



Value based healthcare for rare diseases: efficiency, efficacy, equity

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Abstract

The paper reviews the literature available on value based health care and relates it to rare diseases. Starting from the economic definition of value and healthcare evaluation, efficacy and efficiency, it includes the equity dimension to define value-based healthcare. It embraces also the cultural framework associated to the concepts of health and disease, normal and pathological, right or wrong for the patient. The paper highlights that a prevention and recovery view and global evaluation of costs/benefits ratio for rare diseases make difficult and limited the applicability of the value-based approach to rare diseases. Since epidemiology of rare diseases identified a series of difficulties in applying value-based public health strategies to rare diseases, the paper underlines the necessity of new culture of health and well-being, radically re-examining how to organise the delivery of prevention, and healthcare services, and finding alternative ways of empowering and giving voice to vulnerable and marginalised groups.

Key words

- healthcare
- rare diseases
- equity
- vulnerability
- resilience

INTRODUCTION

The expression “value-based healthcare” was first introduced in 2006 by Michael E. Porter in a book published in collaboration with Elizabeth Olmsted Teisberg [1]. It should not be surprising that this proposal came from an academic known for his theories on economics and particularly business strategies and competition. Rising health care costs are a major global challenge and health systems should also be evaluated from an economic and financial point of view. A number of factors contribute to the financial crisis of the health systems, including ageing populations and the permanently increasing costs of medical technology and pharmaceutical products. However, an underlying and misunderstood source of healthcare’s escalating costs has been the inability of healthcare provider organisations (such as large hospitals and sanitary structures) to properly measure and manage the true costs and value of healthcare.

In this book Porter apply to health systems a concept of business management proposed in his 1985 best-seller *Competitive advantage: creating and sustaining superior performance* and known as “global value chain” (GVCs), that is the full range of activities that are required to bring a product from its conception, through its design, its sourced raw materials and intermediate inputs, its marketing, its distribution and its support to the final consumer. In the health care marketplace the “final consumer” is the patient and according to Porter, “value-based care” seems to carry the promise to signifi-

cantly reduce overall costs spent on healthcare, linking the prices of diagnostic analyses, drugs and treatments to their actual value to patients: «The way to transform health care is to realign competition with value for patients. Value in health care is the health outcome per dollar of cost expended» (1, p. 20).

In a very influential and seminal paper published in July 2009 in the NEJM on Value Based Healthcare, Porter define value improvement as «better patient outcomes relative to the costs of achieving them. The single most powerful step to improve health outcomes is to just start measuring them at the level of patients with a given medical condition – such as breast cancer or knee or hip arthritis – or in delivering primary and preventative care for patient segments such as healthy adults» [2]. In the conclusions of the paper Porter rises the «big question» if it is possible to move «beyond a reactive and piecemeal approach to a true national health care strategy centred on value», suggesting that the only real solution is «to align everyone in the system around a common goal: doing what’s right for patients».

Two questions emerge from this conclusion: 1. What is a value «right for patients»? 2. Can this concept of value and the relative strategies be applied not only to acute and chronic diseases, such as cancer or diabetes, but also to rare diseases?

MATERIALS AND METHODS

The paper reviews the main literature available on the of value based health care and relates it to rare diseases.

The questions focus on the value “right for patients” and if this concept of value and the relative strategies be applied to rare diseases.

RESULTS

The last quoted passage of Porter's paper bring us directly to the very origins of medical thought and medical practice and to the theoretical and moral basis of medicine and health policies.

Starting from classical times, from the origins of the western medical thought, medicine has acquired a double status: it is a special form of knowledge and a knowledge-based social practice. The Greeks had a single expression for designating this double nature, *iatrike technè*, translated in Latin with *Ars medica* and in modern language as Medical Art. Medicine is not only a scientific discipline and its activities must be evaluated with two different sets of criteria, based respectively on knowledge and in value, looking at what is ‘true’ but also at what it is “good”. Therefore, criteria of truth must be accompanied by criteria of value. The physician does not have as sole basis for his or her decision a “criterion of truth” (the rules used to judge the accuracy of statements and actions) but also a “criterion of value” (the moral appropriateness and utility for the patient).

For this reason medicine is an “applied science”, which links together knowledge, ethical and practical principles [3]. As a science it requires an epistemology, a theory of knowledge; as an ‘applied’ practice it requires a theory of congruence between actions, possible results and their value. In clinical medicine, therefore, each medical act must be scientifically grounded but also have a value, primarily for the patient. This remains the basis of the patient-physician individual relationship.

