinical problem was important and the approach to managing the problem was appropriate (5). This point is a cultural process as well as practical. This cultural process in linked to the last step that is generate feedback about the changed behaviours and learning from this.

The result of this cycle is the enhancement of the value of the health care system. This virtuous cycle must be continuously undertaken to achieve a continuous improvement in the quality of the health system.

Not all this argumentations are sufficient to create a value-based health care system. Another success factor should be the use of outcome data to readjust incentives in the health system so that stakeholders are encouraged to optimize health value. When such incentives are actualized, the system itself drives changes in the ways that all involved

stakeholders such clinicians practice, payers reimburse, and suppliers of drugs and medical devices develop and deliver products and services.

In this direction, the initiatives adopted by the English health care system improving care of elderly patients with a hip fracture are virtuous. Beside the publication of an Orthopaedic Blue Book guideline (6) and the creation of a National Hip Fracture Database (7), the British health system has established a best practice tariff. This action incentives individual trusts financially for providing gold-standard care, defined by a set of criteria, and results in an improvement of outcomes for patients (8).

1.1.2 Centrality of the patient

Recognizing the centrality of the patient, compared to the actions of healthcare professionals, means shifting the focus from individual services, visit or technology to the entire sequence of care (made by health professionals and performances) that is activated to resolve the episode of disease.

In fact, the course of treatment of a patient, in relation to the disease that manifests itself, often does not end in a single episode or a single hospitalization, and patient not necessarily close its requirements in an acute care facility. For example, a predominantly or alternatively territorial or rehabilitation path could follow, that require the integration and organization of several health professionals (Figure 2).

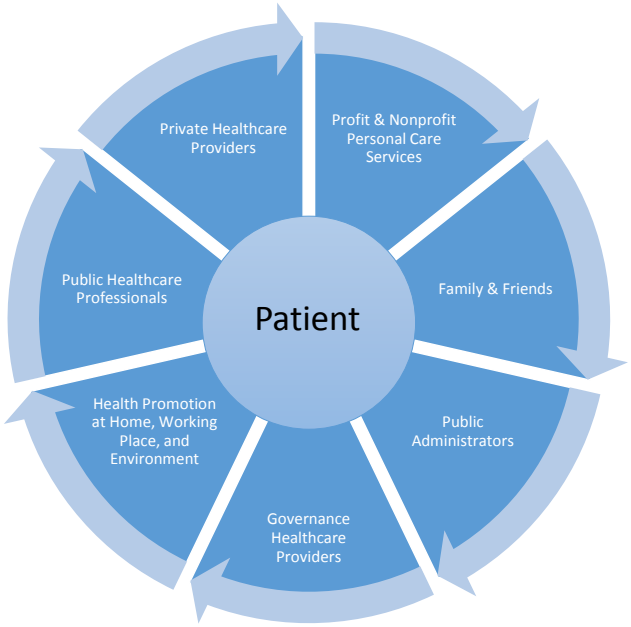


Figure 2. *Patient-centred vision of care.*

In the patient-centred view, many other actors are involved and could contribute to the wellbeing of the patient. Obviously, the family, friends, social relationships and not least new planning of working place and environment, the patient working ambient, urban planning, and the new proposals of ambient assisted living can give great assistance and strong support and create the condition for healthy lifestyle. Overall a general public government is call to design new health promotion politics dealing with the incidence of weak economic grow and demographic changes (9).

1.1.3 Create effective Healthcare Leadership

Organisational culture is defined as "the values and beliefs that characterise organisations as transmitted by the socialisation experiences newcomers have, the decisions made by management, and the stories and myths people tell and re-tell about their organisations" (10). A recent study about different approaches to reforming the NHS in England argue that culture change within organisations is fundamental to health services that must adapt to be able to deliver continually improving, high quality and compassionate care (11). To respond to current and future challenges, organisational cultures in health care must be nurtured in parallel with changes in systems, processes and structures and the key influence on culture is the leadership of an organisation (12).

To ensure high quality care, there has to be direction, alignment and commitment to a shared, holistic view of care that includes commitment to improving linkages with other providers and to achieving system goals such as continuity of care. This in turn implies alignment across different parts of organisations, different providers and other groups. Ensuring the key cultural elements requires leadership that creates direction, alignment and commitment in relation to these cultural elements (13).

Of course, many researches focused on personality traits associated with leadership effectiveness, including high energy level and stress tolerance, self-confidence, emotional maturity, personal integrity, socialized power motivation, and achievement orientation (14). Other studies focalized on the competencies related to managerial effectiveness, including skills, knowledge, motivations, self-image and some specific comportments. One of these researches suggests the following competencies are important for leaders (15):

Technical competence. It includes knowledge about health care services, treatments and technologies, knowledge about the organization, its strategy, structure and processes, and knowledge about the organization setting. Technical competence gains the respect of colleagues and co-workers.

Conceptual skills. It means have the ability to analyse, plan and make decisions when internal and external organizations interface, and when they are difficult to analyse and manage. This is essential to organizational functioning, so leaders who have conceptual skills will increase the confidence of colleagues and co-workers within the organization.

Interpersonal skills are fundamental: understanding the needs and feelings of colleagues and co-workers, monitoring the effects of own actions and being aware of emotional reactions to others are indispensable.

Perhaps most important than the personal skills are the behaviours that a leader develops and transmits. Such behaviours could be (14):

Task oriented, which means explicatory, planning, monitoring operations, and problem solving.

Relations oriented which means encourage trust and cooperation, supporting, developing, identifying, empowering people. This behaviour is important for the relationships with colleagues and co-workers.

Change oriented which means promoting and visualizing change, encouraging innovation, facilitating collective learning, ensure necessary resources are available. This is really an indispensable component.

External networking which means external monitoring and representing.

Leadership behaviours is the most influential factor in affecting organizational culture, it models change of organizational structures, which turn into motivate and support staff to deliver high-quality care (3).

Thus, let us see how leadership might affect organizational cultures, climates, and clinical outcomes in health care.

The Faculty of Medical Leadership and Management (FMLM), the King's Fund and the Center for Creative Leadership (16) reviewed the world literature concerned with relating

effective healthcare leadership and clinical outcome (12). The review demonstrated that the quality of healthcare experienced by patients is inextricably linked to the culture, climate[1] and support experienced by staff (3). In particular, studies have revealed that a culture that emphasizes cohesion and involvement appears to have a positive impact on healthcare and is more often associated with high inpatient satisfaction, and fewer complaints (17) (18). Another study proposed that the cultural characteristics valued by leaders and managers will be associated with specific organisational outcomes such as fewer patient complaints and higher staff morale (19).

Another relevant finding is that leader's behaviours influence the dominant culture of the organization. Encouraging team working and a new culture, this has a positive impact on quality improvement and stakeholder satisfaction (19) (18) (20). Several large-scale studies have shown that organizations which promote effective team working, where staff are involved, and have distributed management, perform better (21) (22). Research into the influence of organizational climate in the healthcare environment indicates that staff satisfaction is directly related to patient approval, satisfaction and clinical outcomes, up to and including mortality with lower death rates (23) (24) (25).

Summing up, an effective healthcare leadership creates organizational culture and positive climate, in turn lead to quality of care and better outcomes for patients (Figure 3).

Figure 3. *From an effective health care leadership to better outcomes for patients.*

[1] Climate is "the shared meaning employees attach to the policies, practices and procedures they experience and the behaviours they observe getting rewarded, supported and expected" (10).

Of course, organizational cultures of this nature take time and consistent energy to develop. It is usual to think of evidence use in order to inform clinical decisions, but it is not so obvious to think that evidence are used with the aim of determine the optimal culture of leadership, climate and systems (3). In addition, it is not so obvious to think that an efficient leadership, which carries a positive climate and a culture, harbours to better clinical outcomes.

1.2 Tools and dimensions to create value-based Healthcare

1.2.1 Data management and Clinical Governance

"In God we trust, all others must bring data." These are the words of William Edwards Deming[2], a celebrated American statistician, and consultant. In Japan, from 1950 onwards he trained top business managers how to improve many aspects of their business through the application of statistical methods. His theories had a great impact on Japanese manufacturing, and his influence on worldwide management is immense. Deming was one of the developer of Total Quality Management (TQM) theory.

A definition of TQM is "A strategic, integrated management system for achieving customer satisfaction which involves all managers and employers and uses quantitative methods to continuously improve an organization's process." (26). TQM funds its theory on the following elements (27):

- focus is on the customer;
- continuous improvement and training. A comprehensive TQM program is not just one shot review of processes, It's a continuous, dynamic, and institutionalized system which can be used over and over again;
- process management. The very core of continuous improvement is managing processes. Management processes needs to be assessed to determine where they are redundant, complex, or ineffective;
- statistical methods (managing by fact). In the TQM world, solid data was needed to use as the basis for making decisions;

[2] William Edwards Deming (1900 –1993) was an American engineer, statistician, professor, author, lecturer, and management consultant.

- employee involvement and teamwork. This point is fundamental, because without involvement and empowerment of the employee, the program, or other effort will not succeed. To maximize employee empowerment there must be a responsibility to meaningful training.
- management commitment and leadership;
- cost of quality;
- construction industry-specific factors (quality of standards, constructability analyses).

Total Quality Management (TQM) is, therefore, a comprehensive and structured approach to organizational management that pursues the continuous improvement of the quality of products and services through ongoing refinements in response to continuous feedback to customers.

TQM can be applied to any type of organization; it originated in the manufacturing sector and has then been adapted for use in almost every type of organization. By the mid-1990s the world of health care have adopted these management theories and a massive change of health directional models that use terminology, and methods typically of the industrial world was assumed. Since the Healthcare world is greatly different from the industrial world, adopting industrial management theories blindly it would be a useless operation or perhaps harmful. Thus, an important work has been done to shape and adapt to the health care context the industrial theories and methods.

In this definition and shaping process, Clinical Governance assumes a pivotal role. The most widely used definition of Clinical Governance is as follows:

> *"A framework through which NHS organisations are accountable for continually improving the quality of their services and safeguarding high standards of care by creating an environment in which excellence in clinical care will flourish."* (28).

In short, it is doing the right thing, at the right time, for the right people, the application of the best evidence to a patient's problem, in the way the patient wishes, by an appropriately trained and resourced individual or team (29). However, that is not all: that individual or team must work within an organization that is accountable for the actions of its staff, values its staff (appraises and develops them), minimizes risks, and learns from good practice, and

indeed mistakes (30). Seven main elements sustain clinical governance: clinical effectiveness and research, clinical audit, risk management, education and training, patient and public involvement, using information and information technology, staffing and staff management Figure 4.

Figure 4. *Clinical governance is an aggregation of service improvement processes that are regulated by a single ideology.*

Clinical Effectiveness & Research

Clinical effectiveness means ensuring that everything is designed to provide the best outcomes for patients i.e. that you do "the right thing to the right person at the right time in the right place". It is the ability of a health care intervention to obtain the desired results, for example the reduction of mortality, morbidity, or the improving o the quality of life. In other words, the effectiveness identifies the extent of the benefits gained from health care.

In practice, it means:

- adopting an evidence-based approach in the management of patients;
- changing the practice, developing new protocols or guidelines based on experience and evidence if current practice is shown inadequate;

- implementing guidelines, and other national standards to ensure optimal care (when they are not archaic by more recent and more effective treatments);
- conducting research to develop the body of evidence available and therefore enhancing the level of care provided to patients in future.

Clinical Audit

As asserted by Avedis Donabedian[3], the quality of a health service is the level at which it conforms to established adequacy or excellence standards (31). Therefore, the aim of the audit process is to ensure that clinical practice is continuously monitored and that deficiencies in relation to set standards of care are improved. It is a way that physicians, nurses and other healthcare professionals can measure the quality of the care they offer. It allows them to compare their performance against a standard to see how they are doing and identify opportunities for improvement. Changes can then be made, followed by further audits to see if these changes have been successful.

Risk Management

Risk Management involves having robust systems in place to understand, monitor and minimize the risks to patients and staff and to learn from mistakes. When things go wrong in the delivery of care, physicians and other clinical staff should feel safe admitting it and be able to learn and share what they have learnt.

This includes:

- complying with protocols (hand washing, discarding sharps, identifying patients correctly etc.);
- learning from mistakes and near-misses (informally for small issues, formally for the bigger events);
- reporting any significant adverse events via critical incidents forms, looking closely at complaints etc.;
- assessing the risks identified for their probability of occurrence and the impact they could have if an incident did occur. Implementing processes to reduce the risk and

[3] Avedis Donabedian (1919 – 2000) was a physician and founder of the study of quality in health care and medical outcomes research.

its impact (the level of implementation will often depend on the budget available and the seriousness of the risk);

- promoting a blame-free culture to encourage everyone to report problems and mistakes.

Education and training

This requires providing appropriate support available to enable staff to be competent in doing their jobs and to develop their skills so that they are up to date. Professional development needs to continue through lifelong learning.

In practice, for physicians, this involves:

- attending courses and conferences (commonly referred to as Continuous Professional Development - CPD);
- taking relevant exams;
- regular assessment, designed to ensure that training is appropriate;
- appraisals (which are a means of identifying and discussing weaknesses, and opportunities for personal development);

Patient and Public Involvement

The involvement is about ensuring that the services provided suit patients, that patient and public feedback is used to improve services into day-to-day practice to ensure an increased level of quality and appropriateness, and that patients and the public are involved in the development of services and the monitoring of treatment outcomes.

Users have the right to participate in the delivery and evaluation of health services and their involvement can bring many benefits. Thus, citizens should contribute to define a shared language, improve the appropriateness of the request, identify priorities, expectations and needs, provide information on the results in the short and long term, provide opportunities to detect and solve problems, and develop knowledge of the social perception of health. Questionnaires, patient associations, social media, and living labs are the actual instruments that are currently applied at local and national level to broaden the patient empowerment.

WHO defines empowerment as “a process through which people gain greater control over decisions and actions affecting their health” and should be seen as both an individual and a community process (32). Effective empowerment strategies include:

> “- increasing citizens’ skills, control over resources and access to information relevant to public health development;
>
> - using small group efforts, which enhance critical consciousness on public health issues, to build supportive environments and a deeper sense of community;
>
> - promoting community action through collective involvement in decision-making and participation in all phases of public health planning, implementation and evaluation, use of lay helpers and leaders, advocacy and leadership training and organizational capacity development;
>
> - strengthening healthy public policy by organizational and inter-organizational actions, transfer of power and decision-making authority to participants of interventions, and promotion of governmental and institutional accountability and transparency;
>
> - being sensitive to the health care needs defined by community members themselves.” (33).

Using Information & IT

This aspect of clinical governance is about ensuring that:

- patient data is accurate and updated;
- privacy of patient data is respected;
- full and appropriate use of the date is made to measure quality of outcomes (for example through audits) and to develop services contextualized to local needs.
- flows of information, records, data quality, and information systems.

Staffing & Staff Management

This relates to need for

- appropriate recruitment and management of staff;
- ensuring that underperformance is identified and addressed;
- encouraging staff retention by motivating and developing staff;

- providing good working conditions.

1.2.2 Accountability

With accountability, we mean an ethical and formal obligation to report, answer some of the results of the activities, and give evidence in a transparent manner to what was achieved. This activity is carried out with useful tools to help people understand the various management outcomes to both internal and external recipients of the organization and institutions (34). The attitude to the reporting of the results in applying the principles of independence, transparency, and accountability, regardless of the legal requirements and should arise from the desire of managers to spread the use of information to improve the quality of decision making and performance achieved. In addition, the same politicians also should show the same aspiration, in order to gain full legitimacy to remain in the role assigned to them by citizens (35).

We will try to explain why a culture of accountability is important in health care.

The primary reasons include improved quality of patient care and value for money spent on health care services. Publishing transparently the costs of health care services and programs assigns a more tangible value to the invested resources. Increasing the accountability of employees will also reduce overuse, misuse, and underuse of resources while better spending the existing resources. This aspect is closely related to the appropriateness of the health performances. Accountability also improves the quality of patient care by increasing the use of evidence-based medicine and performance measurement with the aim of reducing inappropriate care (36). Furthermore, accountability encourages the assessment of evidence from process and outcome measures by using feedback from performance measurement to improve processes and outcomes of health care activities. Finally, accountability is synonymous with the utilization of evidence-based practices, such as clinical practice guidelines, while enhancing learning and reducing variability. Intuitively, if employees and organizations are holding themselves more accountable, then the desire to learn and use evidence-based practices and performance measurement tools will be increased, thus creating continuous assessment, learning, and change. Consequently, variability in health care will decrease as a result of a culture that emphasizes accountability (37).

1.2.3 Appropriateness

Appropriateness is a complex issue with various dimensions and definitions and these differ between countries. However, most definitions of appropriateness address a number of key requirements: that care is effective (based on valid evidence); efficient (cost-effectiveness); and consistent with the ethical principles and preferences of the relevant individual, community or society. The priorities given to each of these dimensions vary in different populations. Appropriateness contains a judgment regarding care at different decision levels (such as health care delivery, health care policy, and research and development) that summarizes clinical, public health, economic, social, ethical and legal considerations. It is therefore important to consider who makes the judgment, on what evidence and following which process of consultation (38).

Of course, a health intervention ought to be appropriate in terms of professional and organizational way. Professional appropriateness means that the service must be delivered to the right patient at the right time and for the right duration.

Organizational appropriateness means that the service is to be provided in the right setting and with the right professional. The improvement of appropriateness should maximize the probability of favourable effects (effectiveness), minimize adverse events (safety), and, of course, optimize the resources.

Furthermore, ethical values play a central role in determining the priorities given to components of appropriateness and it must be accepted that defining appropriateness is, to a large degree, a socio-political process, involving multiple players and preferences (38).

1.2.4 Ethical principles and priority setting

It is generally acknowledged that priority setting in health care is primarily a socio-political rather than clinical process. Over the last years there has been an international trend searching for priority setting systems based on micro-level rational decision rules, towards the development of “meta-rules” that inform the process of priority setting (39). This is commonly known as the principles-based approach to priority setting. The Scandinavian countries have been very active in this debate. In Sweden, for example, a national Priorities Commission has established three ethical principles to inform policy on priority setting (40). These were, in order of importance: human dignity (equal rights for all), need and solidarity

(identifying those at greatest need and supporting those less able to exercise their rights) and lastly cost-efficiency.

We must spend a few more words about the equity of access. Equity of access refers to the ability of a single user to access to health services and to have the same effectiveness. The concept of equity evokes the need to respond to user requests and in particular those of the weakest. It is indissolubly linked to the concept of equality and effectiveness in response to the needs and the quality of services to create "public value" (41).

An equitable health system should ensure essential services to all citizens, regardless of age, gender, race, religion, residence, educational, and socioeconomic levels.

In addition, a period equity and an intergenerational equity can also be defined. The first can be considered as the ability, in a historical moment, to provide users fairness of conditions and a qualitative and quantitative satisfaction of expectations with regard to the required sacrifices. Intergenerational equity is attributable to the relations between successive generations and refers to the ability of the health service to offer a homogeneous relationship between benefits and sacrifices, avoiding benefiting a generation at the expense of another.

1.2.5 Evaluation

It is now clear the critical importance that the evaluation of healthcare interventions assumes as a method able to offer a continuous improvement in the quality of care and health services.

For completeness, we also provide definitions of evaluation. Probably the most frequently given definition is “Evaluation is the systematic assessment of the worth or merit of some object.” (42).

This definition is nearly perfect. Better perhaps could be a definition that emphasizes the information-processing and feedback functions of evaluation. A more complete definition provided by William M.K. Trochim[4] could be

[4] Dr. W.M.K. Trochim received his Ph.D. from the Department of Psychology at Northwestern University in the area of Methodology and Evaluation Research. Among many roles, he was the 2008 President of the American Evaluation Association (AEA), has served multiple terms on its Board of Directors and is the Chair of the AEA Evaluation Policy Task Force.

"Evaluation is the systematic acquisition and assessment of information to provide useful feedback about some object." (43) (44).

Both definitions agree that evaluation is a "systematic" attempt and both deliberately use the ambiguous term "object" which could refer to a program, policy, technology, service, person, need, activity, and so on. The latter definition emphasizes acquiring and assessing information rather than assessing worth or merit because all evaluation work involves collecting and examining through data, making judgements about the validity of the information and of inferences we derive from it, whether or not an assessment of worth or merit results.

The generic goal of most evaluations is to provide "useful feedback" to a variety of actors including promoters, contributors, users, administrators, staff, and other relevant stakeholders. Most often, feedback is perceived as "useful" if it supports in decision-making. However, the relationship between an evaluation and its impact is not simple. More studies that seem critical sometimes fail to influence short-term decisions, and studies that initially seem to have no influence can have a delayed impact when conditions that are more congenial arise. Despite this, there is broad consensus that the major goal of evaluation should be to influence decision-making or policy formulation providing empirically driven feedback (45).

Evaluation is a complex term used in most fields of human activity and in different disciplines. In the company context evaluation has a purely economic meaning "having money", then estimate and express in monetary terms the quality and quantity of an object (46).

In an organizational meaning, however, it corresponds to judge the compliance or appropriateness of a behaviour, an action or a result compared to an expected paragon. In a second meaning the word "assess" overlaps with the word "confirm" and the person who implements the audit, the evaluator, judges the behaviours, actions, and results achieved in the company management. This process takes place in an alternative or parallel manner on multiple levels: at the level of individuals (micro), on the business joints (meso), at the level of companies or group of companies (macro).

The evaluation process considered as verification and production of judgments about behaviour and results is an essential part of governance management systems of public companies. In particular, in some interpretations evaluation systems are considered as mechanisms that increase the rationality of the decision-making process and business functionality. They are organizational variables that can guide the behaviour of individuals and the individual results to the strategic and operational objectives of the company.

Some studies, however, have shown many critical issues associated with the use of these mechanisms in the context of the public. Because of the difficulty in reconciling the external accountability, linked to public liability, with monitoring requirements and assessments related to internal managerial purposes, the risk could be that an approach to routine motivated only by the legislative obligation emerges (47). A balance among structural and behavioural aspects is therefore needed, as well as an action aiming to harmonize organizational and informative elements, at a micro, meso, macro levels in order to facilitate the achievement of business goals. In this sense, the systems of planning and control and the evaluation must be integrated for the influence they exercise on behaviours and thus on the company's results. Programming and control systems are based on the definition of a set of objectives to be reached and on the concurrent and subsequent verification of the degree of achievement of these objectives to guide decision-making.

The assessment must be a phase of the planning and control; this stage must be strongly linked to the development of information systems, and to the evaluation of the compliance of the results relating to the objectives. It is also important to determine the period of time that is considered necessary for the achievement of the assigned aims.

It has already been said that the evaluation should be an integral part of the planning phase as well as the control. We must specify this aspect explaining the planning and evaluation cycle.

The planning & evaluation cycle

Often, evaluation is construed as part of a larger managerial or administrative process, referred as the planning and evaluation cycle (Figure 5). This distinction between planning and evaluation is not always clear. Usually, the first stage of such a cycle, the planning phase, is designed to elaborate a set of potential actions, programs, or technologies, and

select the best for implementation. Depending on the organization and the problems being addressed, a planning process could involve any or all of these stages (48):

- formulation of the problem, issue or interest;
- the comprehensive conceptualization of the major alternatives and their potential implications;
- evaluation of the alternatives and selection of the best one;
- implementation of the selected alternative.

Although these stages are traditionally considered “planning”, there is a lot of “evaluation” work involved. Evaluators are trained in needs assessment, they use methodologies (such flow chart or conceptual maps) that help in conceptualization and detailing, and they have the skills to help assess alternatives and choose the best one.

In addition, the evaluation phase involves a sequence of stages that typically includes:

- the formulation of the major objectives, goals, and hypotheses of the program or technology;
- the conceptualization and operationalization of the major components of the evaluation program, participants, setting, and measures;
- the design of the evaluation, detailing how these components will be coordinated;
- the analysis of the information, both qualitative and quantitative;
- the utilization of evaluation results.

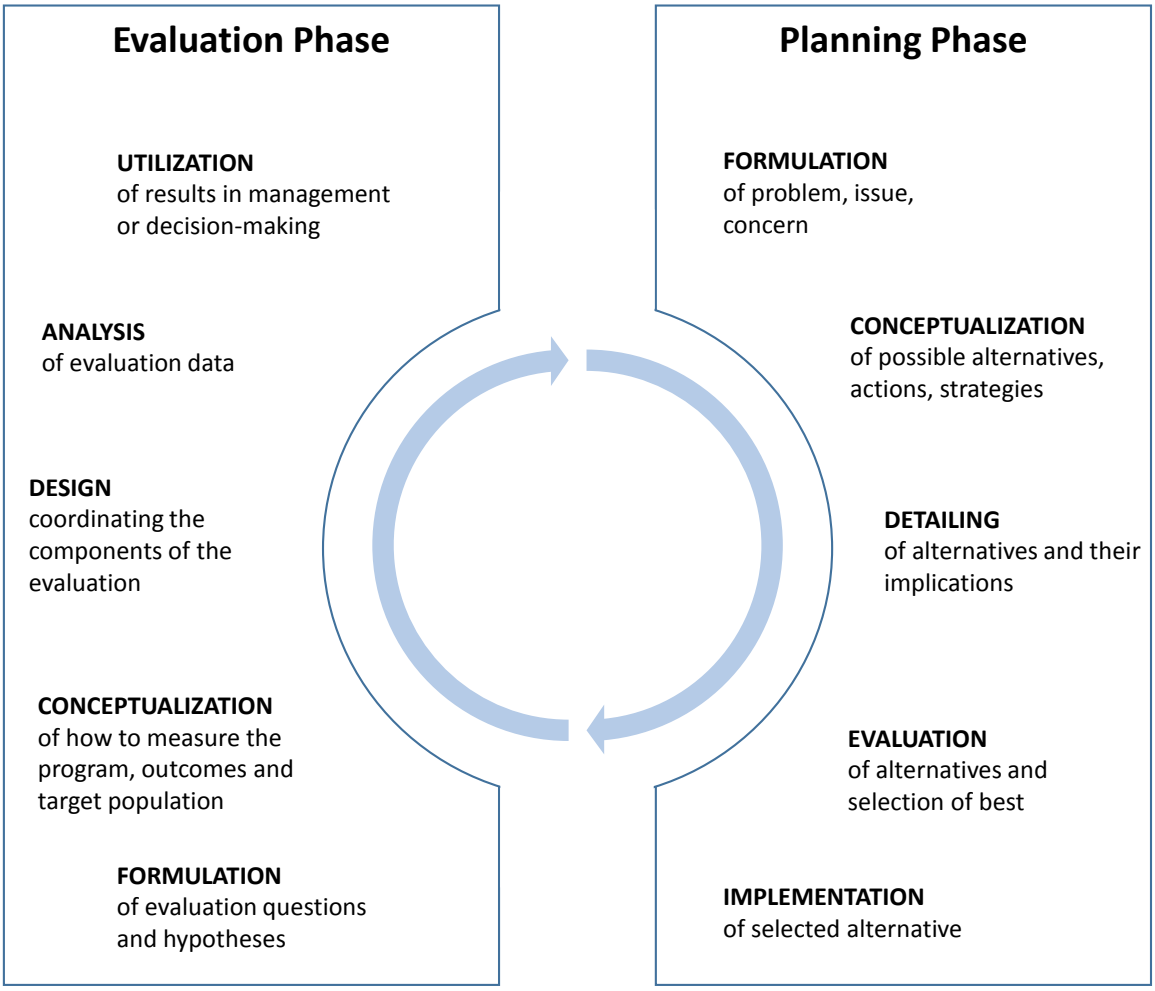


Figure 5. *Planning and evaluation cycle (modified by W.M.K. Trochim, 1992 (43)).*

Some evaluation strategies comprehend the most general fields in which the evaluators work.

- "Scientific-experimental models" are probably the most historically dominant evaluation strategies. Taking their values and methods from the sciences, they emphasize the desirability of impartiality, accuracy, objectivity and the validity of the evidence generated;
- the second class of strategies are "management-oriented systems models". They emphasize comprehensiveness in evaluation, placing evaluation within a larger framework of organizational activities, and very often they came from the industrial world;
- "qualitative-anthropological models". They emphasize the importance of observation, the need to retain the phenomenological quality of the evaluation context and the value of subjective human interpretation in the evaluation process;

- "participant-oriented models". As the term suggests, they emphasize the central importance of the evaluation participants, especially clients and users of the service.

In this work, the focus is on the scientific-experimental models and on a summative assessment type. Summative evaluations examine the effects or outcomes of some object. They summarize it by describing what happens subsequent to the delivery of a programme or technology, assessing whether the object can be said to have caused the outcome, determining the overall impact of the causal factor beyond only the immediate target outcomes, and estimating the relative costs associated with the object (49).

Summative evaluation can be subdivided in:

- "outcomes evaluations" that investigate whether the performance or technology caused demonstrable effects on specific targeted outcomes;
- "impact evaluation" assesses the overall intended or unintended effects of a service as a whole;
- "cost-effectiveness" and "cost-benefit analysis" report questions on efficiency by standardizing outcomes in terms of costs, values, and quality-adjusted life year (QALY);
- "meta-analysis" integrates the outcome estimate from multiple studies to arrive at a combined judgment on an evaluation question.

Indicators

A famous statement attributed to Florence Nightingale[5] appropriately captures the performance–quality–management relationship: "The ultimate goal is to manage quality. But you cannot manage it until you have a way to measure it, and you cannot measure it until you can monitor it" (1) (2). To achieve this goal is mandatory to define appropriate indicators and measures able to capture health and health system-related trends and factors (50). Healthcare stakeholders agree on the meaning and role of these performance indicators for making decisions and steering health systems (51). Most of these indicators are process and/or outcome measures, emphasizing the focus on desired results and the

[5] Florence Nightingale (1820 - 1910) was a celebrated English social reformer and statistician, and the founder of modern nursing.

processes that yield these outcomes. According to the SMART paradigm these indicators have to monitor target that are considered to be Specific, Measurable, Achievable, Relevant, and Time-limited, and relate to national and local healthcare systems objectives as embodied in its core principles of provision of universal and comprehensive services, patient responsiveness, staff value, and support, reducing health inequalities, quality improvement, and fair funding (52).

Evaluating a healthcare performance requires an adequate information support, a set of indicators to assess effectiveness, efficiency and user satisfaction. Given the complexity of health care systems, there are disagreements on the selection of indicators. The construction of the indicators is most often based on empirical form from administrative data, clinical data, or from ad hoc dataset made. Regardless of their origin, indicators must meet certain requirements. They must be (53):

- quantifiable, so as to allow calculations, analysis, comparison;
- of simple construction and use, having to understanding the essence of a phenomenon;
- relevant, having to build the base on which to make choices;
- sensitive and specific;
- integrated into a system that through the use of multiple indicators provide a picture as complete as possible of the phenomenon that one wants to understand.

Indicators can be defined as "variables with high information content that allows a summary assessment of complex phenomena, providing sufficient information to guide decision-making" (54).

1.3 Implementing the value-based Healthcare

1.3.1 Organizational models

Due to advances in science, medicine, and technology, the length of life is much extended; this leads to meet the needs of an older population and therefore more exposed to risk of developing one or more comorbid conditions. The best quality of care in this case is not only the management of one chronicity, but also the management of multiple chronic illness, which will require the intervention of several professionals and different services

over time. It is also not sufficient to manage the chronicity but it is important to make the patient feel healthy even in sickness. Although the concept of health is roughly linked to the idea of a sick body, a damaged organ or pathological physiological functions, this approach is not able to grasp the complexities comprised in what to be healthy means. In 1946 the World Health Organization (WHO 1946) defined health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (55).

The management of complex situations, having in mind this extended meaning of health, requires the definition of new organization design and models.

Organizational design typically refers to the decomposition of the organization into subparts and to those processes that integrate the subparts to support the strategy and achieve organizational aims (56). As already seen, one of the aim of value-based healthcare is to produce a shift in the concept of care from volume and intensity of services toward high-value, patient-centred care (57).

Within this new paradigm, the organization design should change from a vertical approach to disease towards a transversal, personalized one. The health-related processes must necessarily take place horizontally, involving the entire services link to a specific health question, considering the different involved stakeholders, the relationship between them and their degree of coordination.

The implementation of care pathways directly impacts this necessity with the aims to give a quality of life as high as possible, or at least with a good level of shared acceptability.

A care pathway is a multidisciplinary process of specific structured actions, based on evidences, undertaken by different actors (stakeholders), each with their own responsibilities, limits to respect and decisions to deal with. Therefore, the clinical pathways are seen themselves as organizational model.

1.3.2 The importance of approach to Healthcare through the Clinical pathways

The complexity of the health system can create situations that lead to variability, defects in appropriateness and continuity and poor integration in care; all these conditions facilitate the possibility of errors and therefore of low or inadequate quality of care.

When a complex object is analysed, it is used to break up the analysis and proceed by "functions". In the world of health, this break up corresponds mostly to an analysis by "structure" (Operational Unit) to which attribute clinic and organization responsibility of the specific clinical moment. However, it could happen that in spite of high-verified quality for the single service, we could have no assurance on the quality of the entire care pathway and on the outcome, which is the mixture of many separate interventions. The pathways are based on the principle that the variability is not caused only by the clinical performance, but also, and often primarily, by the procedures of assistance distribution, and by organizational and operational aspects.

A care pathway contains a number of different elements including a combination of good practice, quality control and improvement, design, planning, and implementation of modification (58). It is viewed as a multi-disciplinary framework of expected care. There is no a single definition of Integrated Care Pathway (ICP) because some institutions link the definition to patient groups or case-types, and others to a particular health condition or pathology.