In philosophical and linguistic terms, the concept of “value” has been applied to two different domains. At the general level, there is a difference between moral value and the value of objects or processes. Moral values are those that have to do with the conduct of persons, usually leading to praise or blame and to an ethical evaluation. The value of objects or processes, on the other hand, is linked to that is economically good for the society and for the individual person. Ethical values and economic values have therefore different domains of application.

In healthcare, however, especially in the case of rare diseases, these two aspects are necessarily linked. An intervention in these field has always an economic value, for the individual and for the society, but cannot be evaluated without taking into account ethical principles, in primis equality and the right to health.

Patient oriented healthcare

According to Michael Porter, the central focus of a value-oriented healthcare system must be on increasing value for patients. This corresponds to a profound change that has occurred in the last decades in the relationships between doctors and patients. In fact, one of the most important change in the health system of the last decades is related to patient and his or her health attitudes and behaviours, a cultural change which includes also the evolution of the role of the physician,

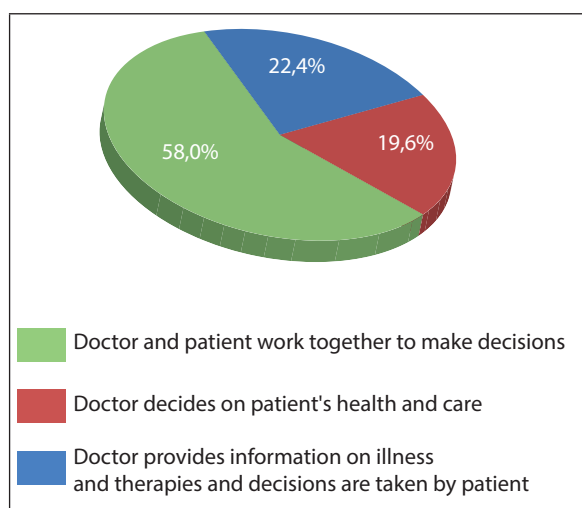


Figure 1

The new set-up of the doctor-patient relationship (val. %). Source: Censis, 2018.

traditional holder of a power based on exclusive medical knowledge. In Italy, from a Censis survey conducted in 2018, it emerges that the majority of Italians considers that the relationships between doctor and patient must be based on collaboration in decisions regarding therapies (Figure 1) [4].

The spread of health information, through the new and traditional media, represented a great driver for the transformation of health demand and the physician, who is the expert by definition, begins to waver in front of an increasingly informed patient, who less and less accepts the asymmetric dimension of the care relationship. In this sense, direct access to health information, above all through a powerful information tool like the Internet, has increased disinter-mediated behaviours of the patient, for example in the choice of health services, or in the exchange of health information among peers [5].

The new patient figure (informed, aware, autonomous, empowered), becomes the protagonist of individual paths of health promotion and protection.

But how to evaluate the value for the patient of the health care delivery?

In the economist's view the evaluation is limited to the economic value, cost effectiveness playing an almost exclusive part in current decisions about the funding of health practices, institutions, and technologies: «Achieving high value for patients must become the overarching goal of health care delivery, with value defined as the health outcomes achieved per dollar spent» [6]. In this context, the “value” in value-based healthcare is derived from measuring health outcomes against the cost of delivering the outcomes. However, the risk is to adopt a purely payer-centred perspective, where “value” means delivering cheap but mediocre services, an advantage for payers, not patients. The focus is on minimising the costs of each intervention and limiting services rather than on maximising value over the entire care cycle. «Lowering Costs and Improving Outcomes» becomes an «Health Imperative», which aims at identifying «a number of factors driving expenditure growth including scientific

uncertainty, perverse economic and practice incentives, system fragmentation, lack of patient involvement, and under-investment in population health». [7]

In the present organisation of the healthcare system, competition seems to be the key word, but competition takes place on discrete services, procedures, tests and interventions rather than on the full care cycle: «Nobody takes an overall care-cycle perspective, including steps to avoid the need for interventions (prevention) and ongoing management of medical conditions to forestall recurrence (disease management). The current structure maintains ways of organising medicine that have long been obsolete. The adverse consequences for patient value are enormous» [1, p. 5]. Value in health care is therefore determined in addressing the patient's health condition over the full cycle of care, from prevention and monitoring to treatment and ongoing management.