1. According to The European Pathway Association: A care pathway is a complex intervention for the mutual decision-making and organization of care processes for a well-defined group of patients during a well-defined period. Defining characteristics of care pathways include:
    - an explicit statement of the goals and key elements of care based on evidence, best practice, and patients' expectations and their characteristics;
    - the facilitation of the communication among the team members and with patients and families;
    - the coordination of the care process by coordinating the roles and sequencing the activities of the multidisciplinary care team, patients and their relatives;
    - the documentation, monitoring, and evaluation of variances and outcomes; and
    - the identification of the appropriate resources.

The aim of a care pathway is to enhance the quality of care across the continuum by improving risk-adjusted patient outcomes, promoting patient safety, increasing patient satisfaction, and optimizing the use of resources (59). Other definitions of clinical pathway are:

2. Journal of Integrated care: An Integrated Care Pathway determines locally agreed, multi-disciplinary practice based on guidelines and evidence, where available, for a specific client group. It forms all or part of the clinical record, documents care given and facilitates the evaluation of outcomes for continuous quality improvement (60).
3. Evidence-based medicine: a care pathway can be defined as a structured multi-disciplinary outline for anticipated care, placed in an appropriate time frame, to help a patient with a specific diagnosis or set of symptoms move through a continuum of care; receiving evidence-based care to maximize positive outcomes (61).
4. Wilson: a multi-disciplinary process of patient focused care which specifies key events, test and assessments, occurring in a timely fashion to produce the best prescribed outcomes, within the resources and activities available, for an appropriate episode of care (62) .

All definitions underlines that care pathways brings together evidence-based multi-disciplinary practice for a particular group of patients, to shape the optimum episode of care for all patients who have a specific condition or who are undergoing specific procedures. Thus in care pathway the focus is on the patient rather than the system.

In Table 1, we summarized the motivations, contents, and purples of an efficient care pathway (58).

Results demonstrated that a clinical pathways designed, conducted and monitored with appropriate steps , improve outcome by providing a mechanism to coordinate care and to reduce fragmentation, and although controversial elements still exist, clinical pathways can have a positive impact on quality in health care (63).

Table 1. *Pillars of care pathway (modified by Wonderlich S, 2007 (58)).*

Reasons for developing a care pathway	Contents of a care pathway	Aims of a care pathway
Ensure the delivery of consistent high quality care	Algorithms defining the planned pathway within a time frame	Provide best evidence-based care
Transfer evidence-based care into practice	Referral, transfer and discharge guidance	Facilitate translation of national directives into local practice
Are patient centred, comprehensive and clinically driven	Local and national standards	Improve multi-disciplinary and multi-agency communication
Reduce unnecessary variation in practice	Evidence-based guidelines	Sustain and make equitable quality standards
Reduce risk	Patient information	Reduce variance in practices
Provide integration of care across organizational boundaries	Information recording – clinical record	Improve clinician/patient communication and satisfaction
Empower training/education and skills transfer	Information recording – variance tracking	Identify research and development questions
Are a tool for systematic action to the continuous improvements in patients care	Information recording – tests, charts, assessments, diagrams, letters, forms, information leaflets, satisfaction questionnaires	Involve team members in service development
Provide evaluation of the impact of service reshape and enhancement	Information recording – scales for measurement and outcomes of clinical effectiveness	
Are a model to support many key local and national programs simultaneously	Information recording – space to add activities or comments to a standard care pathway to individualize care for a specific patient	
Provide an opportunity to involve teams in service restructure		

2 Methods for outcomes evaluation

The measure and the comparative evaluation of the outcomes of health interventions are considered key strategies to promote the quality and equity of health care. The term "outcome" means "the end result of a process" which in this field is the improvement of the state of health of the person or of the population.

The term health intervention refers to all welfare activities in health services for the prevention, diagnosis and treatment. The health intervention is therefore a phenomenon estimated to different levels of care, in which different clinical and organizational responsibility are recognizable. In the case of integrated activities between different care levels and the presence of multi-disciplinary collaborations, evaluation is complex.

Until today most of the observational studies on the comparative outcome evaluation focused on acute hospital care. Recently the outcome assessment is expanding in the context of ambulatory care (territorial medicine or primary care), rehabilitation of post-acute care, organizational models in emergency, and drug treatments in clinical practice. In an outcome study, it is essential to clearly identify the clinical and organizational context that is being evaluated, in order to highlight critical issues, responsibility and promote changes. Evaluation is important for health care services who intend to monitor over time the outcomes of health care interventions in structures, or for a group of patients. Moreover, assessment is important for clinical services or health care professionals who want to test the outcomes difference of different treatments or procedures used in clinical practice. The evaluation also requires a multidisciplinary approach: the outcome evaluation is, in fact, a real study, which requires a protocol design and the development of the methods necessary for its implementation. The evaluation process requires the collaboration of various professionals with different and complementary expertise.

The methodology for the comparative evaluation of health outcomes is a study project that must fulfil the specification of many requests.

2.1 Study hypothesis and goals

The assessment of outcomes can have different purposes.

- Evaluate the **effectiveness** in clinical practice (effectiveness) of health interventions that have already been demonstrated theoretically (efficacy). The observed efficacy in clinical practice is very different from that estimated in experimental studies. The outcome evaluation can provide important notes about the real impact of the treatments in current practice and for the health of patients.
- Evaluate the clinical practice effectiveness of health interventions with no evidence of efficacy. The reference is to the evaluation of health care treatments which are not available or not possible (for ethical, organizational, social, economic reasons) to conduct using randomized controlled trials (RCT). This happens mostly for non-pharmacological interventions, particularly for organizational models, for interventions concerning preventive, diagnostic, therapeutic and rehabilitation technologies.
- **Systematic and comparative evaluation of hospital facilities or medical areas, for accreditation, remuneration, and information to citizens**. The health services can adopt models of accreditation, funding and remuneration of hospital facilities based on the evaluation of performance achieved, as it can be a lot of heterogeneity of treatment outcomes among providers. Users also have the right to choose freely the place of care. Therefore, a proper function of protecting the health and purchasing services requires valid and reproducible efficacy information of the outcomes of all the providing structures.
- **Production of evidence about the relationship between structural and organizational characteristics (for example volume activity) or between different modes of care delivery and effectiveness of care**. Organizational, structural, economic factors may change the effectiveness of health interventions. In particular it is important for the clinical governance and service management to identify factors that, when changed, can improve the effectiveness of treatments. An important example is that of the volume of specific health interventions that are associated with the maximum effectiveness of the treatments: services that provide larger or smaller volumes compared to an estimated threshold may offer treatments less effective than expected, or even have harmful effects. Identifying optimal thresholds of activity is therefore very important for planning, accreditation, and remuneration of providers.

- **Evaluation of changes during time of treatment outcomes**. The rapid development of new technologies and treatments for the diagnosis and treatment of many diseases requires a continuous adjustment of resources (facilities, equipment, organizational models, and professional skills) to the new standards and health goals. Important information on the effectiveness of these changes can be seen by monitoring outcomes over time and comparing them between different patient groups or different structures before and after the change.

2.2 Study designs

Many are the study designs available to make a comparative assessment of outcomes and many classifications of study designs are available. Understanding the classifications and choosing the most appropriate study design for its aims is not always easy and immediate. Among the primary design, the ideal kind of study to evaluate efficacy of medical treatment is the randomized clinical trial (RCT). The great advantage of this type of study is in the randomization of patients in the two (or more) treatment groups. Randomization can attribute the possible outcome differences only to the treatment, because it cancels the possible selection bias of patients and distributes uniformly known and unknown confounders. A weak point of RCTs is their external validity: very often, the results are not used in clinical practice because there is too much difference between the perfect theoretical conditions of the trial and the real conditions and variabilities of the practice.

Observational studies provide analysis of the events and patients in their usual condition, i.e. clinical practice (effectiveness). The data can be collected at the aggregate level for ecological studies or time series, or individually, for studies of transverse or prevalence, longitudinal cohort, case-control, etc. Patients are therefore not randomized in the different groups and this can lead to unbalanced distribution of comorbidities, disease, confounding, etc. So the results of an observational study can be systematically distorted because of the non-random distribution of patient characteristics. Observational studies may have problems of internal validity: the study should not be designed ad hoc only for some specifics needs, patients or aims.

2.3 Study population

The definition of the study population is a key point and some considerations on the criteria for inclusion and exclusion should be made. First, one need to choose the sources of the data. For the identification of the population health information systems, disease registries or clinical documentation collected ad hoc can be used. Critical points of all the clinical documentation are encoding problems, completeness of filler fields, quality and comparability of the data.

- **Inclusion and exclusion criteria**. Once established the source of information, it is necessary to apply specific inclusion and exclusion criteria. They allow the definition of the study population, i.e. the population that will maximize the level of accuracy of the assumptions and the validity of the study results.
- **Enrolment period and sample size**. The choice of the enrolment period depends on the purpose of the study. For example if we want to assess the effectiveness of the introduction of a new technology, the enrolment period must take account when the technology has come into use. Similar considerations should be done to test the effectiveness of a new care path or organizational model. In this case, the researcher has to make sure that two periods with two different organizational models, have a volume of activity sufficiently large and comparable. The enrolment period has consequences on the population size in the study. The sample size is a very important parameter for the statistical power. To calculate the sample size the statistician needs to consider not only the absolute value of the clinical records, but even the portion of expected events (outcomes), the exposed patients, and the estimation of the expected effect. All these parameters are required for the calculation of the sample size.
- **Residence**. According to the hypothesis of the study, different choices about what kind of people based on residence in a given geographical area can be done. The comparison can be done for different regions, different health districts etc.
- **Age classes**. According to the hypotheses of the study, the most appropriate age group must be identified, considering the different incidences of the diseases and their characteristics depending on age. For example, in a study on the clinical

outcomes of hip fracture, it is appropriate to include only patients aged greater than or equal to 65 years.

- **Hospital admission category**. Depending on the aim of the study, choices of inclusion or exclusion related to the type of hospitalization can be made. For example, only ordinary hospitalization, urgent admissions, long-term care admissions, rehabilitation, day hospital etc.
- **Treatment indications or contraindications**. When surgical or therapeutic procedures are studied, it may be appropriate to exclude the conditions in which the intervention is rarely appropriate. In this case, the skills and experience of the clinician is critical in order to identify the best indications or contraindications. For example, while comparing outcomes related to patients who carry out haemodialysis or peritoneal dialysis, patients with previous history of abdominal surgery can be excluded, since they could not support the peritoneal dialysis. In the study of the outcomes of hip fracture, cases of non-operated patients could be excluded from the study, because those patients are different from the rest of the population.

2.4 Exposure

The exposure must be defined a priori while setting an evaluation study. In epidemiological studies, exposure is the main factor used to measure the extent of the association with the outcome. The definition of exposure varies according to the hypothesis in the study. The modality of identification and the quality of the measurement depends on the source of information. The modalities of identification analysed as exposure are: socio-demographic factors, treatments, and time. Depending on the research hypothesis, the goals and the specific context of a study, a variable may be the main factor of exposure or a potential confounder or potential effect modifier.

Socio-demographic factors.

- **Age**. In epidemiological studies, it is essential to take account the age distribution of the population. Age is strongly correlated with the presence of chronic diseases, such as cardiovascular disease, diabetes, osteoarthritis. In general, older people have worse clinical outcomes of young people. Moreover, the signs and symptoms

of disease often differ between young and old. In the assessment of individual clinical risk, age generally has an independent effect of the presence of other factors.

Consequently, in evaluation studies the choice of a range of age rather than another may result in different clinical outcomes with different implications. In many cases the population is studied separately by age groups (adults, the elderly, late elderly).

- **Gender**. Men and women differ in the risk of incidence of various diseases and death in different age categories. Scientific evidence shows that men and women are not only biological and behavioural different, but also in terms of effectiveness and access to treatment. For this reason gender is a very important variable to be considered in any outcome evaluation study.
- **Residence**. The residence is used for several reasons: it can indicate the probability of access to health services by the population under study (for example residence near a great complexity hospital) or it can be a proxy of exposure to factors potentially associated with the outcome (for example environmental pollution, socioeconomic level).
- **Socio-economic level**. The socio-economic factors have a special role. They are able to strongly influence the clinical outcomes but also the access to treatments. Culturally and economically disadvantaged people fall sick more, have higher mortality, are more susceptible to inappropriate therapy, have less access to effective therapies.
- **Treatments**. In outcome studies, any medical intervention can be considered a treatment. Interventions, procedures, specific drug treatments, types of service (for example hospital care versus local care), types of care (for example medical versus surgical), organizational models in emergency assistance (for example hub-spoke networks), prevention interventions (screening), diagnostic and therapeutic healthcare pathways, types of structures (private versus public), volumes of activity (high volume versus low volume), organizational parameters (preoperative stay) can be compared.
- **Time**. Time is the exposure variable of interest in the outcome comparative evaluation between different periods. If we want to study the change during time of an outcome variable of exposure, it is represented by the unit of time chosen

(days, months, years, etc.). As all other exposures considered, the time can be, in turn, a potential effect modifier.

2.5 Outcome

The outcomes of health care interventions include mortality, morbidity, complications, changes in the physical or functional status, quality of life and satisfaction, and use of drugs, etc. The choice of the most appropriate measure of outcome depends on the hypothesis of the study, the aims of the study, the type of study population, the validity and reproducibility of the measurement, the ability to detect expected changes in health status, the ability to detect changes during time and the comparability with other studies.

The classification of outcomes is very extensive. Among all definitions of different types of outcome, in statistics, a proxy or **proxy variable** is a variable that is not by itself directly relevant, but that serves in place of an unobservable or immeasurable variable (64). Therefore, indirect or proxy indicators are used to demonstrate the changes or results where direct measures are not feasible because some objectives are difficult to monitor. It is often necessary to select indirect or proxy indicators that may be easier for evaluators to measure.

- **Mortality**. Mortality is one of the outcomes used for clinical relevance, thanks to the availability of health records, the level of validity and reproducibility. According to the hypothesis of the study, we can measure the short-term mortality in the long term (survival study). The time window of observation (or follow-up) can vary depending on the context and the hypothesis of the study. In-hospital mortality, early in-hospital mortality within a certain period of time, or death at 30, 90, 180 days to 1 year etc., can be measured. If death occurred after discharge, another database with which to check, through the record-linkage procedure, the death of the patient, and informatics skills are indispensable. Very often because of the absence of quality of data in databases, mortality from all causes (overall mortality) is used, but for some diseases, it may be important to examine the specific cause of death. Operationally mortality is a ratio (or percentage) of the number of deaths in the specific period over the study population. For survival studies, a more complex

statistical method is rather used that takes account of the function probability of survival.

- **Morbidity**. The occurrence of a disease is a widely used measure of outcome. For example, the impact of patients with kidney failure, the incidence of cardiovascular events, the incidence of bedsores and hospital infections, the incidence of hospitalization for complications due to treatment can be assessed. In the case of hospitalizations, the rate of hospitalization for a condition can be used.
- **Drug use, access to services, access to treatment.** The use of drugs or the access to specialized services can be used as a proxy measure for disease. However, the meaning varies according to the hypothesis of research and the type of study. For example, the use of pharmacological treatments, both in the acute phase or in the post-acute cases, both in the long-term monitoring of chronic diseases, can be used as an outcome measure. Access to surgery within 48 hours of hospitalization in patients with hip fracture is one of the outcome measures more known in orthopaedic area, as well as the time between the hospital admission and the surgery. These are proxy outcomes that could be linked to mortality, complications, pain, and mobility outcomes.
- **Complications.** A particular example of outcome measure are the complications. These conditions may occur in the natural history of the disease and can be prevented or controlled by medical treatment. We can distinguish acute complications and chronic complications. The definition of complication is difficult both from the conceptual point of view and for the operative. The difficulty is apparent in particular when from the database is not possible to identify the temporal sequence of events.

2.6 Effect modification

In epidemiology, this term is used to describe a situation in which one or more factors modify the relationship between the exposure and the outcome in the study.

It is important to distinguish the “effect modification” by “confounding”, which is defined as the existence of a factor associated with exposure and outcome in question and

responsible, in whole or in part, of the association (or lack of association) observed between exposure and outcome.

The effect modification implies, however, a different effect on the outcome of the exposure as a function of the values assumed by a third factor, called "modifier effect". Therefore, modifier effect is a variable that differentially (positively and negatively) modifies the observed effect of a risk factor on disease status. Different groups have different risk estimates when effect modification is present.

In the context of the outcome, comparative assessment is important to define a priori, based on available evidence or specific research hypotheses, what are the factors that have been interested in investigating the role as potential effect modifiers.

Modification effect is evident in terms of the heterogeneity of measures of association between layers in stratified analysis; in multivariate statistical models, it can be represented by the addition of interaction terms between exposure and factor in the study and assessed by the contribution of these terms to the predictive ability of the model.

In both cases, the hypothesis that there is a phenomenon of effect modification must be formally verified with appropriate statistical tests.

2.7 Confounding

The confounding refers to the case in which the measure of association between exposure and the outcome is "confused" by the effect of another factor. It is said, therefore, that the estimate of effect is suffering from distortion (or bias). By definition, a confounder is a risk factor associated with both outcome and the exposure, which is distributed heterogeneously among the different levels of exposure, but should not be an intermediate factor in the chain of causality between exposure and outcome.

A classic example is given by confounding by age: if we want to compare mortality rates between different regions, the observed difference could be explained by the different age distribution in the compared populations. The interpretation of the differences between regions would not be correct without a standardized measure for age.

Another example of confounding are factors of clinical severity, which, potentially are associated with the outcome, because they are not be uniformly distributed between the compared groups (population groups, treatments, facilities).

There are several techniques to control the confounding and limit the distortion in the effect estimates, including the risk adjustment, propensity-adjustment and the change-in.

A potential confound particularly relevant in this type of study is the clinical severity.

- **Clinical severity**. For clinical severity, we mean all of the clinical features of the individual in a defined time, able to influence the likelihood of adverse events. The clinical severity includes several components. The major determinants of clinical severity are the **pathology** under study and coexisting chronic conditions (comorbidities). It is important to measure the severity of both components, acute and chronic, taking into account their potential influence on different outcomes.

  The disease under study can be more or less serious depending on many factors, such as the duration of the disease, the intensity of current treatments, the number and intensity of aggravations. The time window used in the measurement of gravity into its components, acute and chronic, may vary depending on the context of the specific study, the hypothesis and outcomes. In some cases, in fact, it makes more sense to measure a given variable of gravity in a restricted time to better describe the component of acute gravity. In other cases, it is more useful the measurement a factor in the long term (previous history) to better describe the chronic component of gravity.

  Dealing with clinical severity, **comorbidities** assume great importance. Comorbidities, or concomitant pathologies, are not related in terms of aetiology and pathogenesis with the principal diagnosis. Comorbidities differ from complications that are series of primary diagnosis. The paradigm of comorbidity is a chronic condition, such as diabetes mellitus, chronic obstructive pulmonary disease or chronic ischemic heart disease. In most cases, compared to patients without comorbidities, those who have coexisting chronic diseases have a higher probability of death or acute adverse events that require further diagnosis and therapies. While many clinical trials tend not to include patients with comorbidities to limit estimates effect distortion, observational studies have the advantage of

examining populations and allow a better assessment of the impact of comorbidities on the prognosis and clinical outcome.

In addition, the number of comorbidities is an element of gravity. Number and type of comorbidities may have different importance depending on studied clinical condition, hypothesis and outcomes. The type and number of comorbidities can influence the allocation of patients to a particular exposure or intervention: for example, in a study of the outcomes of hip fracture among the elderly, patients with severe comorbidities are less likely to receive surgery.

Another factor that can influence the results (particularly in studies involving the elderly population) is the functional and cognitive status of the patient that is the set of skills of the person in everyday life from a physical, mental and social point of view.

The level of cognitive function, psychological and psychosocial, can affect both the access to treatment and the outcome.

There are many questionnaires for the measurement of patients' health status, both generic (The Short Form (36) Health Survey, SF-36) and specific for diseases (Acute Physiology and Chronic Health Evaluation-Apache, Barthel activity of daily living index). In the analysis and statistical models that are used for the calculation of the measures of association, it is possible to insert the variables that take into account the severity of the disease and comorbidities, therefore adjusting the measure of association for these variables.

2.8 Bias and quality of a study

As previously mentioned an outcome evaluation study is a veritable experimental design and requires the writing of a protocol that specifies the study population, intervention, exposure, outcomes etc. In planning and conducting a study, it is unfortunately possible to incur into some errors. These errors can be random or systematic. **Random errors** occur due to the chance, which means that multiple measurements of the same outcome can produce different results. Nevertheless, the final average of all the random measurements gives the "true" result. **Systematic errors** occur due to the presence of a factor that systematically distorts the observations in the same direction, that is, multiple replications of the same measurement produce results that are always in the same direction and

"wrong". They affect the estimate of the investigated effect always towards the same direction (65).

Examples of systematic errors comparing two groups of patients are:

- selection bias: systematic differences between baseline characteristics of the groups that are compared;
- performance bias: systematic differences between groups in the provided care, or in exposure to factors other than the interventions of interest;
- detection bias: systematic differences between groups in how outcomes are determined;
- attrition bias: systematic differences between groups in withdrawals from a study;
- reporting bias: systematic differences between reported and unreported findings.

Systematic errors affect the precision of an evaluation project or research, because they negatively affect the estimate of the measured outcome and, in turn, the strength of inferences and of recommendations used by health professionals, researchers, policy makers.

It is important to mention a number of organizations worldwide that are using new standards for developing trustworthy clinical guidelines. One of such approaches, developed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group, offers systematic and transparent guidance in moving from evidence to recommendations (66).

A high quality study aims to implement at best methods for the reduction of bias. In order to facilitate the assessment of the quality of clinical studies, a number of critical appraisal guidelines and design-based quality checklists (67) have been developed by many international organizations. Some well-known and established checklists are Jadad (all areas, RCTs), Pedro (physiotherapy, RCTs), Chalmers (pharmacology, RCTs), DELPHI (all areas, RCTs), New-Castle Ottawa Score (all area, non-randomized studies). As they provide guidance to study evaluation, such checklists should be taken well into account during planning, conduction and reporting of a study, using them as a guide to reduce bias.

Study quality shows a dependence by the study design chosen, according to the evidence pyramid hierarchy (68) which depicts a trade-off between quantity and quality of studies (Figure 6).

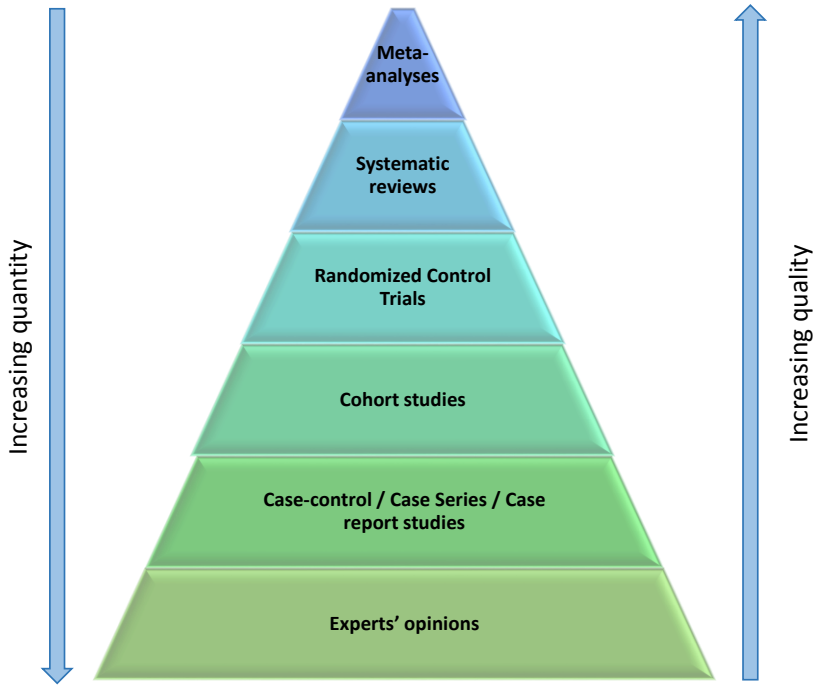


Figure 6. *Evidence pyramid hierarchy shows levels of evidence according to the degree to which they are not open to bias.*

Although the study design showing the highest methodological quality is RCT, not all research questions can be answered through the conduction of a RCT, either because of practical or ethical issues. Moreover, even when evidence is available from high-quality RCTs, evidence from other well designed and conducted study types may still be relevant (69).

2.9 Statistical analysis

Statistical analysis of the data is divided into several phases that can be summarized in a few steps: description of the study population and the phenomenon of investigation; estimation of the "raw" extent of association between exposure and outcome; control of confounding; estimation of measurement association between exposure and outcome "adjusted" for confounding; calculation of the precision of the estimates of association.

- **Description of the study population and the event of investigation**. The description of the population and the investigation event occur by taking back the absolute number of a characteristic or the event within the study population. The

frequencies of occurrence of the phenomenon or the presence of the characteristic in the population (for example number of men and women) are reported. The frequency is calculated as a count of the number of times in which the phenomenon or characteristic is presented, and is directly influenced by the size of the population. It allows quantifying the size of the phenomenon under study, but it tends to increase with the size of the population, does not lend itself to the comparison of the phenomenon among different populations. Then, relative abundance or percentage are calculated; it is well suited for the comparison of features between different populations (as it is not affected by the size of the population), but it is not proper in measuring the extent of the phenomenon under study, if not accompanied by the size of the affected population.

- **Estimate of the "raw" extent of association between exposure and outcome**. The measures of association between an exposure and an outcome quantify the degree of association between exposure and outcome. These shall be calculated by counting the number of times that the outcome is present in the different levels of exposure. Depending on how these counts are combined between levels of exposure, we have several measures of association based on the needs and goals. There are many measures of association, they depend on that outcome, and exposures are quantitative, dichotomous, ordinal, or survival variables. For example, assuming that both the outcome of the exposure are dichotomous variables (presence /absence), the following measures of association may be used: Risk Ratio (RR), Odds Ratio (OR).

  Risk Ratio. It expresses the ratio between the relative frequency of outcome in the exposed (i.e. the ratio between the number of outcomes exposed and the total number of exposed) and the relative frequency of outcome in non-exposed (i.e. the ratio between the number of outcomes non-exposed and total number of non-exposed).

  A RR of 1 denotes a lack of association between exposure and outcome (because the occurrence of outcome does not vary with exposure). Values greater than 1 show a positive association (the presence of exposure is associated with increased occurrence of the outcome), values of less than 1 show a negative association (the presence of exposure is associated with a lower occurrence of the outcome).

Odds Ratio. It expresses the ratio between the odds of outcome in exposed (that is the ratio between the number of outcomes exposed and number of non-outcomes exposed) and the odds of outcome in non-exposed (that is the ratio between the number of outcomes non-exposed and number of non-outcomes non-exposed).

An OR of 1 denotes a lack of association between exposure and outcome (because the occurrence of outcome does not vary with exposure). Values greater than 1 denote a positive association (the presence of exposure is associated with increased occurrence of the outcome) and vice versa for values smaller than 1.

In the case in which the studied event is rare (incidence <10%) among both exposed and non-exposed, the OR takes values very similar to the RR. In such situations, the OR is often called "relative risk". If the outcome of the study is not rare (incidence > 10%), the relative risk must be used.

For example, assuming that we are analysing time to event variable, we have to plan a **survival study**. Time to event variable means that, for each patient, it is measured not only if the outcome occurs, but also the time to episode. The time to event is the length of the period between the start of the observation (beginning date treatment, disease onset date, etc.) and the last observation.

Survival study uses Hazard rate (λ) which is the ratio between the number of events and the length of follow-up in the time interval considered. For the comparison of two or more groups, the **Hazard Ratio** is the measures of associations. HR is the ratio of the two hazard rates in the two groups, assuming that this is maintained over time. The predictive model for survival variables is the Cox proportional hazards regression that provides indeed the HR. The interpretation of HR is the same of RR and OR. Kaplan-Meier estimator is used in order to evaluate and visualize the survival function witch is the conditional cumulative probability to develop the event or conditional cumulative probability being free from event.

Since the previous measures relate to the univariate relationship between exposure and outcome, regardless of other factors potentially responsible for this association, they will be defined "crude" and constitute the preliminary quantification of the relationship between exposure and outcome in the study. In other words, they are useful to give an idea of the size of the relationship between

exposure and outcome, but cannot be interpreted in a causal chain because they say nothing about the possible influence of other descriptive factors.

- **Control of confounding.** Observational studies that compare groups, services, facilities or treatment must aim to take account of the possible heterogeneities existing in the studied populations, especially the differences in patient characteristics that may represent, in itself, a determining factor of care outcome. The main objective of the research is to study the differences in effectiveness between groups, services, facilities or treatments, without the possible confounding effect of uneven distribution (between groups, services, facilities or treatments) of the patients characteristics, which may affect the outcome. Regardless of the statistical methods used, the **risk-adjustment** can be schematized as a process, which calculates, for each of the groups compared, an expected outcome measure based on the relationship between the examined characteristics (risk factors) and the study outcome. The expected outcome is the outcome adjusted for severity. The risk-adjustment consists of two essential components: the construction of the measurement used to describe the a priori risk, simplifying the gravity, and the use of this measure in order to obtain adjusted outcome measures and thus comparable to each other, properly. The analytical procedure used for the construction of the measure of gravity takes the name of "predictive model", as model designed to predict the outcome expected based on risk factors. The classification of the gravity measurements provides, among others, an **empirical approach**. The core of this approach is the need for observational studies to identify confounders and check the effect on the study population. The instrument most frequently used for the construction of an empirical severity measure is the multivariate regression. It may be linear, logistic or Cox, depending on the study outcome that could be respectively a continuous variable (for example systolic blood pressure), dichotomous (for example transfer for worsening yes / no), or survival or waiting time (for example waiting time for replacement surgery of hip fracture, because of hospitalization for fracture). Once built the measure of gravity with the prediction model, the comparison of the results in the groups examined (facilities, populations or treatments) can be done for example with a **direct standardization**. From the operational point of view this method does not provide,

except in the simplest cases, an explicit computation of the different expected outcomes and the use of such values for the comparison between the groups, but the calculation and comparison are carried out simultaneously. The direct standardization provides the application of multivariate statistical models (they could be, depending on outcome, linear, logistic or Cox, see above) in which, in addition to the risk factors variables, there are N-1 dummy variables which represent the N groups being comparing. A dummy variable is a variable that takes the value 1 for the persons belonging to the concerned group and the value 0 for all others.

- **Estimation of measurement association between exposure and outcome "adjusted" for confounding**. While the crude measure of association between exposure and outcome concerns the univariate relationship between exposure and outcome, the adjusted measure of association quantifies the degree of association between exposure and outcome excluding other factors, potentially responsible, in whole or in part of that association. Therefore, the two measures may greatly differ if the adjustment for risk factors is important. The adjusted measure of association between exposure and outcome is the final part of quantifying the relationship between exposure and outcome, therefore, the main result of the study.

  In observational studies it is almost impossible to identify causal relationships between factors in the study because the residual confounding variables unknown or undetected are always possible. The adjusted measure of association between exposure and outcome is the best estimate that the researcher can do on the potential effect of exposure on outcome. Obviously, the result is confined to the data analysed, limited to the study population and the period of observation.
- **Calculation of the precision of the estimates of association**. The random error, unlike the systematic error, is not systematic and concerns the natural variability of any phenomenon, both in observational and experimental studies. Therefore, it does not interfere with the validity of the estimate, but only with its precision. That error tends to decrease as the number of subjects studied increase. In addition, for each given sample size, its effect can be quantified using the methods of inferential statistics. This quantification can be done by calculating the confidence interval or p-value.

The confidence interval is a range of values to which attribute a predetermined probability of containing the true value of the analysed measure.

Operationally, a maximum acceptable threshold error α is chosen a priori (generally 5%, but may vary depending on the context), then the confidence interval with "level of significance" 1-α (thus 95% in the example above) based on available data and probabilistic assumptions on them is calculated.

This interval includes the "true" value measure of association (calculated on the theoretical entire population) with a probability of 95%.

If the measure of association is a ratio (RR, OR, HR), and the 95% confidence interval includes the value 1, we cannot exclude that the groups being compared (exposed and unexposed) are equal in terms of the occurrence of the outcome. Conversely, if the interval does not include the value 1 (for example, is all greater than 1), we can assert that the occurrence of outcome exposed have a different (greater in the example) than non-exposed with a probability equal to 95%.

P-value is the probability (therefore, is a value between 0 and 1) that the difference between the results of the compared groups (exposed and not exposed, or different categories of exposure) is entirely due to the effect of the random error, making the hypothesis (called "null hypothesis") that there is no difference between the true outcome of the groups themselves.

Low values of the p-value (conventionally choosing the threshold of 0.05, but the choice depends on the context and the type of comparison) support the conclusion that the differences in the outcome of the two groups are result of chance with a very small probability. Thus, these differences are "real" in the sense that they cannot be wholly attributed to chance. Conversely, high values of the p-value leave serious doubts about origin of an eventual difference of occurrence of the outcome between exposed and non-exposed, as the probability that the differences are due to chance is great.

The two approaches, the confidence interval and the p-value, are based on the same theoretical assumptions and are therefore strongly correlated. In fact, if the confidence interval to 95% of a measure of the ratio between the two groups does not include the 1 (the two groups have the same outcomes, null hypothesis), the p-value for the comparison between those two groups is less than 5%.

3 Systems performance assessment in Healthcare

3.1 International overview

Health systems are expected to achieve and manage results in line with established objectives and quality standards. Many Countries and international organizations have recently renewed their interest in how their health systems perform. They developed conceptual frameworks for monitoring, measuring, and managing the performance of their health systems to ensure effectiveness, equity, efficiency, and quality (52).

Depending on the type of health care system, priority areas, areas of improvement, quality of care initiatives, and managerial goals, countries conceptualized, designed, and implemented different performance frameworks with different performance dimensions, domains and indicators in order to measure quality of their services (70) (71) (72) (73) (74) (75) (76) (77) (78).

A very well done and comprehensive specialized magazine article that explores, individually, the conceptual bases, effectiveness and its indicators, as well as the quality improvement dynamics of the performance frameworks of the UK, Canada, Australia, US, World Health Organization, and Organisation for Economic Co-operation and Development is in this reference (52).

3.2 National overview – The National Program Outcomes Evaluation

In Italy, among evaluation of health outcomes projects, the most important, solid and institutionalized is the National Program Outcomes – PNE – Programma Nazionale Esiti.

The National Program Outcomes (PNE), established in 2010, is developed by National Agency for Regional Healthcare Services - Agenas - Agenzia Nazionale per i Servizi Sanitari Regionali (79) for the Ministry of Italian Health and provides national comparative evaluations of efficacy, safety, efficiency and quality of care produced within the National Health System (NHS). The areas of evaluation are, as regards the production function individual hospitals, and as regards the function of protection the local health (regions or provinces).

The 2015 edition of PNE on data updated to 2014 analyses 63 indicators of outcome or process, 57 volumes indicators and 26 indicators of hospitalization. The indicators are grouped into ten areas of clinical interest: cardiovascular, surgical procedures, cerebrovascular disease, digestive disease, musculoskeletal, perinatal, respiratory, urogenital, infectious diseases, and hospitalizations.

Main purposes of PNE are:

- observational evaluation of efficacy ("theoretical" one) of health interventions for which there are not possible or available experimental evaluations (Randomized Clinical Trials RCTs);
    - evaluate new treatments or technologies for which there are not possible experimental studies;
- observational evaluation of effectiveness ("operational" one) of health interventions for which experimental evaluations of effectiveness are available;
    - evaluate the difference and the impact between the effectiveness of treatments in experimental conditions compared to that observed in the "services real world";
- comparative evaluation between providers and / or between professionals;
    - with possible applications in terms of accreditation, remuneration, citizens and users information, with publication of the outcome results of all the facilities in order to improve the empowerment of citizens and their associations in the choice and assessment of services;
- comparative evaluation between population groups (for example according to socioeconomic level, residence, etc.);
    - especially for evaluation programs and promoting equity;
- identification of the factors that determine outcomes of care processes;
    - for example estimate what minimum volumes of activity are associated with better outcomes of care and use the minimum volumes as a criterion for accreditation;
- internal and external auditing.

Each of these applications has different methods and various possible approaches of communication, with potential positive and negative effects, costs and benefits; some of

them have already been evaluated in the literature. It requires careful *a priori* assessment to any application, not just from the point of view of health organization, but also economic and social. In particular, any direct information to citizens about the results of individual services and providers require national and regional communication programs aimed at optimizing the positive effects and minimizing the negative ones.

The indicators used by PNE must be documented by scientific protocols based on available literature, with clear definition of measured health outcome (i.e. short-term mortality, hospitalizations for specific conditions etc.). When direct outcomes of health are not validly available or measurable, PNE uses intermediate outcomes or surrogate outcomes, which can be composed, for example, by processes, procedures, periods of time.

Regarding the outcome indicators of care, PNE assessments include:

- production of functions for assigning patients or treatments outcome at the hospital that provided the service. Specific criteria were defined for each indicator;
- the functions of protection and support assigning patients / treatment outcome at the area of residence.

For each of the activities, care processes, preventive, diagnostic, therapeutic and rehabilitative evaluated interventions, shall document, based on the systematic review of the scientific literature, the available evidence of efficacy of treatments.

For health interventions for which scientific evidence of efficiency are available, the PNE evaluates, through systematic reviews of the literature and through empirical analyses on Italian data, the association between volume of activity and outcomes of care; volumes indicators are estimated by specific protocols.

Like all scientific measurements, also the estimates produced by PNE it may be affected by systematic errors and sample bias. PNE ought to use methods of study design and statistical analysis based on current best methodological available knowledge, that make explicit the possibility of error and, where possible, they aim to control its effects.

The results of PNE can be used appropriately only in the context of critical assessment, especially in the context of processes and evaluation of integrated programs at regional and local levels. The measures are thought as a support for clinical and organizational

auditing programs aimed at improving the efficiency and equity in the National Healthcare System. PNE does not produce rankings, report cards, judgments.

It publics and disseminates the results of the evaluations using instruments and formats of communication suitable for specific target populations, differentiating the modes of presentation and communication of results in relation to the characteristics of each target population. In particular:

- directly produces data with high professional competence, through a website dedicated to operators, professionals, managers, administrators and institutions of the NHS, that is of high completeness and scientific complexity profits to a critical evaluation;
- provides, for the communication tools of the NHS dedicated to citizens (portal), clear and easily understandable information also to non-specialist audiences;
- conducts efficiency and impact evaluation studies with different methods of presentation and communication of results.

PNE consists of the national level evaluation functions and regional level evaluation functions. In particular, PNE promotes and supports regional programs of outcome evaluation, which, for the characteristics of greater validity of the regional information systems, can produce additional assessments, sometimes of greater validity than national one.

Agenas through PNE is working with the competent structures of the Ministry of Health, the Regions, the Autonomous Provinces, for the development and integration of all national information systems.

PNE promotes debate and discussion with professionals, their associations and scientific societies, on the issues of outcome assessment.

PNE offers, promotes, supports and manages research and experimental programs for the development of evaluation, statistical and epidemiological methods and their application in the National System.

The indicators are discussed in the PNE Committee, composed of representatives of regions, autonomous provinces, the Ministry of Health and scientific institutions. Planning,

management, design and data analysis and web site management are performed by the Department of Epidemiology of the Lazio region as the centre of the operating PNE Agenas.

The website of the National Programme Outcomes is organized into five sections:

- **Hospital structure of the Local Health Unit**

  In this section, for each selected indicator, the results of all structures hospital / ASL of residence are shown: raw risk, risk-adjusted, adjusted relative risk (compared with Italian average), p-value for the comparison and temporal trends (results for the years 2008-2014). The results are reported with both tables and graphs.

  In addition to the comparison with the Italian average, PNE provides other three comparison options: between two hospitals, with a benchmark, with the previous year.

  In this way, for each selected indicator, one can also visualize the variability between facilities for the selected indicator in the year 2014, the variability in the region and per year, a trend graph for the whole Italy from 2008 to 2014.

- **Instruments for audit**

This section contains the following items:

- the audit for data quality PNE for the selected year. This is the list of hospitals to which the regions have been invited to verify the quality of data based on the results of several indicators that showed anomalous results;
- the results of the verification of data quality carried out in the selected year for the selected indicators;
- clinical risk. The available tools to individual facilities for monitoring the risk of death at 30 days after acute myocardial infarction or coronary artery bypass surgery using the details of their records; they enable the comparison between the observed mortality in the single operating unit and / or structure and the expected mortality based on the models of analysis used in the PNE;
- validation. Hospitals can access to a sample of their medical records for verification of data quality of their hospital discharge;

- monitoring. By entering the own medical records, the hospital can see a chart with the monthly trend of its results and the comparison with the expected values based on the national results. This tool can provide a more timely assessment of the impact of possible implemented clinical-organizational changes in the hospitals.

- **Summary for structure of the Local Health Unit**

This section shows the results of all indicators for structure and Local Heath Unit of residence. The results of "hospitalizations" are shown for residence province or city above 200,000 residents.

- **Informative System of Emergency**

This section presents the results referred only to health care in emergency and urgent Hospitals, using data from the Informative System of the monitoring of the assistance in Emergency and urgent.

- **Regional experimentations**

This section presents the results of regional experimentations relating to new indicators that include the integration of information recorded in Health Informative Systems available only in some regions and not sufficiently present nationwide.

For each indicator of the National Program Outcomes, on the website, the information document (containing the indicator rationale and the bibliography), the operating protocol (definition of the indicator and the selection of the population study) and the predictive model (risk adjustment) are given.

Informative sources and record Linkage criteria

The PNE uses the Hospital Information System (HIS), the informative system of tax register as sources of information, and informative system for emergency-urgency assistance monitoring (EMUR – Sistema informativo per il Monitoraggio dell'assistenza in Emergenza-Urgenza).

Hospital Information System (HIS)

The Hospital Information System collects information of all hospital admissions (in acute and post-acute) registered in Italy.

The hospital discharge summary (SDO – Scheda di Dimissione Ospedaliera) is the tool for collecting information about each patient discharged from public and private hospitals throughout the country. The SDO was established in 1991, after some adjustments in 1993 and 2000, it updated the content and the information flow, defined the general rules for the coding of clinical information (diagnosis, surgical, diagnostic, and therapeutic interventions and procedures) using updated system ICD-9-CM version (80).

The data from SDO include:

- demographic information (identifier patient, gender, date and place of birth, place of residence, etc.);
- health information related to hospitalization (admission date, identification code of the institute, specialty and department of admission, etc.);
- any intra-hospital transfers (date and department);
- information relating to the discharge (date, type of discharge, etc.);
- clinical information at discharge (main diagnosis and five secondary diagnoses, major intervention and 5 secondary proceedings with their dates of execution);
- DRG (Diagnosis Related Groups).

Informative system of tax register

The tax register is a computerized system that manages data and information related to taxpayers in the relationship with the tax authorities. The communes are the primary source of certification of personal data of individuals, because they hold vital records, the register of the resident population and the abroad resident. Notices of death are essential for proper fiscal management of users and timely management of health card. Agenas works in partnership with municipalities to align the data in the municipal and tributaries registers. This makes possible to link to the calculation of the indicators of mortality.

Informative system for emergency-urgency assistance monitoring (EMUR)

Informative system for monitoring assistance in emergency-urgency (EMUR) was established in 2008 and revised in 2012. From 1st January 2012, the regions are required to use and fill them appropriately.

The call number 118 system data includes information relating to the 118 operation centre, the phone call to the number 118, the rescue mission turned from the 118 operation

centre, patient assisted (data without direct identifiers), services provided in the rescue mission, and outcome intervention.

Emergency room data EMUR include the dispensing structure, access and discharge, patient assisted (data without direct identifiers), diagnosis, the service provided and the economic value of access.

Record linkage

Assured the need to guarantee data confidentiality, the use of record linkage techniques in building integrated archives is essential for epidemiology analyses. In addition, to connect information from the same register or different archives is an essential instrument for finding useful information in order to describe and assess, in terms of effectiveness, appropriateness, equity, services and care provided to citizens.

The method of record linkage used is deterministic: it connects statistical units who agree in reference to a specific key identifier.

The reconstruction of the patient's care path or medical history was made through a record linkage within the same hospital discharge summary, or between different hospital discharge summaries and the tax register. This action was useful to:

- count people with a given diagnosis in a given period;
- reconstruct the episode of care (for example, the episode of acute myocardial infarction can be defined through the identification of all patients hospital admissions occurred in a given time interval from the first admission for heart attack);
- identify the incident for the pathologies, defined as those for which there is no evidence of episodes of care for the same condition previous to the evaluated incident;
- characterize patients enrolled in a cohort. Patients can be characterized according to their "a priori" severity, by searching for comorbidities, both in the episode of hospitalization for the disease under study and in previous hospitalizations;
- identify the occurrence of patient outcomes in a given time interval from the hospital admission under study.

4 Study cases - Clinical Pathways

4.1 Survival and efficiency to transplant of Peritoneal Dialysis versus Haemodialysis for patients with chronic kidney disease in the Autonomous Province of Trento[6]

Abstract

In Italy, as well as in the other Western countries, peritoneal dialysis (PD) is still an underutilized method compared to haemodialysis (HD), despite several studies reported similar outcomes. The latest Italian data report a PD prevalence around 10%. In the Autonomous Province of Trento, the increase in the use of PD has been a key governance strategy since 2008. After this decision, incident patient rate has risen from 7% to 47%.

The aim of this work was to assess the impact of such a wide use of PD by comparing HD and PD methods in terms of survival and efficiency to transplant.

We analysed the data related to 223 HD patients and 115 PD patients followed by the nephrology unit of the Santa Chiara Hospital in Trento, from 1st January 2008 to 31th December 2014. The two therapies were compared in terms of survival and efficiency to transplant by computing descriptive statistics, Kaplan-Meier curves, log-rank test and Cox Proportional Hazard Model.

The analysis of the crude survival rate of the populations showed no significant differences between HD and PD, except for aged patients, where PD showed worse survival. Clinical risk factors associated with reduced survival for PD compared to HD patients were cardiovascular disease ($p<0.01$) and diabetes ($p<0.01$). HD displayed significantly lower efficiency to transplant than PD. Cox regression indicated that PD patients had a hazard ratio of receiving a transplant 5 times higher than HD patients ($p<0.0001$).

We can state that an extensive use of peritoneal dialysis had no relapse on mortality, except for aged patients and patients with cardiovascular disease and diabetes, but had a great positive impact on efficiency in view of a transplant.

[6] We are going to submit part of this study for publication on Clinical Journal of the American Society of Nephrology.

Introduction

In Italy, as well as in the other Western countries, peritoneal dialysis (PD) is still an underutilized method compared to haemodialysis (HD). The latest data from the National Registry of Dialysis and Transplantation 2009-2010 reported a prevalence of PD patients around 10%, and an incidence of 10.5%, with a declining trend in recent years. The prevalence varies considerably in different geographical areas (81). The reduced use of PD does not seem justified by safety reasons. Indeed, data derived from both national registries and large observational studies agree that the survival of patients on PD and HD is at least comparable (82) (83) (84) (85).

An attempt to conduct a randomized controlled clinical trial was made in the Netherlands. However only 38 (5%) of 773 eligible subjects provided consent to be randomized to the choice of treatment (86). Of these, 18 patients were randomized to HD, and 20 to PD. The study was substantially underpowered to provide any meaningful conclusion about the primary outcome considered, which was the mean quality-adjusted life year (QALY) score. The secondary outcome was survival, and a significant difference in longer-term (over the first 5 years) survival was observed, which favoured peritoneal dialysis. Nevertheless, due to the small sample size, this result should be considered with caution.

The difficulty to perform randomized controlled trials forced investigators to conduct observational studies based on registry data or ad-hoc collected data to clarify whether or not survival on peritoneal dialysis (PD) and haemodialysis (HD) differed.

These studies vary enormously with regard to population selection criteria, sample size, statistical methodology, definition of treatment, and availability of information on important potential confounders. The results obtained in these studies are conflicting: some authors reported a survival benefit for PD patients (87) (88) (89) (90), others for those on HD (91) (92) (93), while the remaining studies did not found significant differences in mortality (94) (95) (96) (97).

In particular, key features that seem to worsen PD survival are age, combination of age and diabetes mellitus (98), and peripheral arterial disease (99).

On the other hand, Buemi M. et al. reported that in elderly patients and patients with heart disease, peritoneal modality was favourable because it reduced the hemodynamic stress and the incidence of hypotension with respect to HD treatment (100).

Furthermore, several studies suggested PD to be associated with slower decline in residual kidney function (RKF), probably due to a greater hemodynamic stability that reduces ischemic insults to the kidney (101) (102) (103). This aspect helps to improve survival, reduce the need for erythropoietin, optimize control electrolyte and water balance (104) (105) (106).

In addition, PD does not make use of heparin, which reduces the risk of bleeding, such as peptic ulcer bleeding and spontaneous retroperitoneal haemorrhage (107) (108).

PD is potentially useful also in the eventuality of subsequent renal transplantation because it preserves the vascular bed. Furthermore, in terms of transplantation outcome, it seems that patients from PD have less incidence of post-transplant oliguria and better survival. Indeed the effect of pre-transplant modality on development of delayed graft function is still unclear (109). There is only a concern that the incidence of graft thrombosis seems higher in patients transplanted from PD respect HD, although renal survival appears similar (110).

Peritoneal dialysis is also proposed, because it enhances the quality of life in end-stage renal failure patients under dialytic treatment. Several studies have shown that PD patients have a perceived quality of life comparable or even better than those subjected to HD. This evidence is confirmed, especially in the elderly patients (111) (112) (113) (114). Indeed PD can be carried out at home, and offers great flexibility. PD patients should be trained to adapt the therapy prescription to their daily activities. Furthermore, PD clinical visits are scheduled every 4-5 weeks, and the technical simplicity of PD allows patients to perform dialysis while traveling. The increased autonomy and flexibility offered by PD are reflected in higher employment rate for patients treated with this modality (115) (116) (117).

Studies of health economics have shown that peritoneal dialysis is less expensive than haemodialysis, at least in developed countries, thanks to reduced direct and indirect costs. Indeed PD modality decreases staff-to-patient ratio, is associated with reduced use of injectable medications and does not require transportation (110) (118) (119) (120).

In Italy, it is estimated that savings associated with the use of PD with respect to HD are approximately 18,600 euros per patient per years. Indeed, in a recent Italian HTA report, direct, indirect, and social costs were estimated for different dialytic treatments indicating average cost of 57,000 euros per patient per year for HD versus 38,400 euros per patient per year for PD (121). Savings would be much more significant if the PD treatment were offered to a larger group of dialytic patients.

Possible reasons limiting the PD use seem related to the orientation of the dialysis centre and the appropriate information of the patient by dedicated outpatient clinics, or the absence of a partner (81).

The Autonomous Province of Trento is located in the northeast of Italy and hosts about 520,000 inhabitants with seven public hospitals. Within the province, there is a Complex Multi-zone of Nephrology and Dialysis, which has its centre at the Santa Chiara Hospital of Trento. In this facility, there are a Nephrology Ward, HD and PD services, an outpatient Clinic for Chronic Kidney Disease patients and one for kidney transplant recipients. Six limited-care Dialysis Centres are located in the periphery. A program to expand the use of the peritoneal method has been established since 2008, with excellent results as regards the incidence of patients. Indeed, a progressive increase in PD incident patients was observed, with a maximum of 47% in 2013 and a doubling of prevalent patients with respect to the Italian average prevalence (20% versus 10% at the end of 2014).

Aim

The aim of this study was to analyse the impact of a wide use of PD after six years from the beginning of the program, by comparing PD versus HD in terms of overall mortality and efficiency to transplant.

Subjects and Methods

The study is an observational, retrospective cohort study. Data were collected in patients treated at the operating unit of nephrology at the Santa Chiara Hospital in Trento, from 1st January 2008 to 31th December 2014. Patients were observed until 30th September 2015, with a minimum follow-up of 9 months. The total number of incident patients was 487. Adherence to the treatments took place on a voluntary basis, after a deep informative discussion and clinical evaluation with physicians and nurses. Among all incident patients,

334 patients chose and began HD and 153 PD. In order to correct population selection bias and have two comparable groups in terms of chance to perform either dialytic method, exclusion criteria were adopted:

- clinic criteria: we excluded from the analysis patients that could support only one of the two methodologies due to clinical reasons. Clinical contraindications to perform PD were: massive polycystic kidneys, diabetes hard to monitoring, obesity (BMI> 30), previous surgery on the peritoneum, physical inability to perform the method (blindness, right hemisyndrome, deforming rheumatoid arthritis). Clinical contraindications to perform HD were: ischemic heart disease with severe hemodynamic instability, liver disease with refractory ascites, advanced malignancy with an indication to palliative PD in a long-term nursing home;
- we excluded patients died within 30 days from the start of the dialytic treatment. We considered the first 30 days as a period of adjustment to therapies;
- we considered patients who changed the treatment only in the first opted methodology and not in the second one. The patients who changed dialysis modality were censored at the time of the change.

Following exclusion criteria, we analysed data in 223 HD patients and 115 PD patients (Figure 7).

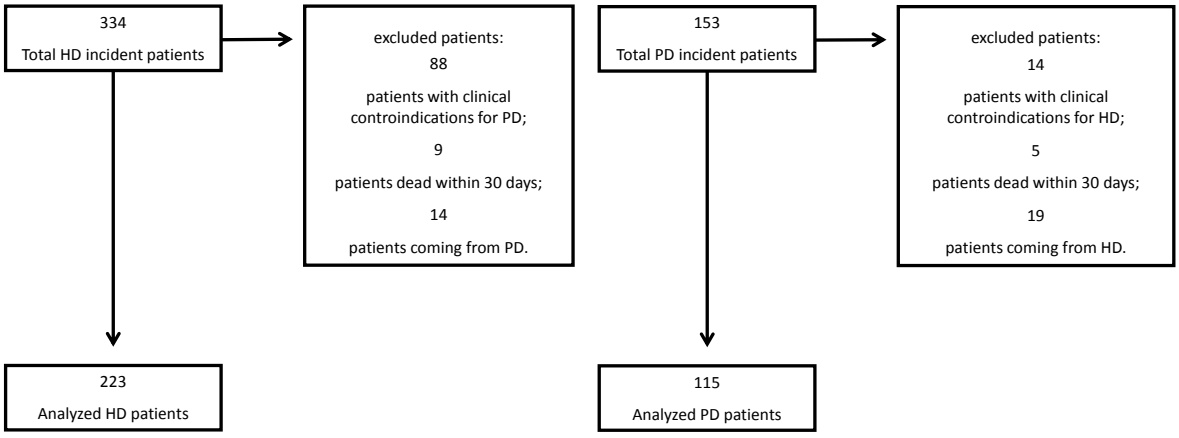


Figure 7. *Flow chart of the study populations.*

Demographic characteristics, survival, and comorbidity data were collected at the start of the dialytic therapy and descended from the Provincial Register of Dialysis Patients.

Descriptive statistics compared the two therapies in terms of survival, and efficiency to transplant. For crude survival study, Kaplan-Meier survival curves were determined for the entire populations and for two subgroups based on patient age (younger than 65 years and equal or older than 65 years). To examine the independent effect of the clinical comorbidities on mortality, six Kaplan-Meier survival curves (one for each considered comorbidity) were calculated. In order to evaluate differences between the curves, log-rank tests were performed. Patients who received a transplant were censored at the time of transplantation. When appropriate, a Univariate Cox Proportional Hazard Model was used to quantify the Hazard Ratio of death in PD patients versus HD patients.

In order to evaluate the efficiency to transplant, the time from the start of dialytic therapies to the transplant or end of follow-up, was further divided into two intervals: “time 1” from the start of the dialysis to the registration in the transplant waiting list, and “time 2” from the registration into the transplant waiting list to the transplant or end of follow-up (Figure 8).

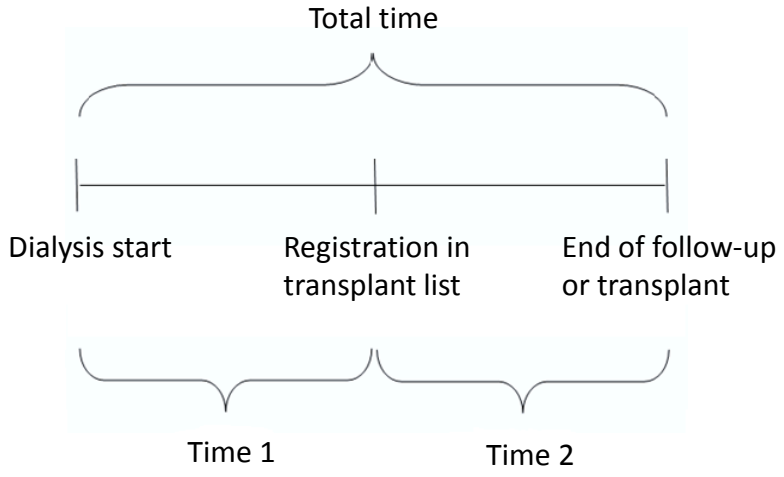


Figure 8. *Diagram of the times used for the Survival analysis investigating the efficiency to transplant. The total time, waiting time for placement in the transplant waiting list (“time 1”), and call time to transplantation after registration in the waiting list (“time 2”) were assessed.*

The total time, the waiting time for placement in transplant waiting list (“time 1”), and the call time to transplantation after registration in waiting list (“time 2”) were assessed by Kaplan-Meier analysis, log-rank test and Univariate Cox Proportional Hazard Model. For the total time and “time 2” the event was the transplant, while for “time 1” the event was the registration in waiting list. Patients died were censored at the time of death.

A second survival study was performed in order to evaluate patient mortality after transplant. To this aim an Intention-to-treat (ITT) analysis was led. In this analysis, patients who stopped dialysis and received a transplant were not censored at the time of transplantation, but remained included in the study until the date of death or the end of follow-up (30th September 2015).

Data were expressed as mean ± SD for normally distributed data, median [IQR] for not normally distributed data, and numbers and percentage for categorical data.

A p-value less than 0.05 indicated statistical significance. All analyses were performed with STATA statistical software, version 13.0 (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA).

Results

Table 2. *Characteristics of study populations*

	HD, n (%)	**PD, n (%)**	**p-value**	**Statistic test**
Total patients	**223**	**115**		
Male	154 (69)	77 (67)	0.69	Pearson's X^2 test
Female	69 (31)	38 (33)	0.69	Pearson's X^2 test
Cardiovascular disease	97 (43)	39 (34)	0.09	Pearson's X^2 test
Diabetes mellitus	**72 (32)**	**24 (21)**	**0.03**	**Pearson's X^2 test**
COPD	33 (15)	16 (14)	0.83	Pearson's X^2 test
Chronic liver disease	**30 (13)**	**7 (6)**	**0.04**	**Pearson's X^2 test**
Cancer	34 (15)	14 (12)	0.44	Pearson's X^2 test
Arterial hypertension	188 (84)	97 (84)	0.99	Pearson's X^2 test
Age at start of dialysis < 65 years	82 (37)	53 (46)	0.10	Pearson's X^2 test
Age at start of dialysis ≥ 65 years	141 (63)	62 (54)	0.10	Pearson's X^2 test
Median age at start of dialysis	70 IQR [59-78]	68 IQR [50-75]	0.06	U Mann-Whitney test

The characteristics of the two groups of patients are shown in Table 2. The two groups displayed differences in the fraction of patients with diabetes mellitus and chronic liver disease. Higher percentages of patients with the two pathologies were present in the HD than PD group (32% vs 21% and 13% vs 6%, respectively).

Survival study - mortality

The analysis of the crude survival rate in the two populations showed no significant difference between HD and PD for the total population and for the patients younger than 65 years. In the subgroup of elderly patients (≥ 65 years), the log-rank test provided a p-value of 0.05, which indicated worse survival for PD versus HD patients (Figure 9). The Cox Proportional Hazard model did not result significant.

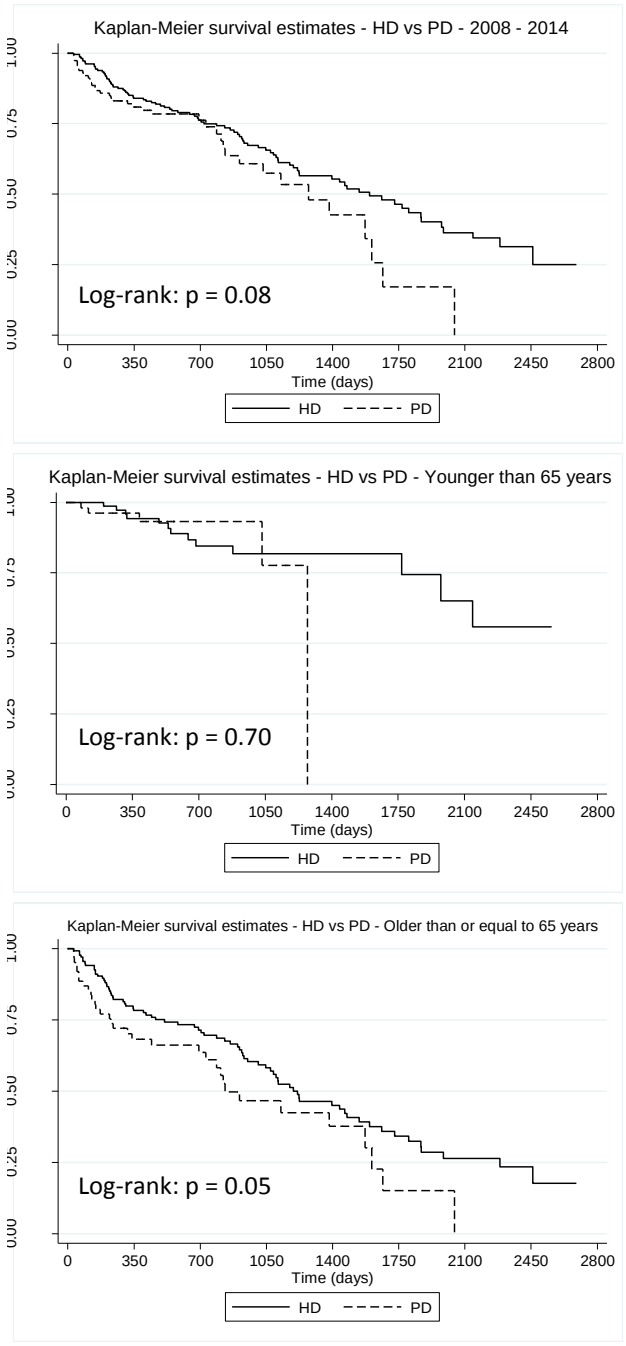
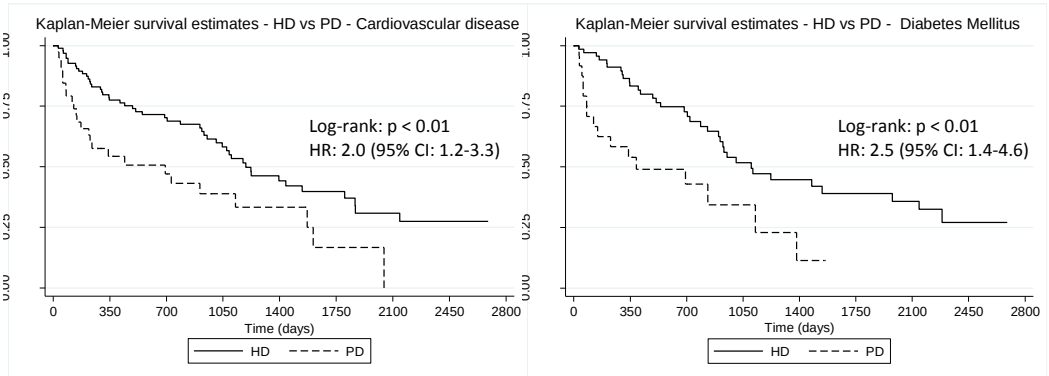


Figure 9. *Kaplan-Meier survival curves for haemodialysis (HD, continuous line) and peritoneal dialysis (PD, dashed line) incident patients from 2008 to 2014 for the entire populations (top), for patients younger than 65 years (centre), and equal or older than 65 years (bottom).*

Clinical risk factors associated with reduced survival in PD versus HD patients were cardiovascular disease and mellitus diabetes (Figure 10).



Univariable Cox proportional hazard model			
	Crude HR	95% CI	p-value
PD	2.0	1.2 – 3.3	0.005
Multivariabile Cox proportional hazard model			
	Adjusted HR	95% CI	p-value
PD	1.8	1.1 – 3.0	0.013

Univariable Cox proportional hazard model			
	Crude HR	95% CI	p-value
PD	2.5	1.4 – 4.6	0.003
Multivariabile Cox proportional hazard model			
	Adjusted HR	95% CI	p-value
PD	2.4	1.3 – 4.5	0.004

***Figure 10**. Kaplan-Meier survival curves, Univariable Cox proportional regression models and Multivariable Cox proportional hazard models comparing haemodialysis (HD, continuous line) and peritoneal dialysis (PD, dashed line) for patients affected by cardiovascular diseases (left) and diabetes mellitus (right).*

In patients with cardiovascular diseases the Cox Proportional Hazard Model provided, a crude Hazard Ratio of death of 2.0 (95% CI 1.2 – 3.3, p=0.005) for PD compared to HD patients. In diabetic patients it provided a crude Hazard Ratio of death of 2.5 (95% CI of 1.4 – 4.6, p=0.003) for PD versus HD patients. When data were adjusted for age, the analysis yielded an adjusted Hazard Ratio of death of 1.8 (95% CI 1.1 – 3.0, p=0.013) for PD versus HD in cardiovascular disease patients, and of 2.4 (95% CI of 1.3 – 4.5, p=0.004) for PD versus HD in diabetes mellitus.

Survival study – Efficiency to transplant

The comparison of the two groups of patients in terms of transplantation, revealed two important aspects. First, a higher percentage of patient was registered in the transplant list in the PD group (48 of 115, 42%) than in the HD group (40 of 223, 18%). Second, among the patients registered in the transplant list, a higher fraction of patients received a transplant in the PD group (42 of 48, 87%) than in the HD group (27 of 40, 67%).

Therefore, HD had significantly lower efficiency than PD in terms of time to transplant. The Total time, the time necessary to be put in the transplant waiting list, and the call time to transplantation after registration were significantly higher in HD than in PD patients with p<0.0001, p=0.0001, and p=0.0006, respectively (Figure 11).