This evaluation includes equality of health outcomes, equality of resource use, and allocation of resources in proportion to the severity of the individual's ill health. Adopting a value-based objective will have profound implications for allocation of resources throughout the healthcare system.

DISCUSSION

From the individual patient to public health

With the development of public health, which deals not with individuals but with populations, another question arises: the traditional synthesis between truth and value is still valid for public health and health promotion?

Classically, the mission of public health has been stated as «the fulfilment of society's programs in assuring conditions in which people can be healthy» [8]. Starting from the Health Reforms in the 19th century, public health agencies have used a large combination of scientific and technological tools (basic science, clinical research, epidemiology, statistics, behavioural research, health care institutions and services, economics, and legislations) to understand and control the causes of health threats, acquiring the right tools to systematically prevent, mitigate, or suppress these causes in entire populations.

But how to attribute a value to the results of a public health programme, the activities of an institution, the quality of a preventive or health promotion intervention?

In 1972 Archibald Leman Cochrane exposed in a lecture the results of his analysis of the activities of the National Health Service in UK. His lecture (and the short book that resulted from it) was entitled *Effectiveness and Efficiency*, and the two words became the guideposts of health care in many countries [9]. Effectiveness means the adequateness to accomplish a purpose and producing the intended or expected results. Efficiency means performing or functioning in the best possible manner with the least waste of time, effort and especially money. Treatments and health practices must be measured and evaluated by their outcomes and their costs. Cochrane's lecture led directly to the ascent of evidence-based medicine and indirectly to health reforms based on the pursuit of efficient and effective outcomes in value-based models.

However, the lecture's and book's title left out a third essential word, that Cochrane considered of the same

importance than the first two: equity. Cochrane suggested in fact three criteria for establishing priorities in care and prevention: Efficiency, Efficacy, Equity. If the first two "Es" deal with economic value, the third has a fundamental ethical aspect and moral value.

Too often, the economic values remain dominant and the third dimension, "Equity", is neglected. Equity is a concept which derive directly from the fundamental Right to Health included in the Constitution of the WHO: «The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being ...» (Preamble). The objective of the World Health Organization has been defined as «the attainment by all peoples of the highest possible level of health» (Art. 1) [10]. Accordingly, any policy and activity which impairs an equal enjoyment of the right to health and produces discrimination in access to health care is ruled off. Equity as a consequence is a fundamental value in health care and public health.

A further step in the definition of value in health care and public health has the increasing consciousness of the importance of the social determinants of health, starting with the Commission created by WHO and chaired by Sir Michael Marmot. The final report of the Commission, *Closing the gap in one generation*, underlines the need to take into considerations and the different levels of the factors which can modify the health status of an individual or a population [11]. As a matter of fact, complex interactions exist between age, sex, and constitutional factors, with individual lifestyle factors, social and community networks, and finally general socio-economic, cultural and environmental conditions [12]. Socio-economic and political context, governance, cultural values, living and working conditions, besides behaviours and biological factors determines the distribution of health and well-being, as well as health inequities.

In Italy, several surveys carried out in the last years by Censis, related to representative samples of about 1000 Italian adults, show some important changes in their health attitudes, opinions and behaviours. First of all, the increasing relevance attributed by Italians to lifestyles and environmental conditions as determinants of health on which it is possible to act [13].

A new perspective is taking on a growing weight, with a more informed and empowered patient, becoming the protagonist of promoting one's health and new lifestyle habits and health-oriented behaviours.

A rich literature on social determinants of health emphasises the negative consequences on health experienced by citizens who are in situations of social disadvantage, because of greater exposure to risk factors, more consistent vulnerability to illness and disability, lower life expectancy. The importance of personal resources is evident also by considering a simple indicator as the declared state of health of the ISTAT survey on the health condition of the Italians [14]. The percentage of people (within groups of the same age) who declare themselves to be healthy increases as the level of education (as proxy of social status) increases, as well as, on the other hand, the share of those with at least two chronic diseases increases when the level of education decreases

Culture matters ...

Values are embodied in medical knowledge and health practices and the personal experience of health and well-being is fundamentally determined by the cultural contexts that contribute to make its meaning. These frameworks and beliefs inform also the actions of policy-makers and health care practitioners as well as the people they care for.