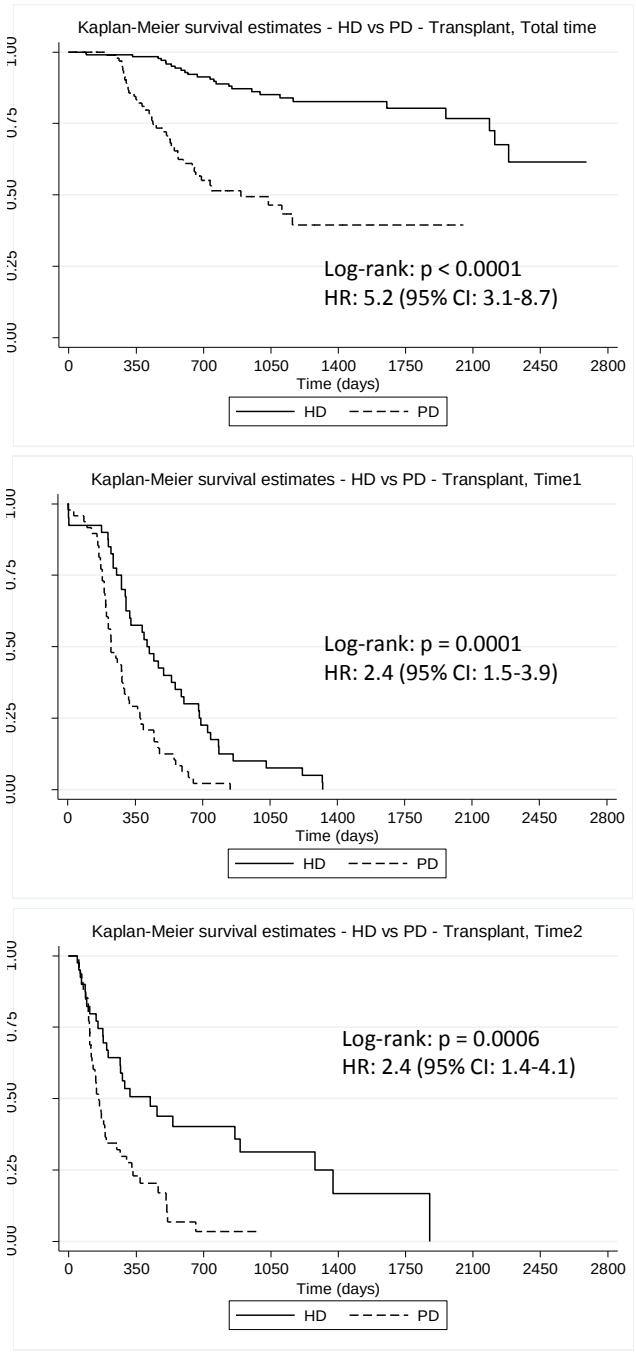


Figure 11. *Kaplan-Meier survival curves comparing haemodialysis (HD) and peritoneal dialysis (PD) in terms of efficiency to transplant. The total time is the time since dialysis start to transplantation. "Time 1" is the time since dialysis start to registration in transplant waiting list. "Time 2" is the time since registration in transplant waiting list to transplantation.*

Cox proportional hazard model indicated that PD patients had a hazard ratio (HR) of receiving a transplant 5.2 times higher than HD patients (95% CI 3.1 - 8.7, p<0.0001). PD patients had a HR of being included in the transplant list of 2.4 times higher than HD patients (95% CI 1.5 – 3.9, p<0.001), and a HR of being called for transplant after registration in waiting list of 2.4 times higher than HD (95% CI 1.4 – 4.1, p=0.001) (Table 3).

Table 3. *Cox proportional hazard model for peritoneal dialysis (PD) compared to haemodialysis (HD) patients.*

Cox proportional hazard model for 'risk-increase' of receiving a transplant – Total time			
	Crude HR	95% CI	p-value
PD	5.2	3.1 – 8.7	< 0.0001
Cox proportional hazard model for 'risk-increase' of registration in the transplant waiting list – Time 1			
	Crude HR	95% CI	p-value
PD	2.4	1.5 – 3.9	< 0.001
Cox proportional hazard model for 'risk-increase' of calling for transplantation – Time 2			
	Crude HR	95% CI	p-value
PD	2.4	1.4 – 4.1	0.001

The total time is the time since dialysis start to transplantation. "Time 1" is the time since dialysis start to registration in the transplant waiting list. "Time 2" is the time since registration in the transplant waiting list to transplantation.

Survival study – Intention to treat analysis (ITT)

The Intention-to-treat analysis for mortality showed no significant difference between HD patients and PD patients for the entire population and for the two age subgroups (Figure 12). It is worth notice that this survival was not only related to the dialytic method, but to the combination of dialysis and transplantation.

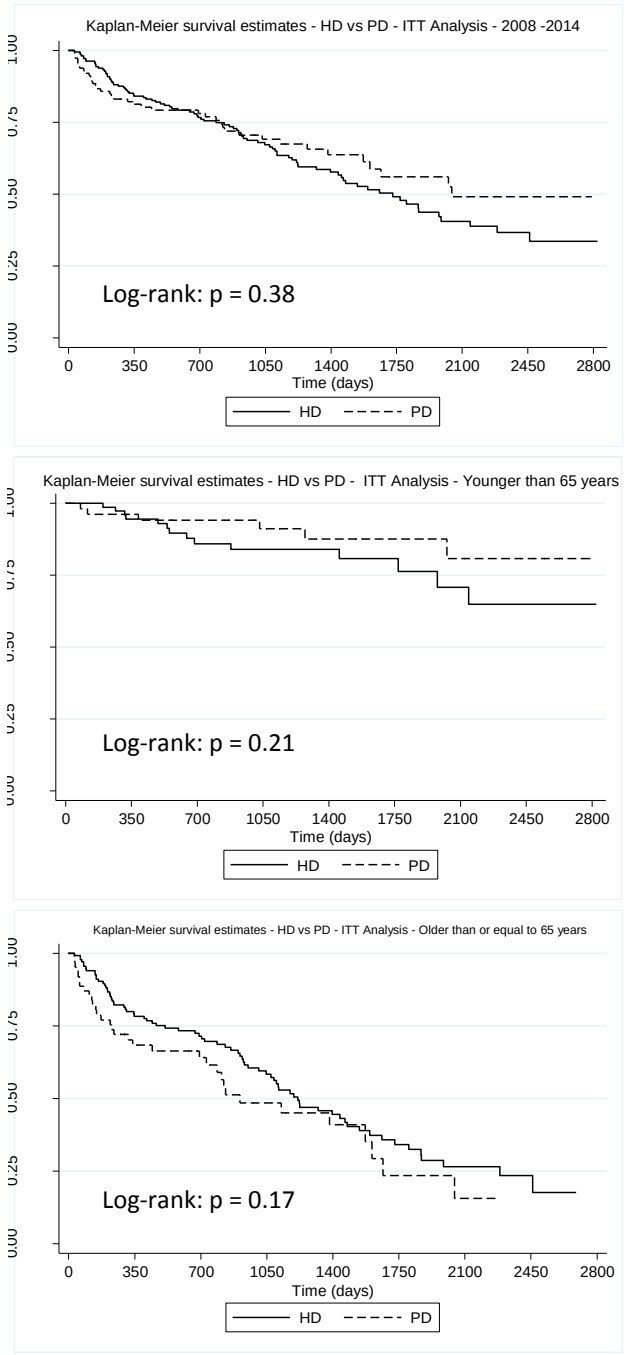


Figure 12. *Kaplan-Meier survival curves in an intention-to-treat analysis for haemodialysis (HD, continuous line) and peritoneal dialysis (PD, dashed line) incident patients from 2008 to 2014 for the entire populations (top), for patients younger than 65 years (centre), and equal or older than 65 years (bottom). . Patients who stopped dialysis and received a transplant were not censored at the time of transplantation, but remained included in the study until the date of death or the end of follow-up (30th September 2015).*

Discussion

In Italy as well as in Western countries peritoneal dialysis is underused in comparison with haemodialysis. This occurs despite the numerous studies suggesting peritoneal dialysis to be comparable to haemodialysis in terms of efficacy, safety, and economic costs, and to be more advantageous for patients in terms of quality of life.

The present study aimed to evaluate the impact of a wider use of PD in the Autonomous Province of Trento, in terms of survival and efficiency to transplant. With this purpose, we designed a comparative study between the incident patients on the two dialytic methods and analysed data from 223 HD patients and 115 PD incident patients over a period of seven years with a minimum follow-up of nine months.

In order to obtain comparable populations in terms of clinical opportunity to perform either dialytic method, some exclusion criteria were applied. In fact, the choice of dialysis method involves many aspects. Although it should be a personal choice of the patient according to his/her own preferences and lifestyles, clinical and ambient conditions put limitations that need to be accurately evaluated with the clinicians. Indeed not all clinical conditions are equivalent for haemodialysis or peritoneal dialysis choice. As an example PD is not indicated in elderly patients with severe diabetes mellitus (98), and in patients with subclinical peripheral artery disease (99). On the other hand, hemodynamic instability, inability to anticoagulate, and lack of access to circulation constitute contraindications for HD. The cognitive status of the patient and the presence or absence of relatives and caregivers can also influence the choice of peritoneal dialysis, since this requires a minimum of skills, hygienic condition, and patient empowerment. Thus, despite a rigorous application of clinical inclusion and exclusion criteria, the two groups were not completely balanced for mellitus diabetes and chronic liver disease. We chose not to further purify populations and to maintain these differences to better represent the real population undertaking dialytic treatment. In this way, greater emphasis was given to a pragmatic instead of explanatory approach (122).

Overall mortality was comparable in the two groups for the entire population and for the population aged less than 65 years. Haemodialysis seemed to show better survival for elderly patients, for patients affected by cardiovascular disease and by diabetes mellitus. However, the intention-to-treat analysis, in which survival analysis reckoned for the

combination of dialysis and transplantation, did not result in survival differences between the two dialytic treatments. This finding was mainly due to the efficiency to transplant found in the PD group, where a noticeable reduction in the time to transplantation was observed.

Although disputed by a recent analysis (123), the literature generally reports better survival for PD patients compared to HD patients in the first years of treatment (83). Our study did not confirm this result. Indeed the survival curve was higher in HD than in PD patients in the first two years. One explanation of this difference could be that we offered PD to a larger population (47% of incident) without making any selection towards HD for unstable or fragile patients.

Concerning the analysis of the subgroup of elderly patients, our study confirmed some literature data, which indicated a worse survival in elderly PD patients (124).

Some studies in the literature demonstrated that the risk of death was significantly increased in PD patients compared with HD patients with subclinical peripheral artery disease (99), congestive heart failure (125), coronary artery disease and myocardial infarction (126) (127). On the other hand, PD was suggested as a viable option to control volume overload and improve outcomes in refractory congestive heart failure patients (128). In our study, HD showed superior survival than PD in patients affected by cardiovascular disease.

As regards patients with diabetes mellitus and end-stage kidney disease, our study showed a better survival for HD compared to PD patients. The method that can lead to longer survival in these patients is still debated in literature. A recent systematic review analysed mortality outcome in diabetic patients performing HD and PD. The analysis of 25 observational studies led to conclude that available evidence was inconsistent because survival varied across study designs, follow-up periods and patient subgroups (129).

With regard to transplants, the literature shows that peritoneal dialysis has commonly a larger number of patients registered in the list. According to the data from national registers, this result seems due to the lower age of PD patients and the higher prevalence of first dialysis experience (130) (131). However, an advantage of PD in terms of call time to transplant has not been reported yet. In our study, which enlarged the floor for

peritoneal dialysis, patients' age was comparable between the two groups, and PD reduced the time to transplant.

A detailed analysis of our data indicated that a slowdown in the call to transplant could be partially explained by the fact that some HD patients had a previous history of kidney transplant. This made more difficult to find a matching organ for the patients due to their state of hyper-immunization.

Another significant finding of our study is the more rapid inclusion in the transplant list for patients on peritoneal dialysis. We tried to identify two possible explanations:

- Organizational explanation. Peritoneal dialysis has a unique provincial centre at the Santa Chiara Hospital of Trento, while haemodialysis is present in seven public hospitals throughout the whole province. It is possible that the presence of a single doctor for patients on PD facilitated faster transmission of information for the arrangements of the registration in the transplant list, by directing patients to the transplant ambulatory. Regarding HD patients, it is possible that the communication on the path to registration in the transplant list is fragmented and thus delayed because there are many physicians and there is no standardized iter. In addition, although patients went to the hospital three times a week, they did not always see a physician, especially in centres with limited care. Finally, the frequent hospital admissions to perform HD may have negatively affected the planning of examinations required for inclusion in the transplant list.
- Psychological and attitudinal explanation. Patients who perform peritoneal dialysis are often more independent, determined and involved in their own care process. They are able to efficiently plan the useful examinations necessary for inclusion in the transplant list. This more active attitude is also noticeable from the higher percentage of patients enrolled in the transplant list. Moreover, those PD patients have to manage dialysis every day by themselves, and this element can be a strong incentive to obtain a quick inclusion in the list.

We performed an observational retrospective cohort study. This fact limited the power of the results, but, as demonstrated by a previous attempt of RCT study (ref RCT), dialytic treatment randomization is not easily accepted by patients.

Conclusions

The aim of this work was to assess the impact, in terms of survival, of a wide use of peritoneal dialysis in patients with end-stage kidney disease in the Province of Trento. According to our data set, the choice of peritoneal dialysis can be considered a great opportunity in terms of survival, especially in younger patients not suffering from severe diabetes, nor from severe heart disease. Moreover, considering the complete course of treatment, composed of dialysis and transplantation, the two treatments were comparable.

4.2 Evaluation of an Orthogeriatric care pathway for the management of fragility fractures in elderly patients

Abstract

Osteoporotic fractures are becoming a major healthcare problem in countries characterized by an increasing number of older adults. Because patients suffering a hip fracture are more likely to be elderly, frail, and to have multiple co-morbidities, these fractures are usually associated with high mortality, disability, and remarkable social and economic healthcare costs. International guidelines indicate that early treatment of these patients and multidisciplinary approaches may improve clinical outcomes and organizational outcomes.

Similarly, to other developed countries, the Italian PNE established a section of six indicators to evaluate the performance of Italian hospitals on this issue.

According to the PNE, from 2005 to 2011 the S. Chiara Hospital of Trento, performed worse than the national average with regard to the *time to surgery*, while it showed better results in terms of mortality at thirty days. In order to improve these outcomes and achieve the average national *time to surgery*, an orthogeriatric clinical care pathway was started in June 2012 in this hospital, which involved five hospital operational units (O.U.).

The aim of this work was to compare the outcomes in patients older than 65 years, admitted for hip fractures to the S. Chiara hospital of Trento in two different periods: before and after the introduction of the orthogeriatric clinical pathway.

The clinical pathway of Orthogeriatrics started at the Operational Unit (O.U.) of Orthopaedics of the Santa Chiara Hospital of Trento in the second half of 2012. The clinical pathway was prescribed for patients hospitalized after the fracture of the proximal femur, being ≥ 75 year old and having unstable or high complexity (pluripathology) medical conditions. The presence of a Geriatrician in the orthopaedic ward was assured every morning. All hospital admissions for hip fractures in patients older than 65 years, from 1st January 2012 to 30th June 2012 fed the pre-pathway patient group, while all hospital admissions for hip fractures from 1st July to 31st December 2012 fed the post-pathway patient group. Patients with conservative or in-hospital fractures and patients from the departments of anaesthesia and intensive care were excluded from the analysis. The two groups were compared by evaluating the number of patients operated within 48 hours after hospital admission (Pearson's chi-squared test), the distributions of time intervals between hospital access and surgery (Mann–Whitney U test), the mortality at 1, 3, 6, and 8 months (Kaplan-Meier survival curves and log-rank test), and the average length of stay of hospitalization (Student's t-test).

Outcomes related to 141 patients treated from January to June 2012 (pre-pathway) and to 168 patients admitted from July to December 2012 (post-pathway) were analysed. The percentage of patients operated within 48 hours increased from 16.3% in the pre-pathway group to 25.6% in the post-pathway group. The exposition to the orthogeriatric pathway led to an increased relative risk of being operated within 48 hours (RR = 1.57, p = 0.047). The median time between hospital access and surgery decreased from 97.0 hours in pre-path patients to 72.5 hours in post-path patients ($p<0.01$). The average length of stay and its standard deviation significantly decreased in the post-pathway compared to pre-pathway patients ($p<0.01$). In terms of mortality, the survival curves showed no difference between the two groups for each of the considered intervals (p=0.09, p=0.36, p=0.70, and p=0.54).

The introduction of the orthogeriatric clinical pathway for the care of elderly patients with hip fracture, led to an improvement of key outcomes. The *time to surgery* and the average length of stay decreased without affecting the good performance on survival already achieved. In addition, the multidisciplinary involvement on a common commitment led to

the development of team working and an organizational culture that remained as added value.

Introduction

Osteoporotic fractures are becoming a major healthcare problem in countries characterized by an increasing number of older adults (132). A recent study demonstrated that the burden of hip fragility fractures in Italy was comparable to that of acute myocardial infarction and stroke (133). The National United Kingdom Hip Fracture Database reported a mortality of 10% at one month and 33% at one year for elderly patients suffering hip fracture in 2011 (134). For the same year, the Italian PNE reported a raw percentage of mortality at one month of 6.0%, with a slow decrease to 5.6% in 2014 (79).

Because patients suffering a hip fracture are more likely to be elderly and frail, and to present multiple co-morbidities, these fractures are associated with high mortality and disability, and produce to high social and economic healthcare costs.

The British Orthopaedic Association (6) estimated more than 70,000 hip fractures per year in UK resulting in a cost of about £2 billion a year. According to the British Orthopaedic Association, this incidence is expected to increase until 91,500 by 2015 and 101,000 in 2020, with an associated increase in annual expenditure. The majority of this expenditure is accounted for by hospital bed days with a further substantial contribution coming from health and social aftercare.

International guidelines indicate that early treatment of these patients and multidisciplinary approaches may improve clinical outcomes, such as mortality and complications, and organizational outcomes, such as the length of stay and the health care costs.

In particular, the International guidelines provide guidance on many aspects of patient care, such as the approach to anaesthesia, analgesia, surgical procedure, mobilization strategies, timing for surgery, multidisciplinary approach, etc.

Early and appropriate surgery for hip fractures is the most effective form of pain alleviation, which potentially accelerates rehabilitation and reduces complications. No specific time interval threshold has been identified (up to 24 hours) within the current literature, below which a reduction in delay show no further benefit. Surgery is recommended to be

performed on the day of or the day after admission, based on pragmatic, organizational and humanitarian considerations (135) (136). The meta-analysis performed by Moja et al. in 2012 (137) , (137), including 35 independent studies and 191,873 patients concluded that surgical delay is associated with a significant increase in the risk of death and pressure sores. This means that orthopaedic surgery services should ensure that the majority of patients are operated within one or two days.

Another issue related to the timing of surgery is the identification and proper treatment of comorbidities that could jeopardize or delay the surgery, such anaemia, anticoagulation, volume depletion, electrolyte imbalance, uncontrolled diabetes, uncontrolled heart failure, correctable cardiac arrhythmia or ischaemia, acute chest infection, exacerbation of chronic chest conditions. Therefore, multidisciplinary care is central to the management of frail older people with multiple medical, psychological and social problems (138). As concerns the multidisciplinary management, one of the many indications reported in the NICE guidelines is to offer patients, since the admission, a formal, acute orthogeriatric or orthopaedic ward-based hip fracture programme that includes all of the following steps:

- orthogeriatric assessment;
- rapid optimization of fitness for surgery;
- early identification of individual goals for multidisciplinary rehabilitation to recover mobility and independence, and to facilitate return to the pre-fracture residence and long-term wellbeing;
- continued, coordinated, orthogeriatric and multidisciplinary review;
- integration with related services, particularly mental and bone health, fall prevention, primary care and social services.

Furthermore, individual studies demonstrated that the introduction of clinical pathways on the treatment of these patients led to better outcomes. Those studies assessed a comprehensive care pathway for patients with hip fracture, showing significantly reduced preoperative fasting time and length of hospital stay (139) (140), without a negative impact on associated clinical and functional outcomes (141). Friedman et al. demonstrated improved outcomes, such as shorter times to surgery, fewer postoperative infections and overall complications, shorter length of stay, fewer cardiac complications, and fewer cases

of thromboembolism, delirium, and infection, thanks to co-management with geriatricians (142).

Because of the great incidence of hip fractures in the elderly and the relevant socio-economic impact, the Italian PNE established a section of six indicators to evaluate the performance of Italian hospitals. These indicators are volumes of admissions, mortality at 30 days, volumes of surgeries, surgery within 2 days, waiting days for surgery, and rate of hospital admissions.

According to the PNE, from 2005 to 2011 the S. Chiara Hospital of Trento performed worse than the national average with regard to the fraction of patients operated within 48 hours after hospital admission and to the time elapsed between hospital access and surgery, while it showed better results in terms of mortality at thirty days, see Appendix 1 (79).

In order to improve these outcomes and achieve the average national *time to surgery*, an orthogeriatric clinical care pathway was started in June 2012 in this hospital, which involved five hospital operational units (O.U.).

Aim

The aim of this work was to compare the outcomes in patients older than 65 years, admitted for hip fractures to the S. Chiara hospital of Trento in two different periods: before and after the introduction of the orthogeriatric clinical pathway.

Methods

The clinical care pathway of Orthogeriatrics started in the Operational Unit (O.U.) of Orthopaedics at the Santa Chiara Hospital of Trento in the second half of 2012. The pathway started after several meetings between professionals of different O.U., in order to provide multidisciplinary approach in healing orthogeriatric patients. The operational units involved were: the Emergency Room, Orthopaedics and Traumatology, Anaesthesia and Intensive Care, Geriatrics, and Cardiology. The clinical pathway was prescribed for patients hospitalized at the Orthopaedics O.U. of the Santa Chiara Hospital of Trento after the fracture of the proximal femur, being ≥ 75 years old, and having unstable or high complexity (pluripathology) medical conditions. The presence of a Geriatrician was assured every morning in the orthopaedic ward, from Monday to Friday, and, by consulting, in the remaining hours/days and on holidays. In addition, a new protocol for the evaluation of

cardiac surgery risk was developed. Finally, six to 12 beds in the orthopaedic ward were dedicated for orthogeriatric pathway patients.

The clinical care pathway includes:

- the early setting of the patient on his arrival in the emergency department;
- the quick and complete setting of the patient with an orthogeriatric model by multidimensional and multidisciplinary evaluation: activities of daily living - ADL, assessment of pain, nutritional status and hydration during both preoperative and postoperative phases;
- the application of a new protocol for the evaluation of cardiac surgery risk.

A flow diagram of the two options that a patient might undergo is shown in Figure 13.

All hospital admissions for hip fracture of patients aged over 65 years, from 1st January 2012 to 30th June 2012 fed the pre-pathway patient group, while all hospital admissions for hip fracture from 1st July to 31st December 2012 fed the post-path-way patient group.

Patients with conservative fractures (non-operated) or in-hospital fractures, and patients from the department of anaesthesia and intensive care were excluded from the analysis.

The two groups were compared by evaluating the following outcomes:

- number of patients operated within 48 hours after hospital admission (Pearson's chi-squared test);
- the distributions of time interval between hospital access and surgery (Mann–Whitney U test);
- mortality at 1, 3, 6, and 8 months (Kaplan-Meier survival curves and log-rank test);
- the average length of stay of hospitalization (Student’s t-test).

Variables were expressed as median and [IQR], and as percentages of the total.

Geriatricians involved in the clinical pathway collected data related to patients *ad hoc*. The analysis of data was possible thanks to a patient informed consent.

A p-value less than 0.05 indicated statistical significance. All analyses were performed using STATA 13.1 Statistics/Data analysis, StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA.

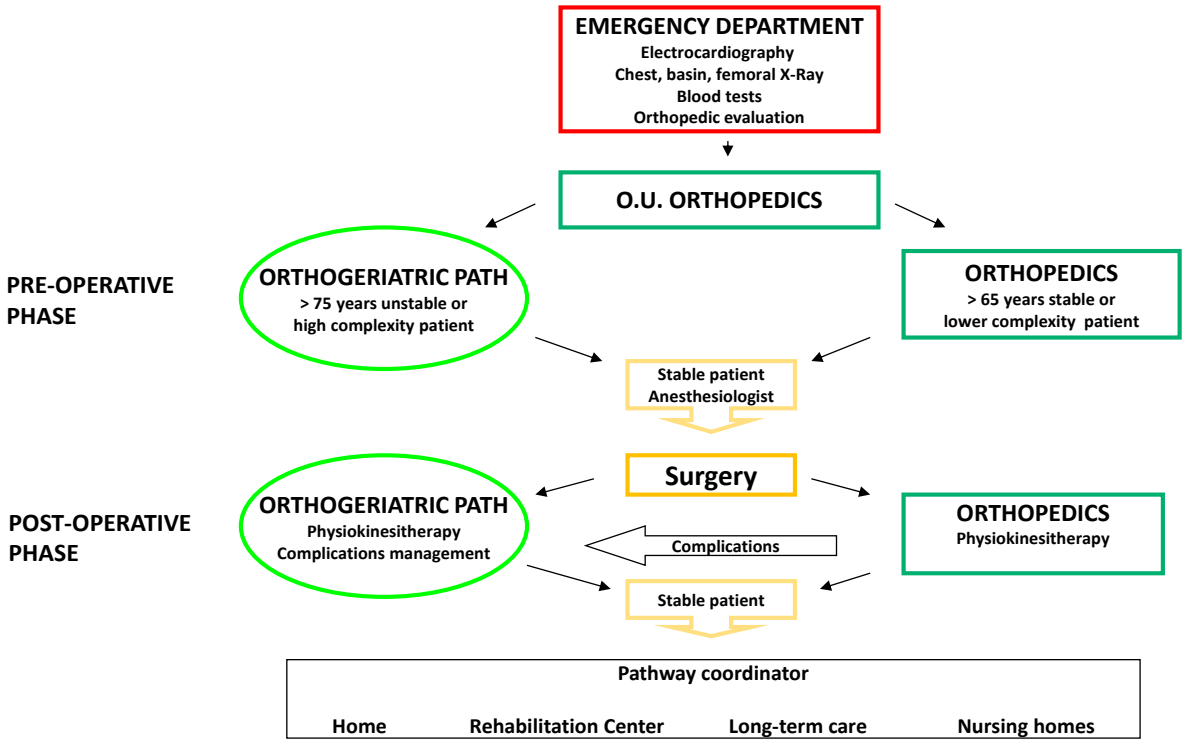


Figure 13. *Flow diagram of the two options that an elderly patient with hip fracture might follow after the introduction of the clinical orthogeriatric pathway in July 2012. Patient admitted to the Emergency Room from January 2012 to June 2012 were addressed only to the right part of the flow chart, independently of their age.*

Results

The outcomes related to 141 patients treated from January to June 2012 (pre-pathway) and to 168 patients admitted from July to December 2012 (post-pathway) were analysed. The characteristics of the two patients' groups are shown in Table 4. In both groups, the percentage of women was higher (75% and 83% in pre and post-pathway, respectively) than the percentage of men. The median age and IQR were 86 [81-89] years in the pre-pathway group and 85 [80-89] years in the post-pathway group (Table 4). Four outcomes were evaluated: patients operated within 48 hours after hospital admission, the median time between hospital admission and surgery, the mortality, and the average length of stay.

Table 4. *Characteristics of the two groups of patients.*

Characteristics of the two group's patients			
	Pre-pathway	**Post-pathway**	
Total patients, n	**141**	**168**	
Male, n (%)	35 (25)	28 (17)	p = 0,09
Female, n (%)	106 (75)	138 (83)	p = 0,09
Total median age [IQR] years	86 [81-89]	85 [80-89]	p = 0,40
Male median age [IQR] years	84 [78-89]	85 [81-90]	p = 0,56
Female median age [IQR] years	86 [83-89]	85 [79-89]	p = 0,20

Patients operated within 48 hours from the hospital admission

The number of patients operated within 48 hours increased from 16.3% in pre-path patients to 25.6% in post-path patients. The exposition to the orthogeriatric pathway increased of 57% the relative risk of being operated within 48 hours after hospital admission (Table 5).

Table 5. *Numbers, percentages, and Relative Risk in patients operated within or after 48 hours following hospital admission.*

	Operated patients		
	After 48 hours **n (%)**	**Within 48 hours** **n (%)**	Total
Pre-pathway	118 (83.7)	23 (**16.3**)	141
Post-pathway	125 (74.4)	43 (**25.6**)	168
Total	243	66	309
	RR = 1.57 (95% CI: 0.99 – 2.47), p = 0.047		

Median time from hospital admission to surgery

Regarding the distribution of the time interval between hospital access and surgery, the Mann-Whitney U test provided a p<0.01. Data showed that the median time decreased from 97.0 hours in pre-path patients to 72.5 in post-path patients (Table 6, Figure 14).

Table 6. *Median time and interquartile range [IQR] between hospital admission and surgery in pre-pathway and post-pathway patients.*

	Median time since admission to surgery [IQR]		
	hours	**days**	**Mann–Whitney U test**
Pre-pathway	97.0 [68-139]	4 [3-6]	**p < 0.01**
Post-pathway	72.5 [48-113.5]	3 [2-5]	

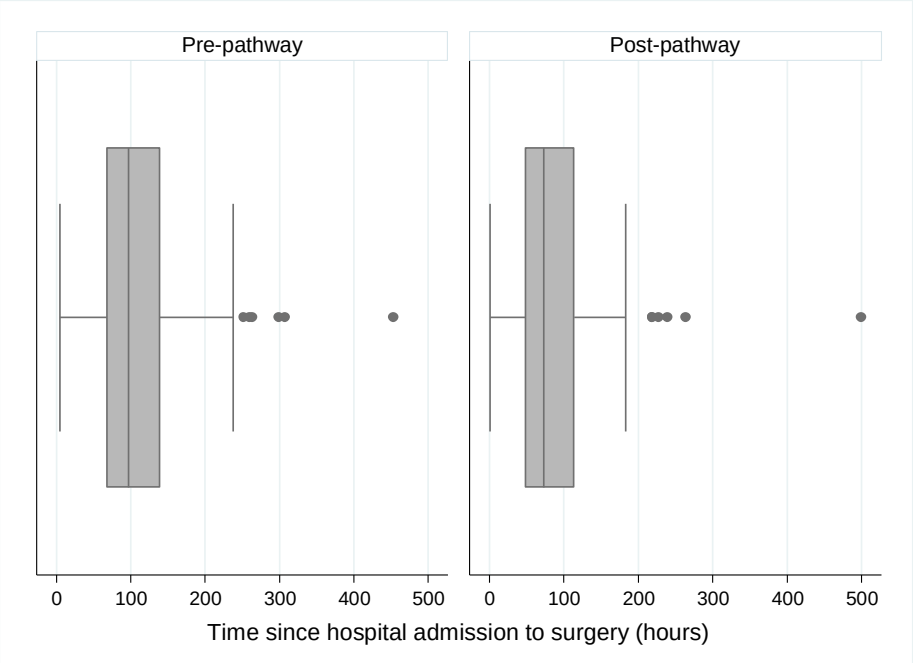


Figure 14. *Box plot of the distributions of the time interval between hospital admission and surgery in pre-pathway and post-pathway groups.*

Mortality

Raw mortality at one month was 4.3% in pre-pathway and 1.2% in post-pathway patients, while crude mortality at 8 months were 18.4% and 10.7%, respectively. The survival study was performed at one, three, six, and 8 months after hospital discharge. The comparisons between pre-pathway and post-pathway Kaplan-Meier curves were performed with a log-rank test. There was no significant difference between the survival curves of the two groups for each of the considered intervals (Figure 15). Mortality did not worsen, remaining within the fluctuations of random factors (p=0.09, p=0.36, p=0.70, and p=0.54).

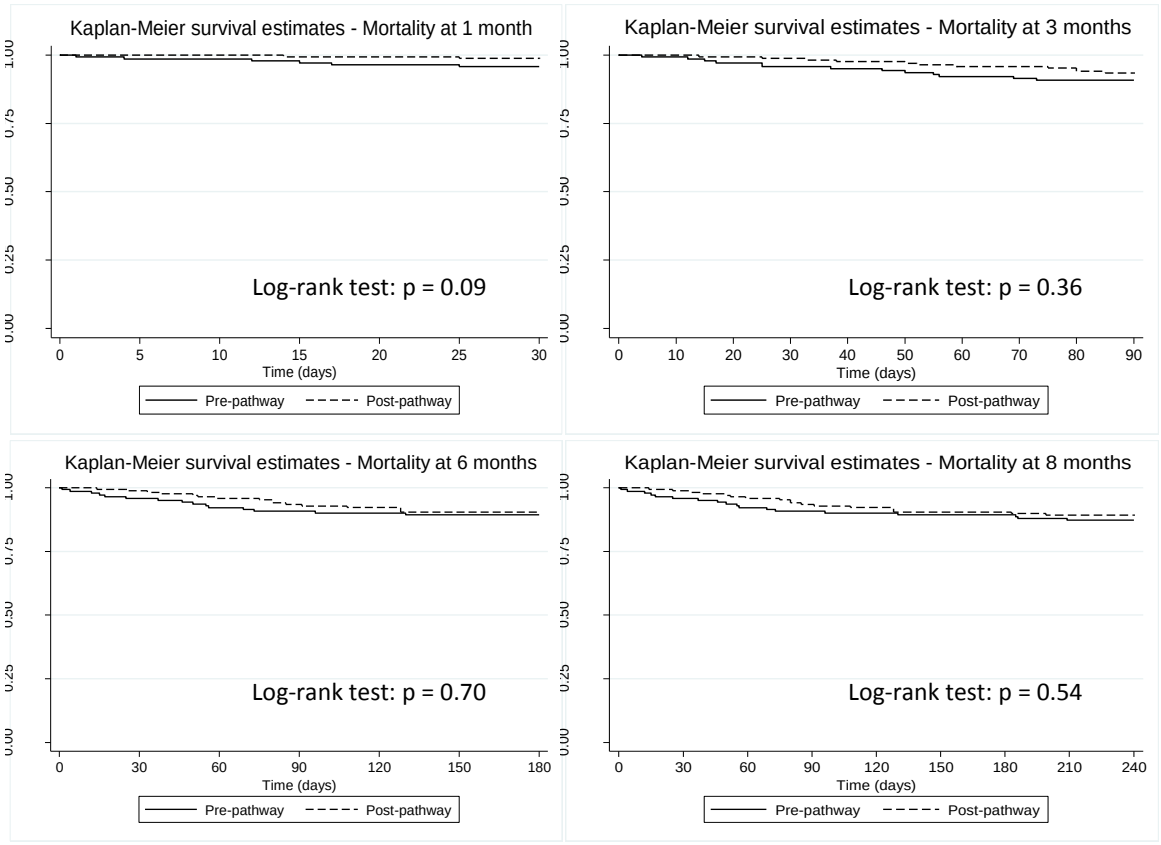


Figure 15. *Kaplan-Meier survival curves at different periods in the pre-pathway and post-pathway patient groups. For each of the considered intervals there is no difference between the survival curves.*

Average length of stay (ALOS)

The average length of stay (ALOS) significantly decreased in the post-pathway compared to the pre-pathway patients (11 versus 15 days, p<0.01). Furthermore, the standard deviation of ALOS was lower in the post-path patients than in the pre-path group (4 versus 6 days, see Table 7).

Table 7. *Average length of stay and standard deviation for pre-pathway and post-pathway patients.*

	Mean ± standard deviation (days)	**Student's t-test**
Pre-pathway	15 ± 6	**p < 0.01**
Post-pathway	11 ± 4	

Discussion

The aim of this work was to compare the outcomes of elderly patients admitted for hip fractures to the S. Chiara hospital of Trento in two different periods: before and after the introduction of the orthogeriatric clinical pathway. In particular, we focused on the fraction of operated patients within 48 hours after hospital admission, and the time interval between hospital admission and surgery. Outcomes related to 141 pre-pathway patients and to 168 post-pathway patients were compared.

The introduction of a clinical pathway including a specific orthogeriatric approach for patients over 75 years with hip fractures significantly increased the percentage of operated patients within 48 hours after hospital admission. Similarly, the time between hospital admission and surgery showed a notable shortening in the post-pathway patients.

The improvement of patient management through the orthogeriatric pathway was also demonstrated by the reduction of the average length of stay and its standard deviation, which indicated a reduced inter patient variability of care and total hospitalization.

These results are consistent with literature data, which indicated that the introduction of a clinical pathway and the co-management with geriatricians could reduce preoperative fasting time and length of hospital stay (139) (140) (142).

As reported in the previous chapters, the aims of implementing a clinical pathway include the reduction of errors and variability among patients, and the integration and coordination of different health professionals and operational units in order to achieve better outcomes (58).

In this study, the clinical pathway brought to the involvement of five different operative units and their professionals, leading to the development of team working capability and the improvement of an organizational culture. An indirect but official confirmation of this ameliorative cultural approach came by the yearly monitoring made from the Italian PNE (79). Indeed, as reported in Appendix 1, the Santa Chiara Hospital showed a continuous improvement of the performance of hip fracture treatment in elderly patients since the introduction of orthogeriatric pathway. As main feature, the PNE highlighted the increase of the number of patients operated within 48 hours after hospital admission, which raised from 22.2% in 2012 to 50.8% in 2014, thus achieving the Italian average benchmark.

International guidelines indicate that healthcare professionals should deliver care that minimizes the patients' risk of delirium, maximizes their independence, and allow early inclusion in an appropriate rehabilitation setting (135). These considerations lead us to the limitations of this study. It would be of crucial importance to evaluate, beside the mortality and proxy outcomes, also the long-period efficacy of the acute intervention. For this purpose, it would be mandatory to verify whether the treatment was successful to provide patients with the same mobility and cognitive level they had before the fracture. The evaluation of these issues is not easy, because it requires to establish in advance specific indexes and scores for assessment, and to store them in a dataset. In addition, the evaluation of the mobility should include the rehabilitation program, which is not always made within public facilities with obtainable data. Finally, it would be useful to know how many patients move to domicile, long-term care, rehabilitation centres, and nursing homes. All these steps require continuous and coordinated actions among the hospitals, the community and all the professionals involved. At the time of this study, it was not possible to obtain such information.

Conclusions

The introduction of the orthogeriatric clinical pathway for the care of elderly patients with hip fracture, led to the improvement of key outcomes. The proportion of patients operated within 48 hours after admission increased, the waiting median time for surgery decreased, and the average length of stay decreased without affecting the good performance on survival already achieved.

In addition, the multidisciplinary involvement on a common commitment led to the development of team working and an organizational culture that remained as added values. These allowed continuing the ameliorative approach in the subsequent years as demonstrated by national PNE data.

Furthermore, the preliminary results provided by this study urge to devise a more complete evaluation protocol aiming to extend the analysis to the years 2011 and 2013, to expand the information about the itineraries that patients underwent after hospital discharge, and to investigate the effects of the pathway on the functional and cognitive outcomes.

Appendix 1 – Overview of Santa Chiara Hospital outcomes made by National Program Outcomes

The Italian PNE, established in 2010 and managed by Agenas, is a National Program aimed to monitor Italian hospitals on a selected panel of performance indicators. Among these, the PNE considered the surgery treatment of hip fracture in elderly as relevant, and provided six specific indicators for it: volumes of admissions, mortality at 30 days, volumes of surgeries, surgery within 2 days, waiting days for surgery, and rate of hospital admissions. Three of these, concern with volume activity, while the other three are more focused on clinical organization and surgery outcome. In Figures 16, 17, and 18, we reported the trend of the three main indicators concerning time to surgery and mortality, over a 7-year period at the turn of the organizational change at the Santa Chiara Hospital of Trento.

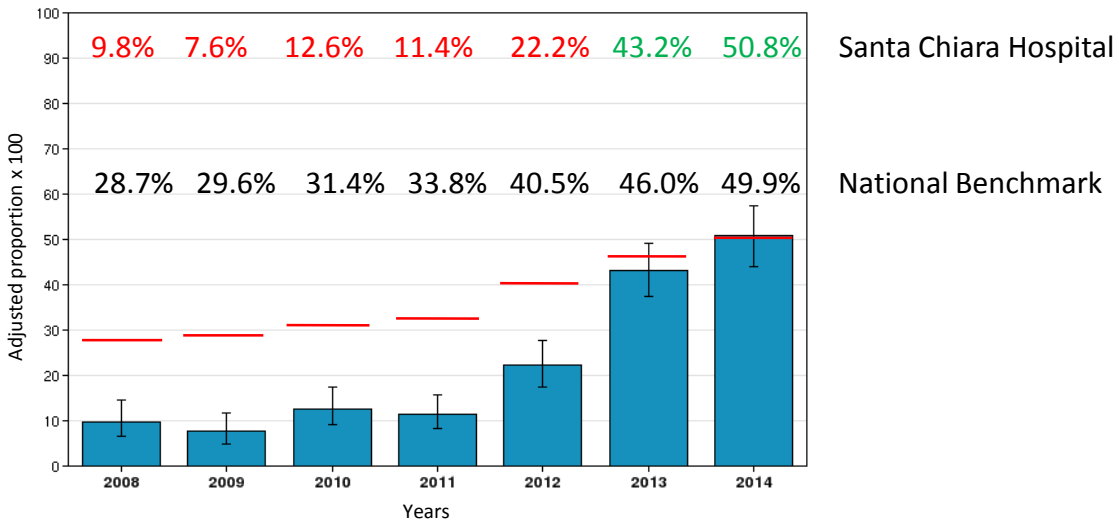


Figure 16. *Trend over years of the indicator "fraction of patients operated within 2 days" for the Santa Chiara Hospital of Trento compared to the national benchmark (red line). The national benchmark values and the Santa Chiara Hospital performance are reported as lines and bars, respectively. A progressive increase is present and the hospital reaches the average Italian benchmark in 2013. Performance out of confidence interval are reported as red values, while green indicates values within the confidence interval, as stated by yearly Italian National Programme Outcomes monitoring. The commitment on orthogeriatric care pathway started in July 2012.*

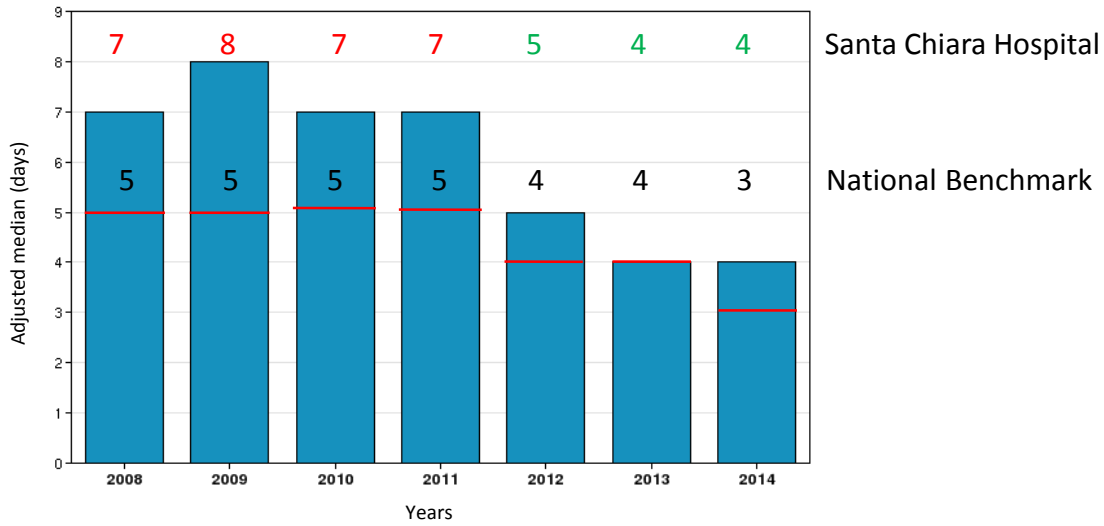


Figure 17. *Trend over years of the indicator "waiting days for surgery" for the Santa Chiara Hospital of Trento compared to the national benchmark (red line). The national benchmark values and the Santa Chiara Hospital performance are reported as lines and bars, respectively. A progressive decrease is present and the hospital reaches the average Italian benchmark in 2013. Performance out of confidence interval are reported as red values, while green indicates values within the confidence interval, as stated by yearly Italian National Programme Outcomes monitoring. The commitment on orthogeriatric care pathway started in July 2012.*

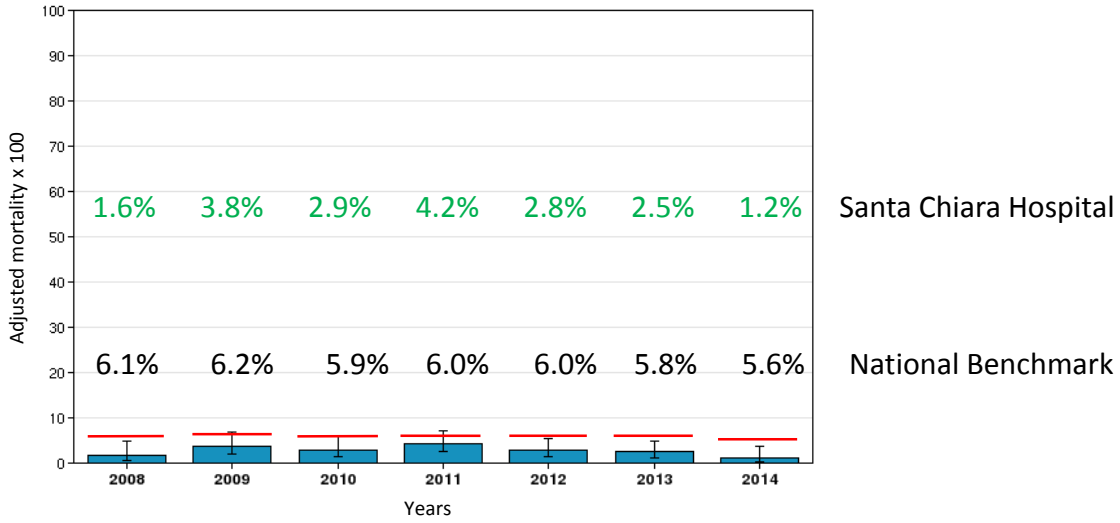


Figure 18. *Trend over years of the indicator "mortality at 30 days" for the Santa Chiara Hospital of Trento compared to the national benchmark (red line). The national benchmark values and the Santa Chiara Hospital performance are reported as lines and bars, respectively. Mortality outcome is continuously decreasing, and becomes significantly lower than the Italian benchmark in 2012. Green percentages indicate values within the confidence interval or better performance compared to the national benchmark, as stated by yearly Italian National Programme Outcomes monitoring. The commitment on orthogeriatric care pathway started in July 2012.*

5 Study cases - Organizational models

5.1 Application of National Early Warning Score (NEWS) as a stratification tool on admission in an Italian Acute Medical Ward: a perspective study[7]

Abstract

Aim of this work was assessing the performance of the National Early Warning Score (NEWS) as a bedside score for stratification of clinical instability and effective management of patients at risk of deterioration assigned to different settings of care after admission in an acute internal medicine ward.

We conducted a perspective cohort single centre study on 2,677 unselected patients consecutively admitted from July 2013 to March 2015 in the Internal Medicine ward of the main hospital of the Autonomous Province of Trento, Italy. The NEWS was collected on ward admission, assessing the following parameters: cardiac and respiratory frequency, body temperature, arteriosus systolic blood pressure, consciousness state, oxygen saturation, and need for oxygen therapy. Based on the score, we defined three risk categories for clinical deterioration: low score (NEWS: 0-4); medium score (NEWS: 5-6); and high score (NEWS ≥ 7). We considered the following adverse outcomes: total in-hospital mortality, early in-hospital mortality (<72 hours), urgent transfers to a higher intensity of care, and combined outcomes of mortality and transfer to a higher intensity of care. To quantify the association between outcome and NEWS, we used a Univariable Logistic Regression model. In addition, as secondary goal, we investigated NEWS performance in predicting adverse events linked to sudden cardiac events and chronic hypoxemic conditions.

For all the outcomes, we found a meaningful increase in the odds ratio of patients with medium and high scores in comparison with those patients with low score. For patients with NEWS >4 versus patients with NEWS <4, the risk of early death increased from 12 to 36 times, total mortality from 3.5 to 9 times, and urgent transfers from 3.5 to 7 times. Similar results were found for assessment of combined outcomes. In patients with sudden

[7] Part of this study has been submitted to Resuscitation.

cardiac events, lower scores were significantly associated with higher risk of transfer to a higher intensity of care. In patients affected by chronic hypoxemia, adverse outcomes occurred less in medium and high score categories of NEWS.

Our study confirmed that NEWS assessed on ward admission may enable stratification of patients at-risk of clinical deterioration and can be a good predictor of in-hospital serious adverse outcome. However, some sudden cardiac events may underestimate NEWS, while chronic hypoxemia may overestimate it. NEWS, as an adjunct to clinical judgment, can be valuable in planning the most appropriate organization of patient care.

Introduction

In general hospitals, acute care medical wards are the areas catering to the majority of medical admissions. Most of the cases presenting here are complex with often undefined diagnosis and different levels of clinical stability, varying from stable to unstable or critical conditions. The detection of physiological changes and the identification of patients at risk of clinical deterioration during hospital stay is critical to deliver safe and effective acute care in the first place. Patients showing signs of clinical instability are at risk of undergoing inadequate or delayed treatments upon recognition (143) (144). Intensive care admissions may be preventable in 21% of cases and sub-optimal care may be responsible till one-third of hospital deaths (145) (146). It is well known that change of physiological measurements is an indicator of clinical deterioration and consequently serious adverse events (SAE). Published studies show that over 60% of primary adverse events, including death, cardiac arrest, and unplanned transfer in intensive care units, are preceded by documented anomalies in physiological parameters (147) (148) (149). Factors involved in “preventable” serious adverse outcomes frequently include poor clinical monitoring, inadequate interpretation of changes in physiological parameters, and failure to undertake appropriate action (150).

The use of track and trigger systems to monitor physiological parameters to enable early identification and effective management of at-risk or deteriorating adult patients has been recommended in guidelines for the management of acute patients in hospitals (138) (151) (152) (153). These systems can be categorized as single-parameter systems, multiple-parameter systems, aggregate weighted scoring systems, or combination systems. Points derived from the monitoring of vital signs (e.g., pulse rate, breathing rate, blood pressure,

level of consciousness) are allocated in a weighted manner, based on the derangement of variables from “normal” ranges (154). The sum of the allocated points is known as the Early Warning Score (EWS).

A range of different EWS has been proposed and tested for use in hospitals in the United Kingdom, and the NHS for developing a standardized scoring system has put much effort. The National EWS (NEWS) was designed and validated in the UK by using evidence arising from existing tools (including the published VitalPAC EWS) to allow for a common and standardized assessment at a national level, in order to drive the “step change” required in the assessment and response to acute illness (155) (156). The use of track and trigger systems and NEWS to ensure consistency in early recognition and response to patient deterioration has also been recommended in other countries (157) (158) (159).

Early warning scores were originally developed to recognize impending clinical deterioration during hospital stay and to prevent in-hospital adverse outcomes. However, some authors proposed their use to identify medical patients whose baseline physiological measures may predict a worse outcome in order to assign them to an appropriate care level during ward admission (i.e., High Dependence Units, special areas) (160) (161) (162) (163) (164). Each EWS tool has some limits in risk prediction power. Certain patient characteristics or diseases may bias the scores. In the United Kingdom, the guidelines of the Royal College of Physicians (156) and the National Governance Group/National Clinical Guideline Development Group highlighted that using the NEWS does not replace clinical judgment. We assessed the performance of NEWS as predictor of adverse outcomes, such as in-hospital mortality and urgent transfers to intensive care, which is expected when a patient becomes unstable, in an acute care medical ward. As secondary objective, we investigated NEWS performance in predicting adverse events in patients affected by sudden cardiac events (acute coronary syndromes, and arrhythmic events) and chronic hypoxemic conditions.

Methods

We performed a cohort perspective study to assess NEWS performance considering all patients consecutively admitted to the Medical Ward (56 beds) of Santa Chiara Hospital of Trento from July 2013 to March 2015. Santa Chiara Hospital is the main facility of the public hospital system managed by the Healthcare Trust of the Autonomous Province of Trento.

It is a general hospital with over 600 beds and all medical and surgical specialties. It operates as a hub of the acute hospital network of the province. The Autonomous Province of Trento is an alpine region in north-eastern Italy, with over 530,000 inhabitants with an ageing index of 123.

We studied all patients urgently admitted to the Internal Medicine Ward from the Emergency Room, from other acute care hospitals and from the Intensive Care Unit in a post-critical phase (critical care area). All patients were triaged on admission by nursing staff trained to collect and understand the six physiological parameters routinely recorded for NEWS calculation. On admission, nurses collected each of the clinical findings forming the basis of the scoring system: (i) respiratory rate, (ii) oxygen saturation, (iii) temperature, (iv) systolic blood pressure, (v) pulse rate, and (vi) level of consciousness, with assessment of level of response on AVPU scale (Alert, Voice, Pain, and Unresponsive). As recommended by the Royal College of Physicians (156), patients were grouped into the following three trigger levels/risk categories: low score (NEW score, 0-4); medium score (NEW score, 5-6); and high score (NEW score, ≥7). Physicians provided appropriate strategy for response and setting of care relying on NEWS and clinical judgment.

We analysed score distribution and association with the following key outcomes (serious adverse events):

- total in-hospital mortality;
- early in-hospital mortality (within 72 h of admission);
- urgent (unanticipated and unplanned) transfers for clinical deterioration to a higher level of care, including Intensive Care Unit, Intensive Cardiologic Therapy, Intensive Respiratory Unit;
- combined outcome one (early in-hospital mortality and urgent transfers for clinical deterioration);
- combined outcome two (total mortality and urgent transfers for clinical deterioration).

Variables were expressed as median and interquartile rage [IQR], and as percentages of the total. The relationship between NEWS and key outcomes was analysed using a univariable logistic regression model, which provides Odds Ratio (OR) as an association measure. For

each outcome, we calculated the odds ratio of NEWS categories 5-6 (medium score) and ≥7 (high score) compared to NEWS 0-4 (low score).

As a secondary objective, we investigated NEWS performance in predicting adverse events in patients affected by sudden cardiac events (acute coronary syndromes, and arrhythmic events), and chronic hypoxemic conditions.

Among the total in-hospital deaths and the urgent transfers, we counted the number of patients with underlying conditions of cardiac disease in the three aforementioned NEWS categories (low, medium, and high risk). Moreover, NEWS overestimation was investigated by counting the number of patients showing chronic hypoxemic condition in the three NEWS categories from among all patients without any negative events. For each of the considered features a 3 × 2 contingency table and Pearson's chi-squared test ($\chi 2$) were performed. The statistical significance was set with a p-value < 0.05.

Clinical information was obtained using the hospital databases. All patients gave informed consent to data management for the study. All data manipulation was performed using STATA 13.0 (StataCorp LP, Statistics/Data Analysis, 4905 Lakeway Drive College Station, Texas 77845 USA).

Results

We analysed data from 2,677 urgent patients consecutively admitted from July 13, 2013, to March 5, 2015, at the Department of Internal Medicine of the Santa Chiara Hospital in Trento; more than 90% derived from the emergency department. Among 2,677 patients, 1,347 were men (50.3%) with a median age of 70 years (IQR, 59–79), and 1,329 were women (49.7%) with a median age of 76 and (IQR, 64-85) years. Cardiovascular, lung, and infectious diseases (including septicaemia) were the most common causes for hospital admissions (Table 8).

Table 8. *Characteristics of study population.*

Variable	**N (%)**
Hospital admissions	2,677
Male	1,347 (50.3)
Women	1,329 (49.7)
Total median [IQR] age	72 [61 - 82] years
Male median [IQR] age	70 [59 - 79] years
Female median [IQR] age	76 [64 - 85] years
NEWS < 4	1,791 (66.9)
NEWS 5 – 6	417 (15.6)
NEWS ≥ 7	469 (17.5)
Co-morbidities	
Heart diseases	590 (22.0)
Cancer	259 (9.7)
Mellitus diabetes	372 (13.9)
Kidney diseases	141 (5.3)
Dementia	59 (2.2)

NEWS score on admission ranged from 0 to 17. Assessing NEW score distribution by category, 1791 patients (66.9%) reported a NEW score of 0-4, 417 patients (15.6%) reported a score 5-6, and 469 patients (17.5%) resulted in a NEWS of 7 and more.

Frequency distribution of patient scores on admission with absolute frequency are reported in Figure 19. Visual relationship between NEW score and measured outcomes (major adverse events) is shown in Figure 20.

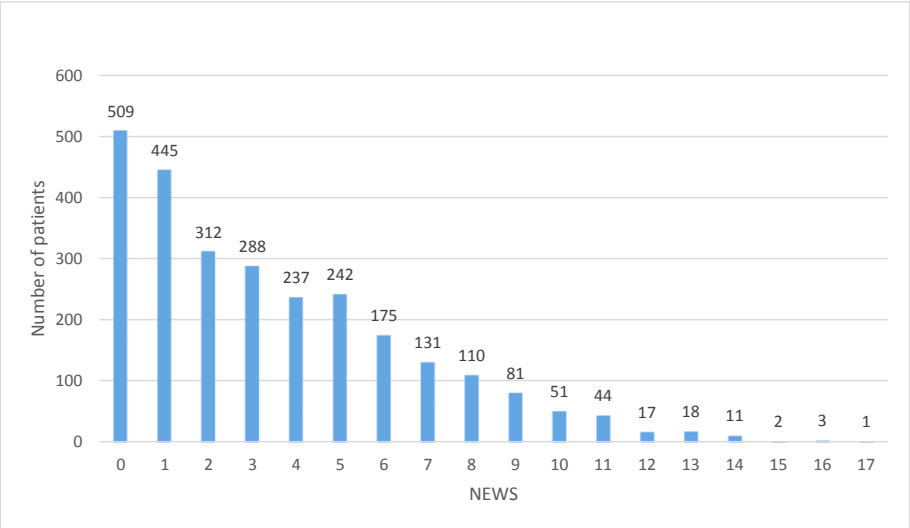


Figure 19. *Absolute distribution of patients based on NEWS.*

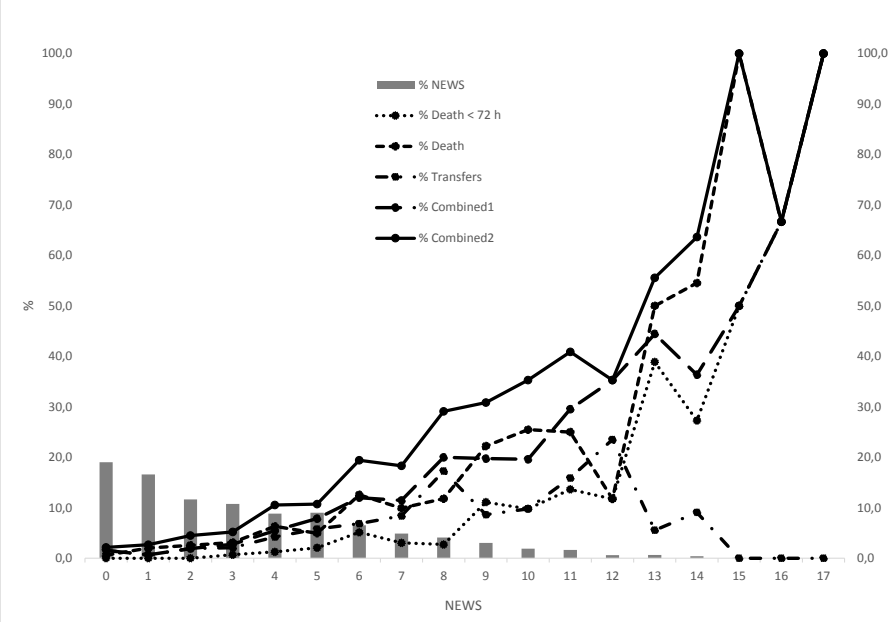


Figure 20. *Relative distribution of NEWS on admission and relationship with evaluated outcomes.*

Total in-hospital mortality

During the study period, 168 (6.3%) of the 2,677 patients died. Forty-four (2.5%) events occurred in the group with NEWS 0-4, 34 (8.2%) in the group with NEWS 5-6, and 90 (19.2%) in the group with NEWS ≥ 7 (Table 9).

The Univariable Logistic Regression Model provided an Odds Ratio of 3.5 (95% CI 2.2–5.6) for the category NEWS 5-6 compared to NEWS 0-4 and an Odds Ratio of 9.4 (95% CI 6.5–13.7) for the category NEWS ≥7 compared to NEWS 0-4 (Table 10).

Among the fatal cases, 8/44 patients (18.2%) with NEWS 0-4, 7/34 patients (20.6%) with NEWS 5-6, and 13/90 patients (14.4%) with NEWS ≥7 were affected by sudden cardiac events. A Pearson's chi-squared test provided a p=0.681, suggesting no differences between number of total in-hospital deaths in cardiac patients among the three categories of clinical risk. (Figure 21).

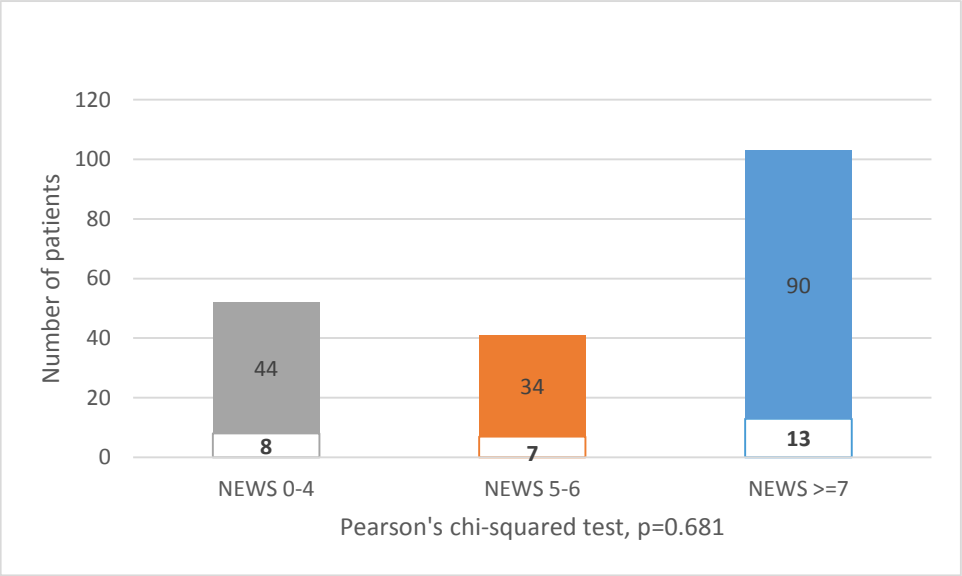


Figure 21. *Relative distribution of in-hospital deaths due to sudden cardiac events in NEWS categories, among total in-hospital deaths. White boxes refer to the fraction of deaths due to sudden cardiac events among the total in-hospital deaths (coloured boxes).*

Early in-hospital mortality (within 72 hours from admission)

Among 2,677 patients, 62 early in-hospital deaths occurred (2.3%). There were 5 (0.3%) events in the group NEWS 0-4, 14 events (3.4%) in the group NEWS 5-6, and 43 events (9.2%) in the group NEWS ≥ 7 (Table 9).

The Univariable Logistic Regression Model provided an Odds Ratio of 12.4 (95% CI 4.4 - 34.6) for the category NEWS 5-6 compared to NEWS 0-4, and an Odds Ratio of 36.1 (95% CI 14.2 – 91.6) for the category NEWS≥7 compared to NEWS 0-4 (Table 10).

Urgent transfers

Among 2,677 patients, 114 urgent transfers occurred (4.3%). We found 33 (1.8%) events in the group with NEWS 0-4, 26 events (6.2%) in the group with NEWS 5-6, and 55 events (11.7%) in the group with NEWS ≥ 7 (Table 9).

The Univariable Logistic Regression Model provided an Odds Ratio of 3.5 (95% CI 2.1–6.0) for the category NEWS 5-6 compared to NEWS 0-4 and an Odds Ratio of 7.1 (95% CI 4.5–11.0) for the category NEWS≥7 compared to NEWS 0-4 (Table 10).

Among the transfer cases, sudden cardiac events were present in 13/33 (39.4%) patients with NEWS 0-4, 9/26 (34.6%) patients with NEWS 5-6, and 4/55 (7.3%) patients with NEWS ≥7. A Pearson's chi-squared test provided a p=0.001, suggesting differences between numbers of transfers due to sudden cardiac events between the three categories of risk. In agreement with the percentages obtained, our findings show that transfers due to sudden cardiac events occurred mainly for low and medium category of risk as assessed by NEWS (Figure 22).

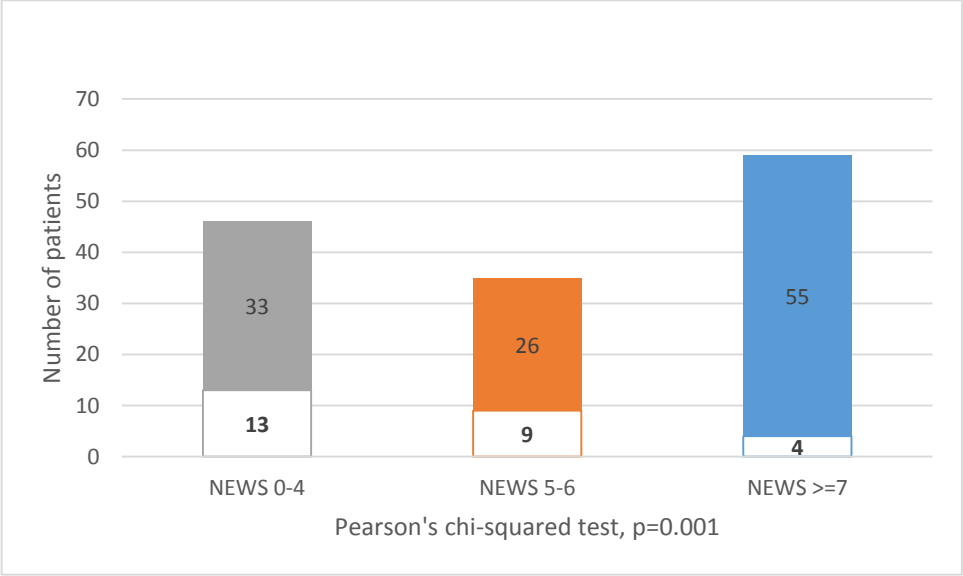


Figure 22. *Relative distribution of urgent transfers due to sudden cardiac events in NEWS categories, among total urgent transfers. White boxes represent the fraction of patients affected by to sudden cardiac events among all patients with urgent transfers (coloured boxes).*

Combined outcome one (early in-hospital mortality and urgent transfers)

Among 2,677 patients, 176 early deaths or unplanned transfers occurred (6.6%). We found 38 (2.2%) events in the group NEWS 0-4, 40 events (9.6%) in the group NEWS 5-6, and 98 events (20.9%) in the group NEWS ≥ 7 (Table 9).

The Univariable Logistic Regression Model provided an Odds Ratio of 4.9 (95% CI 3.1 – 7.7) for the category NEWS 5-6 compared to NEWS 0-4 and an Odds Ratio of 12.2 (95% CI 8.2 – 18.0) for the category NEWS≥7 compared to NEWS 0-4 (Table 10).

Combined outcome 2 (total in-hospital mortality and urgent transfers)

Among 2,677 patients, 282 total deaths or unplanned transfers occurred (10.5%). We found 77 (4.3%) events in the group NEWS 0-4, 60 events (14.4%) in the group NEWS 5-6, and 145 events (30.9%) in the group NEWS ≥ 7 (Table 9).

The Univariable Logistic Regression Model provided an Odds Ratio of 3.7 (95% CI 2.6 – 5.3) for the category NEWS 5-6 compared to NEWS 0-4 and an Odds Ratio of 10.0 (95% CI 7.4 – 13.5) for the category NEWS≥7 compared to NEWS 0-4 (Table 10).