In 2014 a Lancet Commission has suggested a culturally informed approach to health and well-being, indicating that «the systematic neglect of culture in health and health care is the single biggest barrier to the advancement of the highest standard of health worldwide» [15]. Culture, as defined by UNESCO, is not a rigid set of abstract ideas and concepts, but a set of «distinctive spiritual, material, intellectual and emotional features of society of a social group ... [which] encompasses, in addition to art and literature, life styles, ways of living together, value systems, traditions and beliefs» [16].

Culture, in its dynamic and diversity, sets the framework for attribute meaning to events and objects, and is something all members of families, communities and populations share. It frames the sense of reality, determines the parameters within which decisions are taken and actions performed, giving a sense of purpose and direction to life. Organisations, institutions, and professional groups also develop their own culture, which produces diverse schemas of thought and practices.

The concepts of health and disease, and the relative beliefs are part of a cultural framework. Values are embodied in medical knowledge and health practices and they constitute a set of shared values, which defines what is normal and what is pathological [17], what is right or wrong for the patient. Viewing health and care in purely clinical terms leaves health systems ill-equipped to understand the psychological, social and cultural determinants of illness and health. Far from a purely medical discourse, the culture of care, health and well-being is built upon a foundation of shared values and beliefs, that must be taken into account.

Health is not the absence of illness, but a search for well-being in the diverse conditions of life and according to the diverse individual constitutions. Moving from the traditional concepts based on the disease to a more large concept of health linked with the global well-being and the realisation of each individual's life project shifts the accent of health care and public health policy towards people's subjectively defined experiences and perceived needs. In such a way health becomes an objective that should be pursued and promoted through individual and community commitment.

This is particularly true for rare diseases, where the pathological condition is always present, but this does not preclude a search for well-being and the accomplishment of the individual's life project. This cultural change in health establishes the framework for measuring the value of a specific health care measure or public health policy.

Rare diseases and value-based public health

The traditional public health approach has been extremely successful in the developed world, with effective

responses to sudden health crises (e.g., infectious outbreaks), persistent health problems (e.g. chronic or non-communicable diseases), or in controlling environmental risk factors (pollution, accidents, nutrition, water, natural disasters). However, this traditional approach to healthcare seems to have a limited applicability to rare diseases, because the diseases are extremely diverse and the patients are few and scattered across populations.

The applicability to rare diseases of the value-based approach, based primarily on prevention and recovery and on global evaluation of costs/benefits ratio seems therefore limited. Rare diseases are in fact characterised by a large number and broad diversity of disorders. This diversity implies a preventive and therapeutical approach based on individuality. There are very few common traits between the diverse disorders and the category of 'Rare Diseases' is an artificial grouping without clear ways to group together diverse diseases. The unique link between them seems to be the genetical or gestational basis of most of them. As a consequence, public health approaches may not seem suitable for rare diseases, because the primary measures of success relate to the prevention of large numbers of cases, measurable health betterments, and the avoidance of premature deaths.

Rare diseases constitute a fundamental paradox because if on one side diversity and individuality seem to place rare disease outside the realm of public health, on the other side the reasons to apply a public health approach to rare diseases are compelling. Rare diseases are a major public health problem and a priority because persons with rare diseases form a sub-population of large dimensions. At the social level, the diagnosis of a rare disease can severely affect the lives of patients, their families and caregivers, with a substantial economic impact for the individuals and the communities in general. The consequences of this paradox is that the sustainability of health systems for rare diseases share additional challenges to those faced by health systems that are stressed by the current financial crisis.

Rare diseases are serious chronic diseases, usually beginning in childhood and may be life-threatening. As a consequence, they represent for the healthcare system challenges fundamentally different from those of more common diseases. Rarity significantly complicates the tasks, because of the small number of patients, the difficulties in reaching widely dispersed patients, the lack of validated and standardised procedures for care and rehabilitation, and limited clinical expertise and expert centres. For many rare diseases, basic knowledge on the specific cause of the disease, its pathophysiology, the natural course of the disease and the relative epidemiological data is scarce, sometimes totally unavailable. This significantly delays or overrides both diagnosis, care giving and prevention. Case definitions for classification are usually lacking and as a consequence screening strategies and surveillance lack efficiency [18]. The knowledge on rare diseases epidemiology has luckily increased considerably in the last decades [19] and the resulting literature clearly identifies a list of difficulties in applying value-based public health strategies to them:

1. scope and capacity of most registries and databases are limited to the pure medical and clinical discourses; 2. knowledge of most rare diseases is insufficient (“orphan diseases”); 3. longitudinal data collections are scarce; 4. outcomes of treatment and care are diverse and difficult to quantify; 5. diagnosis are difficult and often delayed; 6. the development of therapeutics and treatments is often fragmented and slow; 7. specialised and coordinated medical care are scarce and expensive, because of its complexity and multidimensionality; 8. standards of care for treatment and rehabilitation are not evidence based because health research is necessarily done at small scale.