Table 9. *Number of adverse events per categorized NEWS and patients total percentages.*

	Outcome					
	Death < 72 h, N (%)	**Total Death, N (%)**	**Transfers, N (%)**	**Combined 1, N (%)**	**Combined 2, N (%)**	**Total, N (%)**
NEWS 0-4	5 (0.3)	44 (2.5)	33 (1.8)	38 (2.2)	77 (4.3)	1791
NEWS 5-6	14 (3.4)	34 (8.2)	26 (6.2)	40 (9.6)	60 (14.4)	417
NEWS ≥ 7	43 (9.2)	90 (19.2)	55 (11.7)	98 (20.9)	145 (30.9)	469
Total, N (%)	62 (2.3)	168 (6.3)	114 (4.3)	176 (6.6)	282 (10.5)	2677

Table 10. *Odds ratio for NEWS 5-6 and NEWS≥7 versus NEWS 0-4.*

	NEWS 5-6 vs NEWS 0-4		**NEWS ≥7 vs NEWS 0-4**	
Outcome	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Death < 72	12.4 (4.4 - 34.6)	< 0.0001	36.1 (14.2 – 91.6)	< 0.0001
Total Death	3.5 (2.2 - 5.6)	< 0.0001	9.4 (6.5 – 13.7)	< 0.0001
Transfers	3.5 (2.1 - 6.0)	< 0.0001	7.1 (4.5 – 11.0)	< 0.0001
Combined 1	4.9 (3.1 - 7.7)	< 0.001	12.2 (8.2 – 18.0)	< 0.0001
Combined 2	3.7 (2.6 – 5.3)	< 0.0001	10.0 (7.4 – 13.5)	< 0.0001

Overestimation of NEW score among patients without adverse events

Among 2,395 patients without any negative events, 1,714 patients had NEWS 0-4, 357 had NEWS 5-6, and 324 had NEWS ≥ 7. Among 1,714 non-events with low score, 110 patients were affected by chronic hypoxemic conditions (6.4%), among 357 non-events with medium score, 65 patients were affected by chronic hypoxemic conditions (18.2%), and among 324 non-events with high score, 71 patients were affected by chronic hypoxemic conditions (21.9%). A Pearson's chi-squared test provided a $p<0.0001$, suggesting differences between numbers of non-events with patients with chronic hypoxemic conditions among the three clinical risk categories. In agreement with the percentages obtained, our findings show that patients without negative events affected by chronic hypoxemic conditions occurred mainly in medium and high categories of risk as assessed by NEWS (Figure 23).

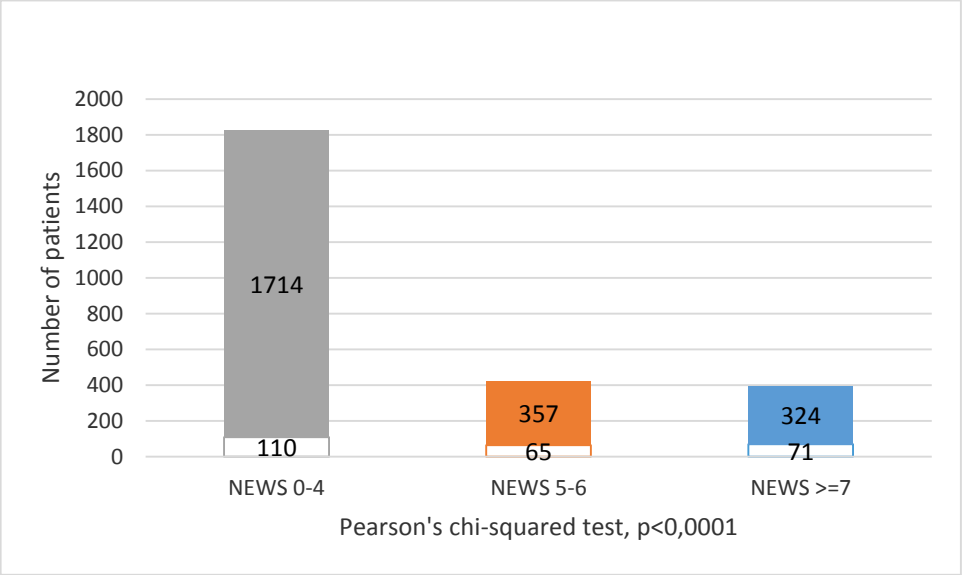


Figure 23. *Relative distribution of non-events patients affected by chronic hypoxemic conditions in the three NEWS categories, among total non-events patients. White boxes represent the fraction of non-events patients affected by chronic hypoxemic conditions on the whole non-events patients (coloured boxes).*

Discussion

This study confirmed the value of NEWS as a predictor of adverse outcomes and tool for stratification of clinical instability and recognition of patients in needs of higher care after medicine ward admission in a large patient population. The higher the NEWS is on admission, the higher are the odds of in-hospital mortality and urgent transfers for

deterioration in intensive wards, with some limitations in patients with cardiac and respiratory conditions, which is common in acute care internal medicine wards.

For all considered adverse outcomes, we observed a meaningful increase in the odds ratio for patients with NEWS categorized as medium and high, compared to those with lower scores. In particular, for patients with NEWS >4 versus patients with NEWS <4, the risk of early death increased from 12 to 36 times, total mortality from 3.5 to 9 times, and urgent transfers from 3.5 to 7 times. Similar results were achieved in the assessment of combined outcomes including early and total mortality associated with urgent transfers.

In internal medicine wards, owing to the high number of urgent admissions and heterogeneity of clinical conditions of patients, it is of utmost importance to standardize the evaluation of acute-illness severity and recognize patients at risk of deterioration in order to provide the right care at the right time.

In our study group, over 15% of admissions showed a medium risk of clinical instability (NEWS 5-6) and 17% showed a high risk (NEWS≥7), confirming literature reports on admissions to medical wards (165).

The NEWS is a based on simple measurement system in which a score is allocated to physiological parameters collected by nursing staff at the bedside, without any additional workload beside routine clinical monitoring activity. Different from scores used for predicting mortality in intensive wards (i.e. Sequential Organ Failure Assessment based models) (166), the NEWS has few variables to assess and does not include other clinical, laboratory, or diuresis data. The scoring system is designed to maximize both sensitivity and (the ability to detect patients at risk of dying) and specificity (minimization of false alarm) for unselected patients admitted to Medical Admissions Units (167).

NEWS was shown to be as good at discriminating risk of acute mortality as the best existing systems and sometimes better than others (156). This means that NEWS will provide an enhanced level of surveillance and clinical review of patients with greater specificity for identifying those at risk of clinical deterioration (156). Thus far, the NEWS is the most sensitive EWS available, whereas single parameter systems and aggregated EWS have insufficient positive predictive value or perform inferiorly (150). The validity of NEWS has been confirmed in a broad retrospective study, where it performed best among 33

aggregated weighted track and trigger systems, as well as two recent perspective studies comparing it with a track and trigger system with single parameters and PARS (Patient at Risk Score) (154) (150) (165) (168). Early Warning Scores were originally developed as bedside tools for early detection and monitoring of clinical deterioration in hospitalized patients and triggering an early response to deranged physiological parameters. However this score may serve as decision rules for the admission of medical patients, to identify patients at risk of deterioration, who might benefit from a high level of attention (163).

In general literature, a positive trend towards better clinical outcomes (improved survival, lower ICU mortality, and decrease in serious adverse event) after the introduction of an EWS System is reported, but these studies were mainly observational, heterogeneous, and used different forms of EWS (150). Studies were mostly conducted in Anglo-Saxon countries and in urban academic settings (152). In addition, it must be noted that various EWS systems are not necessarily equivalent or interchangeable (150), and that it was recommended that they be implemented only if they demonstrate clear benefit to patients and are supported by strong evidence (152).

Despite its value and relative easiness of adoption, which contributed to its implementation in acute medical settings, the NEWS has been studied less than other earlier and widely used scoring systems, such as the Modified Early Warning Score (MEWS), in real-world clinical settings. Studies carried out in internal medicine wards, in many countries, with implementation of the MEWS (Modified Early Warning Score), documented its predicting power in identifying subsets of patients at risk of deterioration (160) (161) (163) (169). Such score differs from NEWS because it does not consider oxygen saturation and oxygen therapy.

The potential of NEWS implementation in clinical practice has yet to be fully realized (170) and is proving complex (171) (172) (173). Although the NEWS has shown its superiority in detecting deteriorating patients, its positive impact on patient safety outcomes remains to be investigated (150). Validation and ongoing evaluation in large studies might be instrumental to the broad dissemination of the tool for healthcare providers and clinical practice in different countries.

To our knowledge, our research may represent the largest perspective study carried out for validation of NEWS as real-world triage tool for identifying patients at-risk of clinical

deterioration, supported by evidence in patients with sudden cardiac events (acute coronary syndromes, and arrhythmic events) and chronic hypoxemic conditions. Although being a single centre study, the setting investigated was a medical ward in a general hospital treating patients with a wide spectrum of clinical conditions from an entire mountainous region.

As for each EWS tool, there are some limits in risk prediction power with a possibility to underestimate (under-triage) or overestimate (over-triage) the real clinical situation in certain circumstances. Concerns were raised about the accuracy of EWS performance in different races and patient subpopulations (174) (175) (176) (177). It is has been reported that some cardiac conditions (i.e., coronary syndromes, rhythm disorders) can be underestimate, while other conditions such as chronic hypoxemia and hyperpyrexia can overestimate clinical instability (178). For this reason, modifications of NEWS have been suggested by some authors to improve specificity while identifying the sickest patients (167) (179).

Our analysis evidenced that a number of cardiac conditions may cause acute worsening without generating higher NEWS scores on admission, as unplanned transfers owing to sudden cardiac events occurred mainly for low and medium category of risk. This may raise safety issues, considering that such patients make up a large proportion of medical ward admissions. On the other side, our data show that patients without adverse events affected by chronic respiratory conditions were distributed mainly in medium and high categories of NEWS. In patients with chronic hypoxemic conditions the “respiratory variables” of the NEWS seem poor discriminators of patients who are clinically deteriorating (179), leading to clinically insignificant triggers (167) and resources for patient management. In other words, there would have been a number of “missed” cases, affected by sudden cardiac events that might require a higher level of care but were assessed as low risk, and a potential number of “false positive” among patients with chronic hypoxemic conditions. As recommended by key medical guidelines, these results reinforce the need to perform a careful and timely risk assessment based equally on the score and clinical judgment to discriminate acute deterioration, and thus help improve patient outcomes and avoid inappropriate care without jeopardizing safety.

Although NEWS score should be always interpreted with caution, stratification of clinical instability can support internal medicine wards in providing enhanced response to acute illness and delivering organizational models based on intensity of care (180) (181) (182) (183). Further studies on the application of NEWS in patients with specific illnesses are needed. In the future, it is possible that change in clinical management will be supported by technological tools and models for disease-specific EWSs (184).

Conclusions

Our study confirms the validity of NEWS as simple and easy triage tool to enable stratification of patients at-risk of clinical deterioration in internal medicine wards. The NEWS, calculated on admission, is a strong predictor of clinical outcomes, including in-hospital mortality and urgent transfers to a higher level of care. However, some clinical condition may have different effects on NEWS scores and safety performances and this must be taken in account when using the NEWS as surveillance and decision making tool in hospitals. Combination of NEWS and clinical judgment may be crucial to identify the safest and appropriate setting of care for ill patients.

Efforts are needed to evaluate performance and organizational changes related to NEWS implementation (supported by competent leadership, education and clinical audit) as an integral part of a system-wide approach to safety through improved identification and management of deteriorating patients in hospitals. Different subgroups of critically ill patients should be specifically analysed. The body of knowledge can be increased by further research addressing the impact of NEWS on resources utilization and cost-effectiveness analysis and potential benefits of new technologies to develop prediction models for adverse outcomes in acute medical care facilities.

5.2 Organizational change in Internal Medicine ward to improve outcomes: a perspective before-after study[8]

Abstract

In medical wards, in order to guarantee safe, sustainable and effective treatments to complex patients, care should be graduated into levels ranging from lower to higher intensity. On the basis of standardised assessment and stratification of patient severity, patients should be allocated in bed areas with progressive level of care and a management of the patient flow strictly related to the clinical instability.

In order to support this assumption, we conducted a perspective observational study on all unselected admissions to the internal medicine ward of the Santa Chiara Hospital of Trento, hub of the hospital network of the Autonomous Province of Trento, Italy from 1st January 2013 to 31st December 2015. During 2013, a standard organizational model (SC) was present, while an organizational model for intensity of medical care (IC) was introduced in 2014 and 2015. In SC, patient admission was performed according to bed availability only. In IC, patients were allocated to three different ward settings (high, middle and post-acute care) based on the stratification of clinical instability done during ward admission. The National Early Warning Score (NEWS) was used for the stratification, as an adjunct to clinical judgment. In order to compare SC and IC models, outcomes related to 1,393 patients managed by standard care (from 1st January 2013 to 31th December 2013) were compared to those related to 1,608 patients managed by intensity of medical care (from 1st January 2015 to 31th December 2015). We considered 2014 as a "switching year".

We assessed the following outcomes: total and early in-hospital mortality (<72 h), number of urgent transfers for clinical deterioration to intensive wards; combined outcomes of urgent transfers with total and early in-hospital mortality, proportion of stepdown patients (from intensive care) and unstable patients transferred from other spoke hospitals of the province.

We demonstrated that the intensity of medical care model, in comparison with standard care, enabled a significant reduction in urgent transfers for clinical deterioration to

[8] We are going to submit part of this study for publication on European Journal of Internal Medicine.

intensive care wards: 5.0% versus 1.7%, p<0.0001, and in combined outcomes (8.2% versus 3.6%, p<0.0001, and 12.2% versus 8.5%, p=0.0007). In addition the model based on Intensity of medical care showed an increase of step-down admissions in internal medicine from intensive care (2.4% versus 4.0%, p=0.018) and a higher proportion of transfers from spoke hospitals (4.3% versus 6.7%, p=0.005).

Results indicates that implementation of an organisational model based on intensity of medical care may improve patient outcomes and enable an efficient bed management and patient flow. Designing differentiated settings of treatment depending on clinical severity and patient needs in acute medical wards may improve quality of service and reduce inappropriate bed use, without negatively impacting on outcomes.

Introduction

Medical wards, laying at the heart of inpatient medicine, are experiencing an increase in workload and number of admissions of complex and frail patients. These represent the majority of urgent hospital admissions, with often undefined diagnosis and different levels of clinical stability, varying from stable to unstable or critical conditions (185) (186) (187). All over the world, acute medical wards are facing the challenge of conjugating optimal levels of safety, effectiveness and patient-centeredness of care with better efficiency in the use of the limited resources available.

Understanding how to better organize health care for general medical patients is an international priority (188). Indeed, more than any other health care setting, general medical wards generate the errors that lead to preventable deaths (189). The detection of physiological changes and the identification of patients at risk of clinical deterioration during hospital stay is critical to deliver safe and effective acute care. Patients showing signs of clinical instability are at risk of undergoing inadequate or delayed treatments upon recognition (143) (144). Intensive care admissions may be preventable in 21% of cases and sub-optimal care may be responsible until one-third of hospital deaths (145) (146).

Among the approaches proposed to solve this dilemma of providing better care at lower cost, there is the new paradigm of organisation around the multifaceted concept of “intensity of medical care” (190) (191) (192) (193) (194). Such approach relies on the classification of patient acuity performed using tools for stratification of severity of patient

conditions and the delivery levels of progressive care, stepping up and down patients, according to clinical instability and complexity of needs.

Patients should be clustered by severity at the time of ward admittance using validated prognostic scores (Early Warning Scores, such as NEWS), in order to identify their clinical risk, and allocated to areas dedicated to patients with homogeneous needs of care (195) (196).

In the ward, patients can be managed and progressively moved (stepped up and down), according to their clinical condition, among ward areas with different, but strongly integrated, levels of care. Addressing these changes requires staffing arrangements, collaboration among medical and nursing staff members, effective clinical protocols and regular feedback on achievements.

Therefore, it is crucial to go beyond traditional organisational models of general medical wards with undifferentiated settings of care, relying on clinical speciality and providing a diluted “average” standard of care for all patients. This may lead to unmet or mismatched needs, especially for critically ill patients, vulnerable to clinical deterioration, resulting in an increased risk of adverse events and suboptimal quality of care (180) (195).

Modes of care may include stand-alone units or incorporation of beds into intensive care units or medical wards. The latter has been less implemented and studied. Areas with “high-intensity of care”, operating as transitional units, were originally born to support Intensive Care Units (ICU) to enable a more appropriate use of beds, allowing management of those patients otherwise inappropriately and unnecessarily admitted to the ICU. These areas provided “step-down” beds in the hope that this move would prevent a later ICU admission or “step-up” beds of patients from general wards or emergency departments (197) (198) (199). This can be a cost-effective solution to provide appropriate critical care outside intensive care units and improve flow of patients requiring more support than regular care, but not full intensive care (200) (201) (202) (203) (204). Such results have been confirmed also when the intermediate area was managed by non-intensivist staff and was structurally separated from ICU (205).

Although structural changes and approaches somehow based on intensity of care in medical wards may have been implemented in acute hospitals, especially in Europe, as part

of reorganizations for improving assessment, treatment and flow of patients, to our knowledge, there are relatively few and fragmented, and mostly retrospective, published data to support the benefits on patient outcomes of such experiences in real contexts of care.

As changes were implemented in the internal medicine ward of Santa Chiara Hospital of Trento, we considered such an opportunity to design a perspective study to evaluate a new organisational model based on intensity of medical care (IC), which replaced the traditional standard of medical care (SC). The new IC model merged systematic assessment of severity with appropriate and graduated response to heterogeneity and complexity of patients, supported by technological and practical changes to promote teamwork, collaboration and performance feedback.

The purpose of our study was to examine the transition and its impact on key clinical and organisational outcomes.

Methods

All the patients consecutively admitted in the Unit of the Internal Medicine of the Santa Chiara hospital in Trento, from 1st January 2013, to 31th December 2015, were included in the study. In the first period, from 1st January 2013 to 31th December 2013, the organization of the ward was based on traditional standard medical care service (SC); in the second one, from 1st January 2014 to 31th December 2015, ward organization was based on intensity of medical care (IC). Almost all patients were admitted to the Internal Medicine Ward from the Emergency Room, from other acute care hospitals and from the Intensive Care Unit in a post-critical phase (critical care area)[9].

[9] Santa Chiara Hospital is the main facility of the public hospital system managed by the Healthcare Trust of the Autonomous Province of Trento, which is the governmental body responsible for all healthcare services in the province. At the time of the study, Santa Chiara Hospital was a large general hospital with over 600 beds and all medical and surgical specialties, including emergency department and multiple intensive care units. The hospital plays a pivotal role in the acute hospital network of the region. Hospital care is provided according to a hub and spoke model encompassing all emergency, surgical and medical wards across the province. The Autonomous Province of Trento is an alpine region in northeastern Italy, with over 530,000 inhabitants with an ageing index of 123. Its surface is equal to 6,212km2; 75% of the territory stretches above 1,000 meters of altitude.

Standard medical care (SC)

Until the end of 2013, the Internal Medicine (IM) ward consisted of three clinical sections, each with its own organization, for a total of 58 beds. The organizational model was traditional with bed assignment reflecting the principle of the "first available bed" only. Telemetry monitored beds, excluding electrocardiography, were non-available. One joint (physician and nurse) ward round was performed daily with clinical revaluations if necessary; sporadically it was possible to perform bedside non-invasive mechanical ventilation.

Intensity of medical care (IC)

Since 2014, the IM Unit has operated with 56 bed differentiated in three integrated ward areas managed by intensity of medical care:

- "High care" area providing "high-intensity" of medical care or "intermediate" care (Intermediate Care Area, ICA) with 8 beds equipped with centralised multiparameters monitoring technology (electrocardiography, pulse oximetry, orthostatic blood pressure); possibility to perform non-invasive ventilation; twice-a-day joint (physician and nurse) ward rounds and clinical revaluations if necessary;
- "Medium care" area, providing a "medium-intensity" of medical care (Medium Care Area, MCA) consisting in 33 beds with the capability of telemetric monitoring (electrocardiography), one daily joint (physician and nurse) ward round and clinical revaluations if necessary;
- "Post-acute area", providing "low-intensity" of medical care (Post-Acute Care Area, PACA) consisting of 13 beds; one daily joint (physician and nurse) ward round and clinical revaluations if necessary. In this area, urgent admissions are not planned, but only transfers of patients in post-acute phase stepping down form higher levels of care (ICA e MCA) needing clinical/functional rehabilitation and/or with discharge problems.

Under this organisational model, patient bed assignment to different areas of the ward follows an assessment on ward admission in a common area and allocation to ICA ("high-intensity" area) or MCA ("medium-intensity" area) depending on the degree of clinical instability and thus risk of clinical deterioration.

Since the beginning of the IC period, all patients were triaged on admission by nursing staff trained to collect and understand the six physiological parameters routinely recorded for NEWS calculation[10]. Physicians provided appropriate strategy for response and setting of care relying on NEWS and clinical judgment.

Statistical analyses and Outcomes

In order to have descriptive and comparative statistics of the outcomes over the three years (2013, 2014, and 2015), 3x2 contingency tables, and Pearson's chi-squared test were calculated for each outcome. In addition, SC and IC were compared in two different steps. The first, comparing outcomes of the SC organizational model in 2013 with the ones of the IC organizational model in 2014. The second, comparing outcomes of the organizational model SC in 2013 with the ones of the organizational model IC in 2015, considering 2014 as a "switching year". For each outcome and for each of the two comparisons, 2x2 contingency tables, Pearson's chi-squared and relative risk (RR) of IC compared to SC were calculated. We performed a multiple comparison correction with the Holm–Bonferroni method. The two organizational models (SC vs IC) were compared, analysing the following patient outcomes:

- early in-hospital mortality (within 72 h of admission);
- total in-hospital mortality;
- urgent (unanticipated and unplanned) transfers for clinical deterioration to a higher level of care (intensive care): Intensive Care Unit (ICU), Intensive Coronary Unit, Intensive Respiratory Unit;
- combined outcome one: early in-hospital mortality and urgent transfers for clinical deterioration;
- combined outcome two: total mortality and urgent transfers for clinical deterioration.

[10] The NEWS is based on simple measurement system in which a score is allocated to physiological parameters collected by nursing staff at bedside, without any additional workload beside routine clinical monitoring activity. On admission, nurses collected each of the clinical findings forming the basis of the scoring system: (i) respiratory rate, (ii) oxygen saturation, (iii) temperature, (iv) systolic blood pressure, (v) pulse rate, and (vi) level of consciousness, with assessment of level of response on AVPU scale (Alert, Voice, Pain, and Unresponsive). As recommended by the Royal College of Physicians (Royal College of Physician 2012), patients were grouped into the following three trigger levels/risk categories: low score (NEW score, 0-4); medium score (NEW score, 5-6); and high score (NEW score, ≥7).

In addition, we assessed the following performances related to management of bed capacity, patient flow and reliability of scoring system:

- proportion of stepdown patients admitted in IM ward transferred from an higher level of care;
- proportion of unstable medical patients transferred in IM ward from spoke hospitals;
- bed occupancy;
- nursing staff to patient ratio.

Data collected for each patient included the following: age, gender, mortality, type of stay, severity of illness (according to NEW scoring system).

The analysed variables were expressed as mean and standard deviation, median and interquartile range [IQR] and as percentages of the total. A p-value less than 0.05 indicated statistical significance. All analyses were performed with STATA statistical software, version 13.0, StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA.

Results

We analysed 4,438 admissions under the different organizational models during a consecutive period of 36 months. We compared 1,393 consecutive unselected admissions during the SC period (January 1 to December 31, 2013), 1,437 consecutive unselected admissions during the IC period in 2014 (January 1 to December 31, 2014), and 1,608 consecutive unselected admissions during IC period in 2015 (January 1 to December 31, 2015).

Table 11. *Characteristics of the study population.*

Characteristics	**Year 2013 SC, n (%)**	**Year 2014 IC, n (%)**	**Year 2015 IC, n (%)**	**p - value**
Total	**1,393**	**1,437**	**1,608**	
Male	695 (50)	675 (47)	788 (49)	n.s. (Pearson's X^2 test)
Female	698 (50)	762 (53)	820 (51)	n.s. (Pearson's X^2 test)
Total median age [IQR] years	72 [62 - 82]	72 [60 - 82]	72 [62 - 83]	n.s. (U Mann-Whitney test)
Male median age [IQR] years	70 [58 - 80]	70 [59 - 78]	71 [59 - 80]	n.s. (U Mann-Whitney test)
Female median age [IQR] years	75 [66 - 84]	73 [62 - 84]	74 [65 - 85]	n.s. (U Mann-Whitney test)
Average weight of DRGs	1.19	1.21	1.20	n.s. (Student's t-test)

Abbreviations: IC = Intensity of medical care; SC = Standard Care; IQR = Interquartile range; DRGs = Diagnosis Related Groups; n.s. = no statistically significant.

The characteristics of the study population (patients treated under SC and IC) are summarised in Table 11. We did not find significant differences in demographic data and average weight of DRGs (Diagnosis Related Groups), during SC and IC periods. Most frequently, cause of admission were cardiovascular diseases, acute respiratory illness and sepsis. Over 95% were urgent medical admissions.

The main results of outcome (patient outcomes and performances) comparison between the two models of care are summarised in the table and commented in the paper.

Table 12. *Studied outcomes and results over three years period.*

2013 (SC) vs 2014 (IC) vs 2015 (IC)				
Outcome	**Year 2013 SC, n (%)**	**Year 2014 IC, n (%)**	**Year 2015 IC, n (%)**	**p-value**
Early in-hospital mortality (<72 h)	44 (3.2%)	37 (2.6%)	31 (1.9%)	0.099
Total in-hospital mortality	100 (7.2%)	111 (7.7%)	109 (6.8%)	0.601
Urgent transfers to intensive care	70 (5.0%)	28 (1.9%)	27 (1.7%)	**< 0.0001**
Combined outcome 1	114 (8.2%)	65 (4.5%)	58 (3.6%)	**< 0.0001**
Combined outcome 2	170 (12.2%)	139 (9.7%)	136 (8.5%)	**0.003**
ICU stepdowns	34 (2.4%)	62 (4.3%)	64 (4.0%)	**0.017**
Transfers from spoke hospitals	60 (4.3%)	108 (7.5%)	107 (6.7%)	**0.001**
Total	**1,393**	**1,437**	**1,608**	

Abbreviations: combined outcome 1= urgent transfers for clinical deterioration and early in-hospital mortality; combined outcome 2= urgent transfer for deterioration and total in-hospital mortality; IC = Intensity of medical care; SC = Standard Care.

Total in-hospital mortality

We did not find differences in total mortality among the three periods: 100 patients (7.2%) under SC model in 2013, 111 patients (7.7%) under IC model in 2014, and 109 patients (6.8%) under IC model in 2015, p=0.601 (Table 12).

Early in-hospital mortality (within 72 hours of admission)

We found a tendency to reduction, albeit non-significant, during the three years: 44 early deaths (3.2%) occurred under SC model in 2013, 37 early deaths (2.6%) under IC model in 2014, and 31 early deaths (1.9%) under IC model in 2015, p=0.099 (Table 12).

Urgent transfers to intensive care

We found a significant difference of urgent transfers to intensive care among the three years (Table 12). The post-hoc analysis indicated a significant reduction of urgent transfers to intensive care from 2013 to 2014 (Table 13). The exposition to the IC organizational model reduced the relative risk of urgent transfers to intensive care by 61% in the first year of IC implementation (Table 13). This significant reduction was confirmed in 2015 (Table 14). The exposition to the IC organizational model reduced the relative risk of urgent transfers to intensive care by 67% in the second year of IC implementation (Table 14).

Combined outcome one (early in-hospital mortality and urgent transfers)

We found a significant reduction in the combined outcome among the three years (Table 12). Post-hoc analysis showed a significant reduction of combined outcome from 2013 to 2014 (Table 13). The first year of exposition to the IC organizational model reduced the relative risk of combined outcome by 45% (Table 13). The reduction on combined outcome was confirmed in the second year of IC model application (Table 14) with a reduced relative risk of 57% for IC patients compared to SC patients (Table 14).

Combined outcome two (total in-hospital mortality and urgent transfers to intensive care)

We found a significant reduction in the combined outcome among the three years (Table 12). Post-hoc analysis indicated a significant reduction of combined outcome from 2013 to 2014 (Table 13). The first year of exposition to the IC organizational model reduced the relative risk of combined outcome by 21% (Table 13). The reduction on combined outcome

was confirmed in the second year of IC model application (Table 14) with a reduced relative risk of 31% for IC patients compared to SC patients (Table 14).

Stepdown admissions from a higher level of care

We found a significant difference in the proportion of stepdown admissions among the three years (Table 12). Post-hoc analysis showed a significant increase in the proportion of stepdown admissions from 2013 to 2014 (Table 13). The exposition to the first year of IC organizational model increased the relative risk in the proportion of stepdown admissions by the IM ward by 77% (Table 13). The increase was confirmed in the second year of IC organizational model (Table 14), with an increased relative risk of 63% (Table 14).

Urgent transfers from spoke hospitals

We found a significant difference in the proportion of admissions from spoke hospitals among the three years (Table 12). Post-hoc analysis showed a significant increase in the proportion of admissions from spoke hospitals from 2013 to 2014 (Table 13). The exposition to the first year of IC organizational model increased the relative risk in the proportion of urgent transfers from spoke hospital by the IM ward by 74% (Table 13). The increase was confirmed in the second year of IC organizational model (Table 14), with an increased relative risk of 54% (Table 14).

Organizational outcomes (bed occupancy and nursing staff to patient ratio)

Be occupancy moved from 85% under SC model in 2013 to 95% under IC model both in 2014 and in 2015. The nursing staff to patient ratio also changed from 1:9 in SC model (2013) to an average of 1:12 in IC model (2014 and 2015). These ratios were 1:4, 1:12, and 1:14 in the ICA, MCA, and PACA respectively.

Table 13. *Studied outcomes and results comparing 2013 (standard Medical Care organizational model) and 2014 (Intensity of Medical Care organizational model).*

2013 (SC) vs 2014 (IC)					
Outcome	**Year 2013 SC, n (%)**	**Year 2014 IC, n (%)**	**RR (95% CI)**	**p-value**	**Post-hoc correction**
Urgent transfers to intensive care	70 (5.0%)	28 (1.9%)	0.39 (0.26-0.59)	**< 0.000001**	*
Combined outcome 1	114 (8.2%)	65 (4.5%)	0.55 (0.41-0.74)	**0.0001**	*
Combined outcome 2	170 (12.2%)	139 (9.7%)	0.79 (0.64-0.98)	**0.031**	*
ICU stepdowns	34 (2.4%)	62 (4.3%)	1.77 (1.18-2.65)	**0.006**	*
Transfers from spoke hospitals	60 (4.3%)	108 (7.5%)	1.74 (1.29-2.36)	**0.0003**	*
Total	**1,393**	**1,437**			

Abbreviations: combined outcome 1= urgent transfers for clinical deterioration and early in-hospital mortality; combined outcome 2= urgent transfer for deterioration and total in-hospital mortality; IC = Intensity of medical care; SC = Standard Care; * = statistical significance after post-hoc correction; n.s. = no statistically significant.

Table 14. *Studied outcomes and results comparing 2013 (Standard Medical Care organizational model) and 2015 (Intensity of Medical Care organizational model).*

2013 (SC) vs 2015 (IC)					
Outcome	**Year 2013 SC, n (%)**	**Year 2015 IC, n (%)**	**RR (95% CI)**	**p-value**	**Post-hoc correction**
Urgent transfers to intensive care	70 (5.0%)	27 (1.7%)	0.33 (0.22-0.51)	**< 0.000001**	*
Combined outcome 1	114 (8.2%)	58 (3.6%)	0.43 (0.32-0.58)	**< 0.000001**	*
Combined outcome 2	170 (12.2%)	136 (8.5%)	0.69 (0.56-0.86)	**0.0007**	*
ICU stepdowns	34 (2.4%)	64 (4.0%)	1.63 (1.09-2.44)	**0.018**	*
Transfers from spoke hospitals	60 (4.3%)	107 (6.7%)	1.54 (1.14-2.09)	**0.005**	*
Total	**1,393**	**1,608**			

Abbreviations: combined outcome 1= urgent transfers for clinical deterioration and early in-hospital mortality; combined outcome 2= urgent transfer for deterioration and total in-hospital mortality; IC = Intensity of medical care; SC = Standard Care; * = statistical significance after post-hoc correction; n.s. = no statistically significant.

Discussion

This before and after study of a multifaceted intervention demonstrated, on a large patient population, over a three years period, that the transition from standard of medical care

(SC) to intensity of medical care (IC), was associated with improved clinical outcomes, more appropriate bed management, and utilization of ICU resources with no harm.

The organisational change determined by IC was associated with a decrease of the number of unplanned transfers for clinical deterioration in intensive care units and a reduction in the combination of unplanned transfers and early and total mortality (combined outcome one and two). Additional positive results were the significant increase in patients transitioning out of intensive care ("stepdown") and transferred for clinical instability from other medical wards of spoke hospitals of the province. The introduction of the IC model positively affected the ward organization management as showed by the features relative to bed occupancy and nursing/patient ratio. Although, our results showed that the model of IC versus SC did not change total mortality, we found a tendency to reduction of early in-hospital mortality over the three years period (3.2% vs 2.6% vs 1.9% on total of admissions, and 42.0% vs 33.3% vs 28.4% on the total of deaths).

Therefore, our data show that systematic triage and stratification of patients based on risk of clinical instability and their allocation to the most appropriate setting for monitoring and treatment may improve clinical management and quality of care.

We are not aware of fully comparable and recent perspective pre-after studies models of "intensity of care" in internal medicine wards, despite such approaches were strongly endorsed, for a long time, at ward and even at hospital level in several countries, including Italy, as key pattern of hospital development and standard of care in response to new clinical challenges and growing environment pressures (206) (181) (207). Evidence of effective interventions to improve the quality and safety of care in medical wards is limited in comparison to other acute hospital settings and it is unclear whether medical wards are truly resistant to some strategies that have shown benefits elsewhere in the hospital (189). Most studies related to systems of internal medicine wards lacked description of important confounding factors and showed little analysis of implementation and durability of the changes proposed (189). Currently, the area is certainly under-researched.