Furthermore, in the case of rare diseases, if the quantitative evaluation of the costs is a relatively easy task, much more difficult is to establish the quantity and especially the quality of the outcomes. The model of “value-based healthcare” is mainly suited for managing chronic diseases or conditions like cancer, diabetes, obesity, high blood pressure, chronic obstructive pulmonary disease (COPD), or heart diseases. Value-based care models focus on helping patients recover from illnesses and injuries more quickly and at a minimum cost.

Can this approach still be valid for a large but sparse population of individuals affected by disabling, life-threatening, and largely unpreventable diseases? How to evaluate a health outcome in a patient with a rare disease?

A positive answer to these questions requires the proposal of a larger view of values, reaffirming that even in the case of rare diseases the main aim of stakeholders, policy makers and institutions in charge of national strategies is to quantify the burden of pathological condition and available resources for sustainable and resilient health system, taking into account the three “Es” proposed by Cochrane, the principles of Efficiency, Efficacy and Equity. But this requires a new culture of health and well-being and the need to radically re-examine how to organise the delivery of prevention, wellness, screening, and routine health maintenance services, finding alternative ways of empowering and giving voice to vulnerable and marginalised groups.

Changing values: vulnerability and resilience

One of the main results of the cultural change in health demand is related to a new patient, who is informed, aware, autonomous, and empowered. The patient’s empowerment is particularly important because can translate into a real growth of health awareness and culture, with positive results in terms of prevention development, increase of ability to recognise symptoms and diseases, enhancement of compliance and effective management of the health conditions. More specifically, the patient’s empowerment can represent a value especially in rare diseases. As in any serious chronic diseases, the patient’s role becomes strategic, because a rare disease is a life-long condition, with a great impact on life possibilities and on daily life activities. Patients, caregivers and families are protagonists in managing the disease and individual and family commitment and resources are strategic for coping with its difficulties. The outcome of cultural changes on health, in terms

of patient’s awareness and accountability, is one of the most important aspects that can impact not only on health behaviours but also on care systems and public health objectives.

For this reason, in recognising the patient’s strategic role, the necessity and the value of his participation in the decisions for the care that concern him and in the management of his chronic conditions, we must also take into account an equally central aspect, health inequalities. Their reduction is an ethical imperative, but also a fundamental value for the enhancement of the patient’s role in the management of rare diseases. Diverse value systems and health views can either promote or limit the equal distribution of health resources. Vulnerable groups face very often barriers to integration and participation.

Vulnerability is at the same time a common everyday term and a rigorous scientific concept. It underlines physical and mental fragility, incapacities to work, to socialise and to realise own life project, to construct and maintain social networks. Vulnerability quite often leads to marginalisation and stigmatisation, to social inequalities and health insecurity. Vulnerable populations and groups often do not become involved in well-being studies, also because they are reluctant to do so, particularly when they feel alienated or marginalised. This can unintentionally reinforce health inequalities and deny certain groups a voice in the decision-making processes that affect their lives. As for the whole society, often the most vulnerable are the most silent.

If vulnerability has a negative acceptance and a passive sense, another word and concept implies an active attitude in coping with difficulties and bad health conditions: resilience.

Resilience is usually defined as an individual’s ability to successfully adapt to life tasks in the face of social disadvantage or highly adverse conditions. Resilience is the ability of an individual or a system to ‘bounce back’ from a negative experience, to continue to function in changing situations or adverse conditions and events, re-establishing and eventually developing personal efficiency and social integration. This implies three different modalities, connected with increasing difficulty of the adverse situations: to absorb its consequences, to adapt to them, and to transform the adversity in the possibility of new developments.

Resilience is not a permanent character trait but a process of building a structured system with gradual discovery of personal abilities and the development of proper coping techniques, that allow to effectively overcome negative conditions or crises. More generally, resilience can be defined as the ability to maintain normative behaviours and realise aimed tasks at the various stages of life, even when the starting conditions of the personal life can be handicapped by a rare disease.