Furthermore, it has been reported that comparing results with other, especially at international level, may not be easy or appropriate because factors such as standardisation of terms, regional/local policies and evidence-based protocols regarding care practices or ICU admission criteria may act as confounder (199) (190).

In a research perspective, we think that some analogies may be found in experiences conducted in hospitals implementing intermediate care units (IMCU), similar to our ICA. Despite encouraging results of some studies, at the moment, evidence is still limited to confirm a positive effect of IMCUs on patient outcomes, efficiency and costs. It is worth underlying that studies on the impact of IMCU are generally rather old, primarily limited to observational, single-centre before/after reports, mainly on surgical patients, with mixed results (208) (199). Recently, a multicentre European study showed for the first time, that adults admitted to hospitals with both Intensive Care Units (ICU) and independent Intermediate Care Units (IMCU) had lower in-hospital mortality than those admitted to ICUs without an IMCU (209).

Overall, until now intermediate care and patient outcomes have received little attention in the international literature, especially for medical wards and recent data are lacking (208). No controlled trials have been reported to date.

The hospital setting for acute unstable patients was obtained with implementation, within the medical ward, of an ICA adequately equipped for monitoring and intervention, similarly to what has been reported in other studies on intermediate care beds. However, the sole implementation of ICA, which could resemble other studies on intermediate care/high dependency units, probably was not enough to explain achieved results in the ward organisation.

Setting up a new model of care requires system-wide changes in practice, that in our case were implemented through strong clinical leadership commitment, alignment and integration of clinical improvement efforts with organizational priorities, medical and nursing staff competencies development, systematic collaboration among physicians and nurses and internal medicine ward and intensive care units, adherence of evidence-based guidelines and protocols. It was also essential to establish an infrastructure for regular feedback on data, processes and performances.

Baseline mortality data on in-hospital mortality of the IM ward of the Santa Chiara Hospital documented from 2010 to 2014 an increase in total mortality from 7.2% to 9.9%, 38% to 42% of all deaths occurred in the first 72. These results prompted immediate attention as the medical area manages a heterogeneous case mix and, as reported in medical literature, some deteriorating situations can go undetected. Outcomes were chosen among those

more frequently proposed in the literature, also for being useful and understandable by all clinical and managerial stakeholder engaged in redesigning the system.

Impact of change, variation of clinical practice and outcomes may be influenced by patient variables and related to complex organisational and context related factors influencing systems of care (210) (211) (212). Influence of interventions on outcomes may require time and "maturity", reflecting the developmental stage and sustainability of various quality improvement strategies and programs (213) (214).

Therefore, factors other than the new organisational model of care might explain changes in outcomes achieved in our study, including mortality and admissions to the ICU and IM ward. As shown in results the patient population treated under SC did not show any meaningful difference from the population treated under IC, both considering demographic data and DRG (as proxy of patient complexity related to workload). We are not aware of any organizational factor that could have skewed our results. To reduce selection bias we included all the patients admitted during the three years periods.

Our experience was implemented in a healthcare system pursuing a long-term comprehensive quality strategy (215), where performances and outcomes monitored at Italian level show a multi-year improvement trend (79).

Among other factors related to performances and outcomes nursing organisation, competencies and staffing levels are under investigation (190) (216) (217). Although a detailed discussion of nurse staffing and organisation lies outside the scope of this paper, it is worth noting that Santa Chiara Hospital, for several years, has been pursuing efforts to implement new models of nursing care, curricula and programs for competencies assessment and development, including analysis of adequate staffing requirements in medical and surgical wards (218) (219). Outcomes may be also linked to unit direction, organisation and curriculum of physicians responsible for graded care options between intensive and conventional ward care.

Our study is perspective and single centre and this limits generalizability to other institutions.

We performed an observational study, which is probably the only options once beds have been reorganised and high dependency beds set up, considering the great pressure to admit patients if capacity permits and ethical issues.

In our study, we used outcome measures, singularly or in combination, widely proposed in studies evaluating performances of EWS, impact of intermediate care models and quality of hospital care (220) (152).

We did not focus on and report any economic and cost related outcomes. Although, we used some quality outcomes that by definition are associated with a more appropriate use of hospital resources. Results show an improvement in bed management and patient flow and a sustained occupancy rate higher than 90%, which seem to provide, according to measured outcomes, a good balance between safety and care efficiency. Our data may point to fact that IC may allow adequate levels of care for patient even with occupation rates between 90% and 100%, otherwise considered, according to literature findings (221), in traditional models of care organisation, posing a higher risk of adverse events for patients. Our findings are indicative that during the investigated period under IC, a lower proportion of urgent transfers to the intensive areas and it was increased number of stepdown patients admitted in MCA that the unit could manage. Considering the importance of availability of hospital beds in ICU for critical or post-surgical patients with a high severity of illness (222) (223) (204), this achievement per se means an optimised management of resources for the hospital system.

The new organisation may be suggestive of more effective functioning of the provincial hospital network with the potential to admit a higher number of acute unstable medical patients transferred from the lower acuity settings of spoke hospitals to the larger and more comprehensive IM ward of Santa Chiara Hospital. A reservoir of beds for patients transfer from wards within the care network is crucial for the Hub & Spoke model. To our knowledge, there is scarce evidence that shows the true benefits of a medical ward hub in support to spoke hospitals translating in changes of clinical and organisational outcomes, underpinning the provision of high quality care.

Some issues concerning practice changes must be further highlighted. The implementation of the model took nearly two years of hard preparatory work in the field, undertaking challenging logistic, organisational and managerial steps with engagement of all the

stakeholders. Regular feedback on achievements, shared with nursing and medical staff, solidified the practice changes and cleared up doubts on the value of the new organisation of care.

Differently from traditional models of care, the IC model, based on graded care options, is not relying on a static and "passive" management but requires a continuous collaborative organisational maintenance and encourages medical and nursing staff to take an active role either in assessment of patient severity and identification of appropriate care settings, based on mechanisms for a dynamic patient management and evidence-based criteria for admission, transfer, and discharge of patients.

We think that models improving risk stratification, patient flow and allowing a homogenous assessment of patient populations, in a general context increasingly faced with change decisions, should be advisable for organisation embracing a new vision of patient care as it may offer to hospitals a systematic way of delivering safe, high quality care to patients across healthcare settings.

Studies could be focused on assessment of the level of acuity, dependence and risk of adverse events for patients, as well as influence of interventions on multiple clinical, organisational and economic outcomes. Certainly one priority in the area is standardization of terms, adoption of validated patient-severity scoring systems to allow rigorous data comparison, among units and models at international level.

Large multicentric trials of interventions are needed to establish a strong base of evidence in this area.

Conclusions

In internal medicine wards, it is of utmost importance to standardize the assessment of acute-illness severity, implement changes in order to establish graded care options between intensive and conventional care and provide to every patient the right intensity of care at the right time throughout the course of hospitalization.

In our study, we sought to determine how IC might improve the provision of adequate levels of care while reducing inappropriate beds use without negatively impacting on patient outcomes.

The new organisation of internal medicine ward areas resulted in improvement of patient outcomes and increased the availability of beds in ICU. Therefore, a model framed on intensity of medical care may be associated with more favourable outcomes.

Intensity of medical care may constitute a bedrock on which other simple, innovative, structured and feasible interventions for quality and safety in the medical ward can build. Careful consideration on a multifaceted interventions and measures of assessment of results is merited. The evidence base can be increased by further research addressing: factors, interventions and outcome, including also patient-relevant as well as staff-reported outcomes, related to implementation models based on intensity of care; in depth analysis of resources utilization; the use of accurate and sustainable tools for multidimensional assessment of severity and complexity; the benefits of new technologies to develop systems with optimal levels of safety and effectiveness in acute medical care facilities. Expanding the body of scientific knowledge specifically pertaining to medical wards should be a priority for all stakeholders of healthcare systems.

6 Conclusions and future developments

This PhD project aimed at disseminating the culture of evaluation research in the Autonomous Province of Trento.

Policy makers, managers, clinicians, healthcare leaders, researchers, and multiple other stakeholders are called to deal with the organisational challenges of redesigning care processes of acute medical wards on an evidence-based and cost-effective approach in their own settings. Decision-making and change management should be based on effective leadership, objective analysis, evidence-based practice and monitoring systems.

In a strained and challenged medical care system, given the abundance of policy guidance, experiences and (sometimes limited) evidence of benefits, it is worth investigating in real contexts of care how changes in care modalities influence outcomes for patients and how they may enable a more rational allocation of resources in medical wards.

We worked on different case studies of clinical relevance, which helped us to practically deal with the matter. The analysis of clinical processes and organizational models allowed us to acquire and develop the methodological and statistical skills necessary for the evaluation of healthcare performance. These methods are now available for wider application. Indeed, the case studies constitute actual demonstrators, which can increase the awareness of health professionals towards outcome evaluation. Evidence that this culture is finally flourishing is represented by the growing interest of local physicians and managers, who asked further analysis and evaluation in their medical area. Due to the analyses here presented, the Trentino healthcare environment increased its awareness of the topic of outcome evaluation and realized its importance. Following this, more evaluation studies are underway now or planned in the next future.

Each study was conducted in close collaboration with the professionals of the specific medical area, so that involved professionals recognized the importance of a scientific, methodological, and statistical approach to inform clinical decisions. Data analysis revealed much about the study population and its characteristics, such as health status and comorbidities. Some known aspects were confirmed by the analysis, but unexpected features or feature proportions arose.

Each evaluation starts with the planning of an evaluation study, which requires the clear definition of the population, intervention, outcomes, the periods of recruitment and follow-up, and the control of clinical, organizational, and technical variables. This step is of fundamental importance: we must pay attention, reflect, and clarify. At this stage, literature research is of paramount importance. It is necessary to set the reference standard, broad the knowledge horizon and set the problem in the appropriate scenario. Since the evaluation results could be partially or completely unexpected, further considerations and additional literature research may be necessary to clarify them.

As mentioned above, practical and theoretical approaches have been actualized on paradigmatic cases. These studies allowed us to capitalize the acquired skills and to support the ameliorative culture of outcome evaluation in the local healthcare system. In particular, we focused on the assessment of clinical pathways and clinical organizational models, because they are strong “allies” to solve or prevent inadequate care or treatments. Indeed, the complexity of the healthcare system can produce variability, defects in appropriateness and continuity, and poor integration in care. Variability is not only related to clinical performance, but also, and often primarily, to the procedures of assistance distribution, and to organizational and operational aspects, which may increase probability of low or inadequate quality of care. Among their several advantages, clinical pathways reduce variation in practice, provide an opportunity to involve teams in service restructure, are patient-centred, comprehensive and clinically driven. They transfer evidence-based care into practice, and ensure the delivery of consistent high quality care. In this way clinical pathways can be considered a tool for a systematic action for the continuous improvement of patient care (58).

As a first study case, we presented an example of how the effort towards change needs evaluation moments to confirm or amend decisions. Since 2008, the local Health Trust has implemented a program aimed to extend the therapeutic offer of peritoneal dialysis (PD) to chronic kidney disease patients. The program has led to a considerable increase in the number of first experience dialytic patients who chose PD. We designed a comparative study that aimed to analyse the impact of a wider use of PD seven years after the beginning of the implementation program. Specifically, PD was compared to Haemodialysis (HD) in terms of overall mortality and efficiency to transplant. The analysis of our data set showed

that PD choice could represent a valid opportunity in terms of survival for all patients, with the exception of elderly patients, especially if affected by diabetes mellitus, and for patients with cardiovascular diseases. Nevertheless, the most surprising result was that the PD showed greater efficiency in view of a transplant. This aspect is likely to be related to differences in the organizational models between the two dialytic methods. Indeed, the PD service has a unique provincial centre at the Santa Chiara Hospital of Trento, while HD services are present in all seven public hospitals throughout the Province. Thus, in view of a transplant, HD presented an inadequate organizational model with respect to PD.

In the case studies treated in chapters four and five, a "flag" raised by the Italian National Outcomes Program (PNE), which compared Italian hospitals to the Italian benchmark, urged our application of clinical pathways to femur fractures. In 2010, the PNE evidenced a lower performance of the Santa Chiara hospital of Trento in terms of timing to surgical treatment of proximal femur fractures in elderly patients. Thanks to this national monitoring, the problem was tackled by the professionals. After a search for international guidelines and literature studies, they agreed that a clinical pathway with a multidisciplinary approach could result in better outcomes. The orthogeriatric pathway solution implemented at the Santa Chiara Hospital improved patients' outcomes, reduced variability among patients, facilitated translation of national and international directives into local practice, increased involvement, coordination and team working of different professionals and operational units.

Concluding this example, we must emphasize that it is not sufficient to solve the problem by a single timely action. On the contrary, a systematic monitoring of interventions and services is needed to ensure continuous improvement or persistence of the quality of care and services over time.

Finally, we presented an assessment of the change of the organizational model in the Internal Medicine ward of the Santa Chiara Hospital in Trento. In the last three years, the ward has led a change from a Standard medical Care (SC) organization to a new organizational model based on Intensity of medical Care (IC). This change in the organizational model needed to be supported by an evaluation of the used tools and an assessment of the outcomes that need an improvement. The first part of such evaluation concerned the assessment of NEWS (National Early Warning Score) as an instrument for

the stratification of clinical instability and effective management of patients at risk of deterioration after admission to the Internal Medicine Ward. Our study confirmed that the NEWS, when evaluated on patient's admission, could be a good predictor of in-hospital serious adverse outcomes and might enable the stratification of patients at risk of clinical deterioration. However, the analysis highlighted also some flaws in the classification of patient risk, such as sudden cardiac events and chronic hypoxemic conditions. The evaluation study led us to conclude that, if correctly used, the NEWS can be a valuable completion to clinical judgement in planning the most appropriate setting of patient care. In the second part of the evaluation study, we tested the effectiveness of the new IC-based organizational model in limiting negative events, such as deaths and unplanned intensive care unit transfers due to clinical deterioration. The comparison of the results of IC versus SC model showed that the application of the new organizational model reduced the number of unplanned and urgent transfers. The reduction of clinical deterioration during hospitalization indicated that the adoption of an organizational model, which combined clinical judgement with the NEW score for early stratification of risk, might improve the quality of care by guaranteeing more appropriate care setting and proper answers to the patient's needs.

In a comprehensive synthesis of the evidence for factors affecting quality and safety on medical wards, interventions were grouped into five themes: staffing levels and team composition; communication and collaboration; care standardisation; early recognition and treatment of the deteriorating patient; and local safety climate (189).

The set up a new model of care requires system-wide changes in practice, that in our case were implemented through strong clinical leadership commitment, alignment and integration of clinical improvement efforts with organizational priorities, medical and nursing staff competencies development, systematic collaboration among physicians and nurses and internal medicine ward and intensive care units, adherence of evidence-based guidelines and protocols. Essential was also establishing an infrastructure for regular feedback on data, processes and performances.

When changes were planned but not implemented, studies here presented were designed in a prospective, observational fashion in order to limit potential sources of bias and confounders. On the contrary, studies were forced to be retrospective when we had to

analyse changes already started. Outcome evaluation in real clinical contexts can be cumbersome, as such kind of evaluation is more prone to biases that can weaken the strength of results and the external validity of the study. However, it constitutes a unique picture of the performance of the specific intervention in the real clinical settings and it is fundamental for leading healthcare improvement and change on the basis of quantitative, reliable data.

The training on specific cases, involving outcome evaluation of more than 4,500 patients, enabled the acquisition of statistical methods and health assessment skills, which are now available for wider application. This work has paved the road to the creation of a Provincial Program for outcome evaluation of clinical and care processes, and contributed to the diffusion of outcome evaluation culture in the clinical setting.

The next steps of this path will be the improvement of areas already analysed by extending the analysis to new outcomes, and the application of the evaluation model to other relevant areas of the health care system, such as cardiology, general surgery, nursing homes, and birth paths.

7 References

1. Eagle CJ, Davies JM. Current models of “quality”--an introduction for anaesthetists. Can J Anaesth J Can Anesthésie. 1993 Sep;40(9):851–62.

2. Kilshaw ME. Implementing an effective quality assurance program. Gelman. Medical Administration in Canadian Hospitals. Canadian Medical Association, Ottawa; 1992.

3. Armit K. Evidence, culture and clinical outcome. Future Hosp J. 2015 Oct 1;2(3):194–6.

4. Progress Toward Value-Based Health Care. www.bcgperspectives.com. Available from: https://www.bcgperspectives.com/content/articles/health_care_public_sector_progress_toward_value_based_health_care/

5. Johnson MJ, May CR. Promoting professional behaviour change in healthcare: what interventions work, and why? A theory-led overview of systematic reviews. BMJ Open. 2015 Sep 1;5(9):e008592.

6. The British Orthopaedic Association. The care of patients with fragility fractures. Guideline BOA2007. The British Orthopaedic Association; 2007.

7. National Hip Fracture Database. http://www.nhfd.co.uk/.

8. Lisk R, Yeong K. Reducing mortality from hip fractures: a systematic quality improvement programme. BMJ Qual Improv Rep. 2014 Jan 1;3(1):u205006.w2103.

9. World Facing an Economic Headwind as Population Ages. BloombergView. Available from: http://www.bloomberg.com/infographics/2013-12-19/world-faces-economic-headwind-as-population-ages.html

10. Schneider B, Barbera KM. The Oxford Handbook of Organisational Climate and Culture. Oxford University Press. 2014.

11. Ham Chris. Reforming the NHS from within. Beyond hierarchy, inspection and markets. The King’s Fund, London; 2014.

12. West M, Armit K, Loewenthal L, Eckert R, West T, Lee A. Leadership and Leadership Development in Health Care: The Evidence Base. Faculty of Medical Leadership and Management, The King’s Fund, London; 2015.

13. Drath WH, McCauley CD, Palus CJ, Van Velsor E O’Connor PMG, McGuire JB. Direction, alignment, commitment: Toward a more integrative ontology of leadership. The Leadership Quarterly. 2008;19 (6), 635–653.

14. Yukl Gary. Leadership in Organizations. England: Pearson Education Limited. 2013.

15. Boyatzis RE. The competent manager: A model for effective performance. Wiley, New York. 1982.

16. Center for Creative Leadership. www.ccl.org/leadership/about/index.aspx?pageId=10.

17. Meterko M, Mohr DC, Young GJ. Teamwork culture and patient satisfaction in hospitals. Med Care. 2004 May;42(5):492–8.

18. West MA, Anderson N. Innovation, Cultural-Values, and the Management of Change in British Hospitals. Work and Stress. 1992;6 (3), 293–310.

19. Davies HTO, Mannion R, Jacobs R, Powell AE, Marshall MN. Exploring the relationship between senior management team culture and hospital performance. Med Care Res Rev MCRR. 2007 Feb;64(1):46–65.

20. Gerowitz MB, Lemieux-Charles L, Heginbothan C, Johnson B. Top management culture and performance in Canadian, UK and US hospitals. Health Serv Manag Res Off J Assoc Univ Programs Health Adm HSMC AUPHA. 1996 May;9(2):69–78.

21. McKee L, West MA, Flin R et al. Understanding the dynamics of organisational culture change: creating safe places for patients and staff. Report SDO/92/2005. London: NIHR SDO; 2010.

22. Dixon-Woods M, Baker R, Charles K, Dawson J, Jerzembek G, Martin G, et al. Culture and behaviour in the English National Health Service: overview of lessons from a large multimethod study. BMJ Qual Saf. 2014 Feb;23(2):106–15.

23. West MA, Guthrie JP, Dawson JR, Borrill CS, Carter M. Reducing patient mortality in hospitals: The role of human resource management. J Organ Behav. 2006;27:983–1002.

24. West MA, Borrill C, Dawson J et al. The link between the management of employees and patient mortality in acute hospitals. Int J Hum Resour Manag. 2002;13:1299–310.

25. West MA, Dawson JF, Admasachew L, Topakas A. NHS staff management and health service quality: results from the NHS staff survey and related data. Report to the Department of Health, London. 2011;

26. Stormy Friday, David G. Cotts. Quality Facility Management: A Marketing and Customer Service Approach. Wiley; 1994.

27. Arditi D, Gunaydin HM. Total quality management in the construction process. Int J Proj Manag. 1997 Aug;15(4):235–43.

28. Department of Health. A first Class Service: Quality in National Health Service. Department of Health, The Stationery Office, London; 1998.

29. Department of Health. The New NHS – Modern and Dependable. Department of Health, White Paper series, The Stationery Office, London; 1997.

30. Care I of M (US) and NA of E (US) R on V& S-DH. Healthcare System Complexities, Impediments, and Failures. 2011; Available from: http://www.ncbi.nlm.nih.gov/books/NBK61963/

31. Donabedian Avedis. An Introduction to Quality Assurance In Healthcare. Oxford University Pres. 2002.

32. World Health Organization. Geneva. Health promotion glossary. 1998.

33. WHO Regional Office for Europe's Health Evidence Network (HEN). What is the evidence on effectiveness of empowerment to improve health? 2006.

34. Humphrey, Miller, Scapens. Accountability and Accountable Management in the UK Public Sector. 1993;6.

35. Roberts J, Scapens R. Accounting systems and systems of accountability — understanding accounting practices in their organisational contexts. Account Organ Soc. 1985;10(4):443–56.

36. Rathwell T, Persaud DD. Running to stand still: change and management in Canadian healthcare. Healthc Manag Forum Can Coll Health Serv Exec Forum Gest Soins Santé Collège Can Dir Serv Santé. 2002;15(3):10–7, 52–60.

37. O'Hagan J, Persaud D. Creating a culture of accountability in health care. Health Care Manag. 2009 Jun;28(2):124–33.

38. WHO-World Health Organization. Appropriateness in Health Care Services: Report on a WHO Workshop ; Koblenz, Germany,; European Health 21 Target 18. WHO, Regional Office for Europe, 2000; 2000.

39. Holm S. The second phase of priority setting. Goodbye to the simple solutions: the second phase of priority setting in health care. BMJ. 1998 Oct 10;317(7164):1000–2.

40. McKee M, Figueras J. Setting priorities, can Britain learn from Sweden? BMJ. 1996 Mar 16;312(7032):691–4.

41. Gimbe news. Pillole di governo clinico. La valutazione multidimensionale della qualità assistenziale. 2009 Mar;vol.2, n.3.

42. Joint Committee. Standards for Educational Evaluation. 1981;

43. William M.K. Trochim. DEVELOPING an EVALUATION CULTURE for INTERNATIONAL AGRICULTURAL RESEARCH. Cornell University. 1992;

44. http://www.socialresearchmethods.net/kb/evaluation.php.

45. Zinovieff MA, Rotem A. Review and Analysis of Training Impact Evaluation Methods, and Proposed Measures to Support a United Nations System Fellowships Evaluation Framework. Prepared for the WHO's Department of Human Resources for Health on behalf of the UN Task Force on Impact Assessment of Fellowships. Geneva; 2008 Jul.

46. Giannessi E. Appunti di economia aziendale. Pisa: Pacini; 1979. 178 p.

47. Giovanelli L. La valutazione delle performance in ambito sanitario. Profili teorici ed evidenze empiriche. G. Giappichelli Editore - Torino; 2013.

48. Nutt PC. Planning Process Archetypes and Their Effectiveness. Decis Sci. 1984 Apr 1;15(2):221–38.

49. Scriven M, In R.W. Tyler, R. Gagne and M. Scriven. The methodology of evaluation. Perspectives on Curriculum Evaluation. Rand McNally. Chicago; 1967.

50. Ibrahim JE. Performance indicators from all perspectives. Int J Qual Health Care J Int Soc Qual Health Care ISQua. 2001 Dec;13(6):431–2.

51. Thompson BL, Harris JR. Performance measures: are we measuring what matters? Am J Prev Med. 2001 May;20(4):291–3.

52. Arah OA, Klazinga NS, Delnoij DMJ, Asbroek AHAT, Custers T. Conceptual frameworks for health systems performance: a quest for effectiveness, quality, and improvement. Int J Qual Health Care. 2003 Oct 1;15(5):377–98.

53. Vannini G, Calamo Specchia F.P. Igiene e metodologia epidemiologica. Principi e argomenti. Unione Tipografico-Editrice Torinese; 1990.

54. Auxilia, Mapelli, Rossi, Pagano, Vittadini. Indicatori per la valutazione di struture sanitarie: uno sguardo d'insieme. Etas, Milano. 2004.

55. Representatives of 61 State, Official Records of The World Health Organization. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference. World Health Organization, New York; 1946.

56. Carroll JS, Rudolph JW. Design of high reliability organizations in health care. Qual Saf Health Care. 2006 Dec;15(Suppl 1):i4–i9.

57. Bozic KJ, Wright JG. Value-Based Healthcare and Orthopaedic Surgery: Editorial Comment. Clin Orthop. 2012 Apr;470(4):1004–5.

58. Wonderlich S, Jones R. Key Topics in Healthcare Management: Understanding the Big Picture. Radcliffe Publishing; 2007. 262 p.

59. European Pathway Association | CARE PATHWAYS. Available from: http://e-p-a.org/care-pathways/

60. Overill S. A pratical guide to care pathways. Int J Integr Care. 1998;93–8.

61. Middleton S, Barnett J, Reeves D. What is an integrated care pathway? 2001;1–8.

62. Wilson J. An introduction to multi-disciplinary pathways of care. Northen Regional Health Authority. Newcastle; 1992;

63. Panella M, Marchisio S, Di Stanislao F. Reducing clinical variations with clinical pathways: do pathways work? Int J Qual Health Care J Int Soc Qual Health Care ISQua. 2003 Dec;15(6):509–21.

64. Upton G, Cook I. A Dictionary of Statistics. 2nd ed. Oxford University Press; 2008. Available from: http://www.oxfordreference.com/view/10.1093/acref/9780199541454.001.0001/acref-9780199541454

65. anonymous. Cochrane Handbook for Systematic Reviews of Interventions | Cochrane Community. Available from: http://community.cochrane.org/handbook

66. Neumann I, Santesso N, Akl EA, Rind DM, Vandvik PO, Alonso-Coello P, et al. A guide for health professionals to interpret and use recommendations in guidelines developed with the GRADE approach. J Clin Epidemiol. 2016 Jan 6;

67. Khan KS, Kunz R, Kleijnen J, Antes G. Five steps to conducting a systematic review. J R Soc Med. 2003 Mar;96(3):118–21.

68. Oxford Centre for Evidence-based Medicine - Levels of Evidence (March 2009). CEBM. 2009. Available from: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

69. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med. 2000 Jun 22;342(25):1887–92.

70. Department of Health. NHS Performance Indicators: A Consultation. 2001.

71. Audit Commission. Aiming to Improve: The Principles of Performance Measurement. Audit Commission, London; 2000.

72. National Health Performance Committee. National Health Performance Framework Report. National Health Performance Committee, Brisbane: Queensland Health; 2001.

73. Canadian Institute for Health Information, Statistics Canada. Canadian Health Information Roadmap Initiative Indicators Framework. Canadian Institute for Health Information, Ottawa; 2000.

74. Institute of Medicine. Crossing the Quality Chasm: A New HealthSystem for the 21st century. Institute of Medicine, Washington, DC: National Academy Press; 2001.

75. Department of Health and Uman Services. Healthy People 2010. Understanding and Improving Health. Department of Health and Uman Services, Washington, DC: US Government Printing Office; 2000.

76. Institute of Medicine. Envisioning the National Health Care Quality Report. Institute of Medicine, Washington, DC: National Academy Press; 2001.

77. McLoughlin V, Leatherman S, Fletcher M, Owen JW. Improving performance using indicators. Recent experiences in the United States, the United Kingdom, and Australia. Int J Qual Health Care J Int Soc Qual Health Care ISQua. 2001 Dec;13(6):455–62.

78. Organisation for Economic Cooperation and Development. OECD Health Data 2001. Organisation for Economic Cooperation and Development, Paris; 2001.

79. Visualizza articoli per tag: PNE - Agenas - Agenzia Nazionale per i servizi sanitari Regionali. Available from: http://www.agenas.it/primo-piano/tag/PNE

80. ICD - ICD-9-CM - International Classification of Diseases, Ninth Revision, Clinical Modification. Available from: http://www.cdc.gov/nchs/icd/icd9cm.htm

81. Viglino G, Neri L, Alloatti S, Cabiddu G, Cocchi R, Limido A, et al. Analysis of the factors conditioning the diffusion of peritoneal dialysis in Italy. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2007 Dec;22(12):3601–5.

82. Mehrotra R, Chiu Y-W, Kalantar-Zadeh K, Bargman J, Vonesh E. Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. Arch Intern Med. 2011 Jan 24;171(2):110–8.

83. Kumar VA, Sidell MA, Jones JP, Vonesh EF. Survival of propensity matched incident peritoneal and hemodialysis patients in a United States health care system. Kidney Int. 2014 Nov;86(5):1016–22.

84. Yeates K, Zhu N, Vonesh E, Trpeski L, Blake P, Fenton S. Hemodialysis and peritoneal dialysis are associated with similar outcomes for end-stage renal disease treatment in Canada. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2012 Sep;27(9):3568–75.

85. Marshall MR, Walker RC, Polkinghorne KR, Lynn KL. Survival on home dialysis in New Zealand. PloS One. 2014;9(5):e96847.

86. Korevaar JC, Feith G, Dekker FW, Van Manen JG, Boeschoten EW, Bossuyt PM, et al. Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment: A randomized controlled trial. Kidney Int. 2003 Dec;64(6):2222–8.

87. Fenton S, Desmeules M, Copleston P, Arbus G, Froment D, Jeffery J, et al. Renal replacement therapy in Canada: a report from the Canadian Organ Replacement Register. Am J Kidney Dis Off J Natl Kidney Found. 1995 Jan;25(1):134–50.

88. Fenton SS, Schaubel DE, Desmeules M, Morrison HI, Mao Y, Copleston P, et al. Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. Am J Kidney Dis Off J Natl Kidney Found. 1997 Sep;30(3):334–42.

89. Schaubel DE, Morrison HI, Fenton SS. Comparing mortality rates on CAPD/CCPD and hemodialysis. The Canadian experience: fact or fiction? Perit Dial Int. 1998 Jan 1;18(5):478–84.

90. Collins AJ, Hao W, Xia H, Ebben JP, Everson SE, Constantini EG, et al. Mortality risks of peritoneal dialysis and hemodialysis. Am J Kidney Dis Off J Natl Kidney Found. 1999 Dec;34(6):1065–74.

91. Bloembergen WE, Port FK, Mauger EA, Wolfe RA. A comparison of mortality between patients treated with hemodialysis and peritoneal dialysis. J Am Soc Nephrol. 1995 Aug 1;6(2):177–83.

92. Locatelli F, Marcelli D, Conte F, Limido A, Lonati F, Malberti F, et al. 1983 to 1992: report on regular dialysis and transplantation in Lombardy. Am J Kidney Dis Off J Natl Kidney Found. 1995 Jan;25(1):196–205.

93. Disney AP. Demography and survival of patients receiving treatment for chronic renal failure in Australia and New Zealand: report on dialysis and renal transplantation treatment from the Australia and New Zealand Dialysis and Transplant Registry. Am J Kidney Dis Off J Natl Kidney Found. 1995 Jan;25(1):165–75.

94. Maiorca R, Cancarini GC, Zubani R, Camerini C, Manili L, Brunori G, et al. CAPD viability: a long-term comparison with hemodialysis. Perit Dial Int. 1996 Jan 1;16(3):276–87.

95. Vonesh EF, Moran J. Mortality in End-Stage Renal Disease A Reassessment of Differences between Patients Treated with Hemodialysis and Peritoneal Dialysis. J Am Soc Nephrol. 1999 Feb 1;10(2):354–65.

96. Murphy SW, Foley RN, Barrett BJ, Kent GM, Morgan J, Barré P, et al. Comparative mortality of hemodialysis and peritoneal dialysis in Canada. Kidney Int. 2000 Apr;57(4):1720–6.

97. Tanna MM, Vonesh EF, Korbet SM. Patient survival among incident peritoneal dialysis and hemodialysis patients in an urban setting. Am J Kidney Dis Off J Natl Kidney Found. 2000 Dec;36(6):1175–82.

98. Winkelmayer WC, Glynn RJ, Mittleman MA, Levin R, Pliskin JS, Avorn J. Comparing mortality of elderly patients on hemodialysis versus peritoneal dialysis: a propensity score approach. J Am Soc Nephrol JASN. 2002 Sep;13(9):2353–62.

99. Liu J-H, Chen J-Y, Lin S-Y, Lin H-H, Ting I-W, Liang C-C, et al. Comparing Survival between peritoneal dialysis and hemodialysis patients with subclinical peripheral artery disease: a 6-year follow-up. Int J Med Sci. 2013;10(4):434–40.

100. Buemi M, Lacquaniti A, Bolignano D, Donato V, Fazio MR, Campo S, et al. Dialysis and the elderly: an underestimated problem. Kidney Blood Press Res. 2008;31(5):330–6.

101. Moist LM, Port FK, Orzol SM, Young EW, Ostbye T, Wolfe RA, et al. Predictors of loss of residual renal function among new dialysis patients. J Am Soc Nephrol JASN. 2000 Mar;11(3):556–64.

102. Misra M, Vonesh E, Van Stone JC, Moore HL, Prowant B, Nolph KD. Effect of cause and time of dropout on the residual GFR: a comparative analysis of the decline of GFR on dialysis. Kidney Int. 2001 Feb;59(2):754–63.

103. Lang SM, Bergner A, Töpfer M, Schiffl H. Preservation of residual renal function in dialysis patients: effects of dialysis-technique-related factors. Perit Dial Int J Int Soc Perit Dial. 2001 Feb;21(1):52–7.

104. Szeto C-C, Wong TY-H, Chow K-M, Leung C-B, Li PK-T. Are peritoneal dialysis patients with and without residual renal function equivalent for survival study? Insight from a retrospective review of the cause of death. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2003 May;18(5):977–82.

105. Termorshuizen F, Korevaar JC, Dekker FW, van Manen JG, Boeschoten EW, Krediet RT, et al. The relative importance of residual renal function compared with peritoneal clearance for patient survival and quality of life: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. Am J Kidney Dis Off J Natl Kidney Found. 2003 Jun;41(6):1293–302.

106. Termorshuizen F, Dekker FW, van Manen JG, Korevaar JC, Boeschoten EW, Krediet RT, et al. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. J Am Soc Nephrol JASN. 2004 Apr;15(4):1061–70.

107. Malek-Marín T, Arenas D, Gil T, Moledous A, Okubo M, Arenas JJ, et al. Spontaneous retroperitoneal hemorrhage in dialysis: a presentation of 5 cases and review of the literature. Clin Nephrol. 2010 Sep;74(3):229–44.

108. Dong R, Guo Z-Y, Ding J-R, Zhou Y-Y, Wu H. Gastrointestinal symptoms: a comparison between patients undergoing peritoneal dialysis and hemodialysis. World J Gastroenterol. 2014 Aug 28;20(32):11370–5.

109. Thomson BKA, Moser M a. J, Marek C, Bloch M, Weernink C, Shoker A, et al. Peritoneal dialysis versus hemodialysis in patients with delayed graft function. Clin Transplant. 2013 Dec;27(6):E709–714.

110. Chaudhary K, Sangha H, Khanna R. Peritoneal dialysis first: rationale. Clin J Am Soc Nephrol CJASN. 2011 Feb;6(2):447–56.

111. Brown E. Peritoneal dialysis: older patients report better quality of life than younger. Evid Based Nurs. 2015 Jul;18(3):93.

112. Griva K, Yu Z, Chan S, Krisnasamy T, Yamin RBA, Zakaria FB, et al. Age is not a contraindication to home-based dialysis - Quality-of-Life outcomes favour older patients on peritoneal dialysis regimes relative to younger patients. J Adv Nurs. 2014 Aug;70(8):1902–14.

113. Theofilou P. Quality of life in patients undergoing hemodialysis or peritoneal dialysis treatment. J Clin Med Res. 2011 May 19;3(3):132–8.

114. Brown EA, Johansson L, Farrington K, Gallagher H, Sensky T, Gordon F, et al. Broadening Options for Long-term Dialysis in the Elderly (BOLDE): differences in quality of life on peritoneal dialysis compared to haemodialysis for older patients. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2010 Nov;25(11):3755–63.

115. Helanterä I, Haapio M, Koskinen P, Grönhagen-Riska C, Finne P. Employment of patients receiving maintenance dialysis and after kidney transplant: a cross-sectional study from Finland. Am J Kidney Dis Off J Natl Kidney Found. 2012 May;59(5):700–6.

116. Julián-Mauro JC, Cuervo J, Rebollo P, Callejo D. Employment status and indirect costs in patients with renal failure: differences between different modalities of renal replacement therapy. Nefrol Publ Of Soc Esp Nefrol. 2013;33(3):333–41.

117. Muehrer RJ, Schatell D, Witten B, Gangnon R, Becker BN, Hofmann RM. Factors affecting employment at initiation of dialysis. Clin J Am Soc Nephrol CJASN. 2011 Mar;6(3):489–96.

118. Karopadi AN, Mason G, Rettore E, Ronco C. Cost of peritoneal dialysis and haemodialysis across the world. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2013 Oct;28(10):2553–69.

119. Baboolal K, McEwan P, Sondhi S, Spiewanowski P, Wechowski J, Wilson K. The cost of renal dialysis in a UK setting--a multicentre study. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2008 Jun;23(6):1982–9.

120. Berger A, Edelsberg J, Inglese GW, Bhattacharyya SK, Oster G. Cost comparison of peritoneal dialysis versus hemodialysis in end-stage renal disease. Am J Manag Care. 2009 Aug;15(8):509–18.

121. Agenas. Adapted HTA REPORT: “Valutazione HTA delle Modalità di dialisi in Italia.”www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/report-hta; 2015.

122. Patsopoulos NA. A pragmatic view on pragmatic trials. Dialogues Clin Neurosci. 2011;13(2):217–24.

123. Merchant AA, Quinn RR, Perl J. Dialysis modality and survival: does the controversy live on? Curr Opin Nephrol Hypertens. 2015 May;24(3):276–83.

124. Han SS, Park JY, Kang S, Kim KH, Ryu D-R, Kim H, et al. Dialysis Modality and Mortality in the Elderly: A Meta-Analysis. Clin J Am Soc Nephrol CJASN. 2015 Jun 5;10(6):983–93.

125. Stack AG, Molony DA, Rahman NS, Dosekun A, Murthy B. Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States. Kidney Int. 2003 Sep;64(3):1071–9.

126. Ganesh SK, Hulbert-Shearon T, Port FK, Eagle K, Stack AG. Mortality differences by dialysis modality among incident ESRD patients with and without coronary artery disease. J Am Soc Nephrol JASN. 2003 Feb;14(2):415–24.

127. Johnson DW, Dent H, Hawley CM, McDonald SP, Rosman JB, Brown FG, et al. Association of dialysis modality and cardiovascular mortality in incident dialysis patients. Clin J Am Soc Nephrol CJASN. 2009 Oct;4(10):1620–8.

128. Lu R, Muciño-Bermejo M-J, Ribeiro LC, Tonini E, Estremadoyro C, Samoni S, et al. Peritoneal dialysis in patients with refractory congestive heart failure: a systematic review. Cardiorenal Med. 2015 Apr;5(2):145–56.

129. Couchoud C, Bolignano D, Nistor I, Jager KJ, Heaf J, Heimburger O, et al. Dialysis modality choice in diabetic patients with end-stage kidney disease: a systematic review of the available evidence. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2015 Feb;30(2):310–20.

130. Patzer RE, Plantinga L, Krisher J, Pastan SO. Dialysis facility and network factors associated with low kidney transplantation rates among United States dialysis facilities. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2014 Jul;14(7):1562–72.

131. Kutner N, Bowles T, Zhang R, Huang Y, Pastan S. Dialysis facility characteristics and variation in employment rates: a national study. Clin J Am Soc Nephrol CJASN. 2008 Jan;3(1):111–6.

132. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 2006 Dec;17(12):1726–33.

133. Piscitelli P, Iolascon G, Argentiero A, Chitano G, Neglia C, Marcucci G, et al. Incidence and costs of hip fractures vs strokes and acute myocardial infarction in Italy: comparative analysis based on national hospitalization records. Clin Interv Aging. 2012;7:575–83.

134. http://www.nhfd.co.uk/.

135. National Clinical Guideline Centre (UK). The Management of Hip Fracture in Adults. London: Royal College of Physicians (UK). Available from: http://www.ncbi.nlm.nih.gov/books/NBK83014/

136. Hip fracture | Guidance and guidelines | NICE. Available from: http://www.nice.org.uk/guidance/cg124/evidence

137. Moja L, Piatti A, Pecoraro V, Ricci C, Virgili G, Salanti G, et al. Timing Matters in Hip Fracture Surgery: Patients Operated within 48 Hours Have Better Outcomes. A Meta-Analysis and Meta-Regression of over 190,000 Patients. PLoS ONE. 2012 Oct 3;7(10):e46175.

138. NICE National Institute for Health and Clinical Excellence. Acutely ill patients in hospital. Recognition of and response to acute illness in adults in hospital. NICE clinical guideline 50. NICE National Institute for Health and Clinical Excellence, London; 2007.

139. Flikweert ER, Izaks GJ, Knobben BAS, Stevens M, Wendt K. The development of a comprehensive multidisciplinary care pathway for patients with a hip fracture: design and results of a clinical trial. BMC Musculoskelet Disord. 2014;15:188.

140. Gupta A. The effectiveness of geriatrician-led comprehensive hip fracture collaborative care in a new acute hip unit based in a general hospital setting in the UK. J R Coll Physicians Edinb. 2014;44(1):20–6.

141. Sánchez-Hernández N, Sáez-López P, Paniagua-Tejo S, Valverde-García JA. Results following the implementation of a clinical pathway in the process of care to elderly patients with osteoporotic hip fracture in a second level hospital. Rev Espanola Cirugia Ortop Traumatol. 2015 Oct 19;

142. Friedman SM, Mendelson DA, Bingham KW, Kates SL. Impact of a comanaged Geriatric Fracture Center on short-term hip fracture outcomes. Arch Intern Med. 2009 Oct 12;169(18):1712–7.

143. Morgan RJM, Williams F, Wright MM. An early warning scoring system for detecting developing critical illness. Clinical Intensive Care. 1997;8:100.

144. NCEPOD. An acute problem? A report of the National Confidential Enquiry into Patient Outcome and Death. NCEPOD, London; 2005.

145. McQuillan P, Pilkington S, Allan A, Taylor B, Short A, Morgan G, et al. Confidential inquiry into quality of care before admission to intensive care. BMJ. 1998 Jun 20;316(7148):1853–8.

146. Seward E, Greig E, Preston S, Harris RA, Borrill Z, Wardle TD, et al. A confidential study of deaths after emergency medical admission: issues relating to quality of care. Clin Med Lond Engl. 2003 Oct;3(5):425–34.

147. Kause J, Smith G, Prytherch D, Parr M, Flabouris A, Hillman K, et al. A comparison of antecedents to cardiac arrests, deaths and emergency intensive care admissions in Australia and New Zealand, and the United Kingdom--the ACADEMIA study. Resuscitation. 2004 Sep;62(3):275–82.

148. Hodgetts TJ, Kenward G, Vlackonikolis I, Payne S, Castle N, Crouch R, et al. Incidence, location and reasons for avoidable in-hospital cardiac arrest in a district general hospital. Resuscitation. 2002 Aug;54(2):115–23.

149. Churpek MM, Yuen TC, Huber MT, Park SY, Hall JB, Edelson DP. Predicting cardiac arrest on the wards: a nested case-control study. Chest. 2012 May;141(5):1170–6.

150. Alam N, Hobbelink EL, van Tienhoven AJ, van de Ven PM, Jansma EP, Nanayakkara PWB. The impact of the use of the Early Warning Score (EWS) on patient outcomes: a systematic review. Resuscitation. 2014 May;85(5):587–94.

151. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. Resuscitation. 2013 Apr;84(4):465–70.

152. Smith MEB, Chiovaro JC, O'Neil M, Kansagara D, Quinones A, Freeman M, et al. Early Warning System Scores: A Systematic Review. Washington (DC): Department of Veterans Affairs; 2014. Available from: http://www.ncbi.nlm.nih.gov/books/NBK259026/

153. Department of Health and NHS Modernisation Agency. The National Outreach Report. Department of Health, London; 2003.

154. Smith GB, Prytherch DR, Schmidt PE, Featherstone PI. Review and performance evaluation of aggregate weighted "track and trigger" systems. Resuscitation. 2008 May;77(2):170–9.

155. Prytherch DR, Smith GB, Schmidt PE, Featherstone PI. ViEWS--Towards a national early warning score for detecting adult inpatient deterioration. Resuscitation. 2010 Aug;81(8):932–7.

156. Royal College of Physicians. National Early Warning Score (NEWS): standardising the assessment of acute-illness severity in NHS. Report of a working party. Royal College of Physicians; 2012.

157. Jenkins PF, Thompson CH, Barton LL. Clinical deterioration in the condition of patients with acute medical illness in Australian hospitals: improving detection and response. Med J Aust. 2011 Jun 6;194(11):596–8.

158. Neary PM, Regan M, Joyce MJ, McAnena OJ, Callanan I. National early warning score (NEWS) - evaluation in surgery. Int J Health Care Qual Assur. 2015;28(3):245–52.

159. Alam N, Vegting IL, Houben E, van Berkel B, Vaughan L, Kramer MHH, et al. Exploring the performance of the national early warning Score (NEWS) in a European emergency department. Resuscitation. 2015 May;90:111–5.

160. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. QJM Mon J Assoc Physicians. 2001 Oct;94(10):521–6.

161. Burch VC, Tarr G, Morroni C. Modified early warning score predicts the need for hospital admission and inhospital mortality. Emerg Med J EMJ. 2008 Oct;25(10):674–8.

162. Groarke JD, Gallagher J, Stack J, Aftab A, Dwyer C, McGovern R, et al. Use of an admission early warning score to predict patient morbidity and mortality and treatment success. Emerg Med J EMJ. 2008 Dec;25(12):803–6.

163. Cei M, Bartolomei C, Mumoli N. In-hospital mortality and morbidity of elderly medical patients can be predicted at admission by the Modified Early Warning Score: a prospective study. Int J Clin Pract. 2009 Apr;63(4):591–5.

164. Scotti E, Pierantonio F. The hospital Internal Medicine specialist today: a literature review and strength, weakness, opportunity, threats (SWOT) analysis to develop a working proposal. Italian Journal of Medicine. 2013;7:278–86.

165. Tirkkonen J, Olkkola KT, Huhtala H, Tenhunen J, Hoppu S. Medical emergency team activation: performance of conventional dichotomised criteria versus national early warning score. Acta Anaesthesiol Scand. 2014 Apr;58(4):411–9.

166. Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: A systematic review. Crit Care. 2008;12(6):R161.

167. Eccles SR, Subbe C, Hancock D, Thomson N. CREWS: Improving specificity whilst maintaining sensitivity of the National Early Warning Score in patients with chronic hypoxaemia. Resuscitation. 2014 Jan 1;85(1):109–11.

168. Abbott TEF, Vaid N, Ip D, Cron N, Wells M, Torrance HDT, et al. A single-centre observational cohort study of admission National Early Warning Score (NEWS). Resuscitation. 2015 Jul;92:89–93.

169. Correia N, Rodrigues RP, Sá MC, Dias P, Lopes L, Paiva A. Improving recognition of patients at risk in a Portuguese general hospital: results from a preliminary study on the early warning score. Int J Emerg Med. 2014 Jul 10;7:22.

170. Capan M, Ivy JS, Rohleder T, Hickman J, Huddleston JM. Individualizing and optimizing the use of early warning scores in acute medical care for deteriorating hospitalized patients. Resuscitation. 2015 Aug;93:107–12.

171. Fox A, Elliott N. Early warning scores: a sign of deterioration in patients and systems. Nurs Manag Harrow Lond Engl 1994. 2015 Apr;22(1):26–31.

172. Odell M. Detection and management of the deteriorating ward patient: an evaluation of nursing practice. J Clin Nurs. 2015 Jan;24(1-2):173–82.

173. Kolic I, Crane S, McCartney S, Perkins Z, Taylor A. Factors affecting response to national early warning score (NEWS). Resuscitation. 2015 May;90:85–90.

174. Cooksley T, Kitlowski E, Haji-Michael P. Effectiveness of Modified Early Warning Score in predicting outcomes in oncology patients. QJM Mon J Assoc Physicians. 2012 Nov;105(11):1083–8.

175. Wheeler I, Price C, Sitch A, Banda P, Kellett J, Nyirenda M, et al. Early Warning Scores Generated in Developed Healthcare Settings Are Not Sufficient at Predicting Early Mortality in Blantyre, Malawi: A Prospective Cohort Study. PLoS ONE. 2013 Mar 29; 8(3). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3612104/

176. Ho LO, Li H, Shahidah N, Koh ZX, Sultana P, Hock Ong ME. Poor performance of the modified early warning score for predicting mortality in critically ill patients presenting to an emergency department. World J Emerg Med. 2013;4(4):273–8.

177. Churpek MM, Yuen TC, Park SY, Gibbons R, Edelson DP. Using Electronic Health Record Data to Develop and Validate a Prediction Model for Adverse Outcomes on the Wards. Crit Care Med. 2014 Apr;42(4):841–8.

178. Chesi G, Nardi R. La stratificazione per severità dei pazienti ricoverati in Medicina Interna: un lavoro ancora incompiuto. Italian Journal of Medicine. 2013;7:231–3.

179. Lobo R, Lynch K, Casserly LF. Cross-sectional audit on the relevance of Elevated National Early Warning Score in medical patients at a Model 2 hospital in Ireland. Ir J Med Sci. 2015 Dec;184(4):893–8.

180. Chesi G, Boni F. Hospitals and organizational models based on the intensity of treatment: the internist's point of view. Italian Journal of Medicine. 2012;6:63–71.

181. Stefani I, Mazzone A. Come organizzare l'Area Medica per affrontare le nuove sfide della complessità clinica e assistenziale. Italian Journal of Medicine. 2014;2:54–9.

182. Sinuff T, Kahnamoui K, Cook DJ, Luce JM, Levy MM, Values Ethics and Rationing in Critical Care Task Force. Rationing critical care beds: a systematic review. Crit Care Med. 2004 Jul;32(7):1588–97.

183. Halpern NA, Pastores SM, Greenstein RJ. Critical care medicine in Unites States 1985-2000: An analysis of bed numbers, use and costs. Critical Care Medicine. 2004;32:1254–9.

184. Badriyah T, Briggs JS, Meredith P, Jarvis SW, Schmidt PE, Featherstone PI, et al. Decision-tree early warning score (DTEWS) validates the design of the National Early Warning Score (NEWS). Resuscitation. 2014 Mar;85(3):418–23.

185. Nardi R, Scanelli G, Borioni D, Grandi M, Sacchetti C, Parenti M, et al. The assessment of complexity in internal medicine patients. The FADOI Medicomplex Study. Eur J Intern Med. 2007 Jul;18(4):283–7.

186. Nardi R, Scanelli G. Multimorbidity and complexity: a current research priority not only in the UK and in primary care, but all over the world and in every care setting. BMJ. 2007 May 17;334:1016.

187. United Nations. Population ageing and development 2012. United Nations, New York. New York; 2012;

188. Pannick S, Davis R, Ashrafian H, Byrne BE, Beveridge I, Athanasiou T, et al. Effects of Interdisciplinary Team Care Interventions on General Medical Wards: A Systematic Review. JAMA Intern Med. 2015 Aug;175(8):1288–98.

189. Pannick S, Beveridge I, Wachter RM, Sevdalis N. Improving the quality and safety of care on the medical ward: A review and synthesis of the evidence base. Eur J Intern Med. 2014 Dec;25(10):874–87.

190. Helay, McKee. Hospitals in a Changing Europe. Open University Press. Buckingham; 2002;

191. Ranhoff AH, Rozzini R, Sabatini T, Cassinadri A, Boffelli S, Ferri M, et al. Subintensive care unit for the elderly: a new model of care for critically ill frail elderly medical patients. Intern Emerg Med. 2006;1(3):197–203.

192. Villa S, Barbieri M, Lega F. Restructuring patient flow logistics around patient care needs: implications and practicalities from three critical cases. Health Care Manag Sci. 2009 Jun;12(2):155–65.

193. Mazzocato P, Savage C, Brommels M, Aronsson H, Thor J. Lean thinking in healthcare: a realist review of the literature. Qual Saf Health Care. 2010 Oct;19(5):376–82.

194. Lega F, Calciolari S. Coevolution of patients and hospitals: how changing epidemiology and technological advances create challenges and drive organizational innovation. J Healthc Manag Am Coll Healthc Exec. 2012 Feb;57(1):17–33; discussion 33–34.

195. Nardi R, Arienti V, Nozzoli C. Organizzazione dell'ospedale per intensità di cure: gli errori da evitare. Italian Journal of Medicine. 2012;6:1–13.

196. Recine U, Pastorelli R, Bruzzese V, et al. The change of hospital internal medicine: a study on patients admitted in internal medicine wards of 8 hospitals of the Lazio area. Italian Journal of Medicine. 2015;7:252–259.

197. Henning RJ, McClish D, Daly B, Nearman H, Franklin C, Jackson D. Clinical characteristics and resource utilization of ICU patients: implications for organization of intensive care. Crit Care Med. 1987 Mar;15(3):264–9.

198. Rosenthal GE, Sirio CA, Shepardson LB, Harper DL, Rotondi AJ, Cooper GS. Use of intensive care units for patients with low severity of illness. Arch Intern Med. 1998 May 25;158(10):1144–51.

199. Vincent J-L, Rubenfeld GD. Does intermediate care improve patient outcomes or reduce costs? Crit Care Lond Engl. 2015;19:89.

200. Nasraway SA, Cohen IL, Dennis RC, Howenstein MA, Nikas DK, Warren J, et al. Guidelines on admission and discharge for adult intermediate care units. American College of Critical Care Medicine of the Society of Critical Care Medicine. Crit Care Med. 1998 Mar;26(3):607–10.

201. Alessandri M, Bartolomei C, Bernardini M et al. Medicina Interna e nuova organizzazione ospedaliera: la proposta di FADOI Toscana. Italian Journal of Medicine. 2007;1:65–9.

202. Bartolomei C, Cei M. L'allocazione dei pazienti in un reparto di Medicina Interna organizzato per intensità di cure: lo studio ADOIT Tri-Co (Triage di Corridoio). Italian Journal of Medicine. 2007;2:31–39.

203. Bollini G, Colombo F, Lolli A. L'intensità assistenziale e la complessità clinica: un progetto di ricerca della Regione Lombardia. Era Futura, Milano. 2011;

204. Fernandes L, Duque S, Silvestre J, Freitas P, Pinto M, Sousa A, et al. Prognostic factors of patients admitted in a medical intermediate care unit: a prospective observational study. Int Arch Med. 2015 Jul 30;8(0). Available from: http://imed.pub/ojs/index.php/iam/article/view/1001

205. Wunsch H, Harrison DA, Jones A, Rowan K. The impact of the organization of high-dependency care on acute hospital mortality and patient flow for critically ill patients. Am J Respir Crit Care Med. 2015 Jan 15;191(2):186–93.

206. Consiglio Direttivo FADOI Emilia Romagna. Medicina Interna e organizzazione ospedaliera per intensità di cure: la posizione di FADOI Emilia Romagna. Italian Journal of Medicine. 2012;6:72–74.

207. Mongardi M, Bassi E, Di Ruscio E. Ospedale per Intensità di cura: strumenti per la classificazione dei pazienti. DGSPS, Servizio Presidi Ospedalieri, Regione Emilia-Romagna. 2015;

208. Prin M, Wunsch H. The role of stepdown beds in hospital care. Am J Respir Crit Care Med. 2014 Dec 1;190(11):1210–6.

209. Capuzzo M, Volta C, Tassinati T, Moreno R, Valentin A, Guidet B, et al. Hospital mortality of adults admitted to Intensive Care Units in hospitals with and without Intermediate Care Units: a multicentre European cohort study. Crit Care Lond Engl. 2014;18(5):551.

210. Mitchell PH, Shortell SM. Adverse outcomes and variations in organization of care delivery. Med Care. 1997 Nov;35(11 Suppl):NS19–32.

211. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, et al. The quality of health care delivered to adults in the United States. N Engl J Med. 2003 Jun 26;348(26):2635–45.

212. Lilford R, Mohammed MA, Spiegelhalter D, Thomson R. Use and misuse of process and outcome data in managing performance of acute medical care: avoiding institutional stigma. Lancet Lond Engl. 2004 Apr 3;363(9415):1147–54.

213. Øvretveit J, Staines A. Sustained improvement? Findings from an independent case study of the Jönköping quality program. Qual Manag Health Care. 2007 Mar;16(1):68–83.

214. Groene O, Mora N, Thompson A, Saez M, Casas M, Suñol R. Is the maturity of hospitals' quality improvement systems associated with measures of quality and patient safety? BMC Health Serv Res. 2011;11:344.

215. Favaretti C, De Pieri P, Torri E, Guarrera G, Fontana F, Debiasi F, et al. An EFQM excellence model for integrated healthcare governance. Int J Health Care Qual Assur. 2015;28(2):156–72.

216. Griffiths P, Sironi C. Care needs and point prevalence of post-acute patients in the acute medical wards of an Italian hospital. Int J Nurs Stud. 2005 Jul;42(5):507–12.

217. Needleman J, Buerhaus P, Pankratz VS, Leibson CL, Stevens SR, Harris M. Nurse staffing and inpatient hospital mortality. N Engl J Med. 2011 Mar 17;364(11):1037–45.

218. Palese A, Cuel M, Zanella P, Zambiasi P, Guarnier A, Allegrini E, et al. Nursing care received by older patients in Italian medical units: findings from an explorative study. Aging Clin Exp Res. 2013 Dec;25(6):707–10.

219. Palese A, Ambrosi E, Prosperi L, Guarnier A, Barelli P, Zambiasi P, et al. Missed nursing care and predicting factors in the Italian medical care setting. Intern Emerg Med. 2015 Sep;10(6):693–702.

220. Berenholtz SM, Dorman T, Ngo K, Pronovost PJ. Qualitative review of intensive care unit quality indicators. J Crit Care. 2002 Mar;17(1):1–12.

221. Serafini F, Fantin G, Brugiolo R, Lamanna O, Aprile A, Presotto F. Outlier Admissions of Medical Patients: Prognostic Implications of Outlying Patients. The Experience of the Hospital of Mestre. Italian Journal of Medicine. 2015;9:299–302.

222. Dhond G, Ridley S, Palmer M. The impact of a high-dependency unit on the workload of an intensive care unit. Anaesthesia. 1998 Sep;53(9):841–7.

223. Edbrooke DL, Minelli C, Mills GH, Iapichino G, Pezzi A, Corbella D, et al. Implications of ICU triage decisions on patient mortality: a cost-effectiveness analysis. Crit Care Lond Engl. 2011;15(1):R56.

Curriculum vitae

In 2008, Marta Rigoni received a Bachelor's Degree in Applied Physics at University of Trento (Italy) with a thesis about applications on photonic crystals of polystyrene spheres.

In 2011, she received a Master's Degree in Physics and Biomedical Technologies at University of Trento (Italy) with a thesis on interactions between biocompatible nanoparticles and two-dimensional and three-dimensional cell cultures.

In 2013, she started an International Doctorate School in Clinical and Experimental Medicine at the University of Modena and Reggio Emilia (Italy) in Public Health, Statistics, and Epidemiology curriculum.

She currently works as Biomedical Statistician Researcher at *Healthcare Research and Implementation Program*, Autonomous Province of Trento, Bruno Kessler Foundation (Trento, Italy). Her competences are in statistical and methodological tools for the definition of clinical and process indicators. She is working with the Department of Health and Social Solidarity on issues of quality, efficacy, and impact of healthcare services at provincial level.

She taught courses on research methodology and medical statistics for healthcare professionals' continuous update for the local Healthcare Trust of Trento.

Scientific contributions and publications

Full paper

- Disertori M, Rigoni M, Pace N, Casolo G, Masè M, Gonzini L, Lucci D, Nollo G, Ravelli F, "Myocardial fibrosis assessment by late gadolinium enhancement is a powerful predictor of ventricular tachyarrhythmias in patients with ventricular dysfunction of ischemic and nonischemic etiology: a meta-analysis.". To be published in JACC Cardiovascolar Imaging.
- Zarantonello D, Laudon A, Dalprà A, Fratton F, Giovannini L, Zulian I, Rigoni M, Torri E, Nollo G, Brunori G, "Caratterizzazione dei pazienti con questionario strutturato per la scelta della terapia renale sostitutiva. L'esperienza della provincia autonoma di Trento (PAT)". Giornale Italiano di Nefrologia. Anno 32, Vol. 1, Gennaio-Febbraio 2015.

Oral comunication

- Spagnolli W, Cozzio S, Peterlana D, Dorigoni S, Vettorato E, Rigoni M, Pace N, Torri E, Nollo G, "An organizational model differentiated by intensity of care may improve outcomes for severely ill medical patients". 20th National Congress FADOI – Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti, Torino, Italy. May 9th-12th 2015.
- F. Tessarolo, E. Bonomi, F. Piccoli, F. Morat, M. Rigoni, I. Caola, M. Barbareschi, P. Caciagli, S. Muraglia, R. Bonmassari, G. Nollo. "Assessing composition of coronary thrombus in STEMI patients. A multiscale approach to charaterize samples obtained by catheter aspiration". Proceedings of the 2nd International Congress on Cardiovascular Technologies. Edited by: Rui César das Neves. Publisher: SCITEPRESS. Rome, 25th to 26th October 2014.
- Rigoni M, Recchi D, Torri E, Nollo G, Pace N, Noro G, "Valutazione di un percorso assistenziale di ortogeriatria per la gestione delle fratture da fragilità nei pazienti anziani". 7° Convegno nazionale SIHTA-Società Italiana di Health Technology Assessment. Roma, Italia. 25-27 Settembre 2014.
- Rigoni M, Torri E, Nollo G, Pace N, Cozzio S, Spagnolli W, "Applicazione di uno score di gravità clinica (National Early Warning Score - NEWS) ai fini prognostici in un Reparto di Medicina Interna". 7° Convegno nazionale SIHTA-Società Italiana di Health Technology Assessment. Roma, Italia. 25-27 Settembre 2014.
- Brunori G, Laudon A, Zarantonello D, Sottini L, Rigoni M, Nollo G, Torri E, "La dialisi peritoneale assistita: un modello di integrazione ospedale-territorio". Convegno Percorsi di integrazione: buone pratiche a confronto. Trento, Italia. 16-17 Giugno 2014.

- Laudon A, Brunori G, Zarantonello D, Sottini L, Rigoni M, Nollo G, Torri E, "Valutazione d'esito in nefrologia: analisi comparativa di trattamenti dialitici in Provincia di Trento". XVII convegno Gruppo di Studio di Dialisi Peritoneale GSDP. Montecatini Terme, Italia. 20-22 Marzo 2014.
- Torri E, Rigoni M, Nollo G, Brunori G, Laudon A, Zarantonello D, Sottini L, "Impatto di modelli organizzativi nella gestione della dialisi peritoneale in una unità operativa multizonale nella Provincia Autonoma di Trento". 6° Congresso Nazionale e 3° Congresso Internazionale SIMM-Società Italiana Medici Manager. Roma, Italia. 21-22 Novembre 2013.
- Nollo G, Rigoni M, Torri E, Brunori G, Laudon A, Zarantonello D, Sottini L, "Valutazione di appropriatezza della dialisi peritoneale in una unità operativa multizonale". 6° Convegno nazionale SIHTA-Società Italiana di Health Technology Assessment. Bari, Italia. 7-9 Novembre 2013.

Poster presentation

- Spagnolli W, Cozzio S, Vettorato E, Dorigoni S, Peterlana D, Rigoni M, Pace N, Torri E, Nollo G, "Usefulness of NEWS (National Early Warning Score) to assess acute-illness severity in an Internal Medicine ward". 20th National Congress FADOI – Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti, Torino, Italy. May 9th-12th 2015.
- Spagnolli W, Cozzio S, Rigoni M, Peterlana D, Dorigoni S, Vettorato E, Grattarola M, Pace N, Torri E, Nollo G, "L'organizzazione per intensità di cura può ridurre l'aggravamento clinico dei pazienti ricoverati in Medicina interna", 10° Conferenza Nazionale GIMBE, Bologna, Italy. March 27th 2015.
- Rigoni M, Recchi D, Torri E, Nollo G, Pace N, Noro G., "Ortogeriatria a Trento: dati preliminari degli outcome a medio termine". 59° Congresso SIGG-Società Italiana di Gerontologia e Geriatria. Bologna, Italia. 26-29 Novembre 2014.
- Brunori G, Laudon A, Zarantonello D, Sottini L, Rigoni M, Nollo G, Torri E., "Comparative analysis of dialytic therapy in the autonomous province of Trento (Italy)". 15th Congress of the International Society for Peritoneal Dialysis. Madrid, Spain. September 7th-10th 2014.

Ringraziamenti

Vorrei ringraziare il Prof. Marco Vinceti per la sua intelligenza, onestà e per aver mantenuto un comportamento impeccabile nel ruolo di mio supervisor. Ringrazio la Provincia Autonoma di Trento – Dipartimento Salute e Solidarietà Sociale per aver finanziato il mio lavoro in questi anni. Un ringraziamento particolare va fatto al Dr. Giandomenico Nollo, innanzitutto per avermi dato l'opportunità di intraprendere questo percorso formativo che è stato assolutamente stimolante ed arricchente sotto molti punti di vista; in secondo luogo, per l'aiuto concreto nella stesura dei lavori e del testo della tesi e per essere un capo che ha a cuore il bene dei suoi collaboratori e del suo gruppo, che tiene in forte considerazione l'aspetto umano e che, proprio per questo motivo, è riuscito a creare un team affiatato e capace. Un immenso grazie ai miei colleghi Dr. Emanuele Torri, Dr. Elisa Morganti, Dr. Michela Masè, Dr. Nicola Pace, senza i quali non sarei riuscita a sviluppare e a terminare il lavoro in questi anni e soprattutto negli ultimi mesi e giorni. Grazie anche agli altri miei colleghi per il loro sostegno quotidiano in questi ultimi tre anni, lavorare con voi mi migliora continuamente e passare del tempo con voi è sempre un piacere!

Devo ringraziare profondamente il Dr. Giuliano Brunori, il Dr. Walter Spagnolli, Dr. Gabriele Noro, Dr. Marcello Disertori, ed i loro preziosi collaboratori, per avermi dato la possibilità di lavorare assieme a loro e di imparare molto dalla loro professionalità, grinta, determinazione e passione.

Non ringrazierò mai abbastanza la mia famiglia, la mia mamma ed il mio papà, per il bene che mi vogliono, per il sostegno che mi danno, per essere sempre le colonne portanti della mia vita. Avrò sempre bisogno di voi, e so che ci sarete. Grazie ai miei nonni, ai miei zii, ai miei cugini, perché mi hanno sempre fatta sentire una persona speciale, amata e fortunata.

Un grazie immenso ai miei amici, la mia seconda famiglia. Non riesco ad immaginarmi senza di voi! Siete tanti ma vi ho tutti nel cuore! Sono stata molto fortunata ad incontrarvi e spero di avere la saggezza e la forza di tenervi sempre vicini!!