Resilience can be linked to individual persons, but it is also a fundamental property of social groups, families, associations, professional teams, and also institutions. Resilience must be developed by all the actors of the health care for rare diseases 99: patients and their families, physicians and caregivers, institutions, associations, institutions, industries, international organ-

isation, NGOs. Evidence suggests that efforts of this type have empowered patients with rare diseases and their organisations as they seek and obtain wider social recognition, more participation in research, and better health care [20].

Fostering individual and community resilience in face of rare disease conditions is the main aim of a value-based healthcare. There are several factors that can develop and sustain a person's or a group's resilience and most of them are value-based: the ability to make realistic plans and being capable of taking the steps necessary to follow them, a positive self-concept and confidence in one's strengths and abilities, communication and problem-solving skills, and the ability to develop and control strong emotions and feelings. Value-based public health can help patients to improve their health, reduce the incidence and the effect of the disease and pathological condition, and live healthier lives [21]. Well-being can be reached even in presence of infirmity or handicap. An individual with a rare disease should enjoy the highest attainable standard of health.

The challenge is to re-evaluate what one takes for granted in healthcare and public health and rethink the spontaneous assumptions about what is health and what will make a person healthier. There are many diverse and interrelated cultural practices that can enhance resilience and values. In the field of rare disease more ambitious objectives are possible within a value-based paradigm: reduce the impact of disease on patient, they relatives and caregivers, and on community; improve the management of associated health conditions; produce a smooth transition between paediatric and adult care; improve the quality of life and life expectancy; enhance the participation of patients in their communities, workplaces, cultural life, and society in general; develop of cultural activities and acquiring more social recognition.

Genomics, epigenomics and rare diseases

With the complete sequence of the human genome we are now in a unique position in the history of medicine to define the genetic basis of human diseases precisely, with optimal sensitivity and specificity. The precise molecular characterisation of human disease will allow us to understand the basis for disease determinism, susceptibility and environmental influence. The recent development of genome-wide analysis seems to be able to offer an explanation for the different phenotypic manifestations of the same disease, to obtain disease prognosis with greater accuracy and to establish new methods and tools for prevention. The aim becomes now to refine and, ideally, personalise disease treatment for optimal therapeutic efficacy. Rare diseases look as unique, individual diseases and the idea of "individual or personalised therapy" seems to be the most promising approach, especially with the development of new personalised biotech products for treating rare diseases.

The new field of epigenetics shown how social contexts and determinants can influence genetic makeup. Epigenetics, defined as the science that studies "the set of modifications to our genetic material that change the ways genes are switched on and off" [22], focuses

not merely on gene expression, but also on how diverse factors in our natural and social environments affect what genes are expressed and the ways in which they are expressed. Environmental factors have a profound effect on gene expression, and in the classic "rainbow" model of the social determinants of health proposed in 1993 by Dahlgren and Whitehead [23], the central core with the age, sex and constitutional factors is not only a set of causal factors for determining upward the individual lifestyle and the general population health conditions, but also the result of a downward causation, which change the ways in which the constitutional factors are expressed along the whole life course.

These scientific developments can produce a paradigmatic change in the concept of health and in public health strategies, thanks to the possibility to personalise prevention, healthcare and promotion of health. Together with the three "Es" proposed by Cochrane (Effectiveness, Efficiency, and Equity) the new paradigm in a value-based medicine and health will be based on 4 "Ps": Preventive, Predictive, Participatory, and Personalised.

CONCLUSIONS

A value-based public health strategy for rare diseases should concentrate on a few objective, clearly defined by a scientific and ethical analysis, which is in general already available in the scientific literature, epidemiological inquires and policy reports. These objectives include the definition of the population impact through epidemiological research adequate for low-prevalence diseases and the evaluation of the costs associated with these diseases, such as medical costs, lifetime productivity loss, financial impact on caregivers, and impact on the employability of patients. Particularly important are the objectives of documenting progression of health status and associated quality of life, evaluate health outcomes (in the largest sense of the term), evaluate and compare health care practices, identifying evidence-based findings on best practices and standards of care, create networks to share research, knowledge and values.

In order to attain these objectives new research strategies based on values are needed, integrating the complexities and individuality of lived experiences into an expanded evidence base on health vulnerabilities that includes assessments of subjectively defined needs, thanks to a narrative and qualitative research and a culture-centred approach.

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