

Framing of scientific knowledge as a new category of health care research

Luis Salvador-Carulla MD PhD,¹ Ana Fernandez PhD,² Rosamond Madden MSc AM,³ Sue Lukersmith M.Erg OT (OT),⁴ Ruth Colagiuri BEd GCHPolMan,⁵ Ghazal Torkfar BHlthSc (PH) MPH⁶ and Joachim Sturmberg MBBS DORACOG MFM FRACGP PhD⁷

¹Professor of Disability and Mental Health, ²Postdoctoral Research Associate, Mental Health Policy Unit, Brain and Mind Research Institute, Centre for Disability Research Policy, Faculty of Health Sciences, The University of Sydney, Sydney, NSW, Australia

³Director, Australian ICF Disability and Rehabilitation Research Program, Centre for Disability Research Policy, Faculty of Health Sciences, The University of Sydney, Sydney, NSW, Australia

⁴PhD Candidate, Centre for Disability Research Policy, Faculty of Health Sciences, The University of Sydney, Sydney, NSW, Australia ⁵Associate Professor, ⁶PhD Candidate, School of Public Health and Menzies Centre for Health Policy, The University of Sydney, Sydney, NSW, Australia

⁷Professor of General Practice, Discipline of General Practice, School of Medicine and Public Health, Newcastle University, Newcastle, NSW, Australia

Keywords

epistemology, evidence-based medicine, framing, practical reasoning, typology of scientific studies

Correspondence

Dr Luis Salvador-Carulla Mental Health Policy Unit, Brain and Mind Research Institute Centre for Disability Research and Policy Faculty of Health Sciences The University of Sydney 75 East Street, Lidcombe, NSW 2141 Australia E-mail: luis.salvador-carulla@sydney.edu.au

Accepted for publication: 24 September 2014

doi:10.1111/jep.12286

Abstract

Rationale The new area of health system research requires a revision of the taxonomy of scientific knowledge that may facilitate a better understanding and representation of complex health phenomena in research discovery, corroboration and implementation. **Method** A position paper by an expert group following and iterative approach.

Results 'Scientific evidence' should be differentiated from 'elicited knowledge' of experts and users, and this latter typology should be described beyond the traditional qualitative framework. Within this context 'framing of scientific knowledge' (FSK) is defined as a group of studies of prior expert knowledge specifically aimed at generating formal scientific frames. To be distinguished from other unstructured frames, FSK must be explicit, standardized, based on the available evidence, agreed by a group of experts and subdued to the principles of commensurability, transparency for corroboration and transferability that characterize scientific research. A preliminary typology of scientific framing studies is presented. This typology includes, among others, health declarations, position papers, expert-based clinical guides, conceptual maps, classifications, expert-driven health atlases and expert-driven studies of costs and burden of illness.

Conclusions This grouping of expert-based studies constitutes a different kind of scientific knowledge and should be clearly differentiated from 'evidence' gathered from experimental and observational studies in health system research.

Introduction

The recognition that many health conditions, health care and health systems are complex phenomena (dynamic, non-linear and non-deterministic) challenges our current understanding of scientific knowledge in medical practice, public health and health policy [1–3]. There are a series of fundamental positions that are relevant to the current debate on the conceptualization and classification of knowledge in health research, particularly in relation to the evidence-based medicine (EBM) model.

The traditional unidimensional grading indexes of the quality of research that place randomized control trials (RCT) at the top, bottom (e.g. 'Levels of Evidence') [4], do not provide a sound ordering of the scientific knowledge for the analysis of complexity in health, especially in health system research [3]. First, observational information arising from different local environments is increasingly being considered to be a separate source of contextual evidence [5,6], and it may produce a type of inferential knowledge driven from data different to the deductive-experimental knowledge typically acquired from randomized controlled trials. In addition, 'scientific evidence' (either experimental/deductive or observational/non-deductive), should be clearly differentiated from 'expert knowledge' that is a different kind of scientific

observational studies in the middle and expert 'opinion' at the

knowledge, which is also critical to explain patterns, associations and interactions of variables in complex phenomena [3].

Apart from the impact on the conceptualization of research designs and its typology, complexity plays a significant role in the reconsideration of classical statistics as the only group of techniques for the analysis of health effects. Under conditions of high uncertainty, classical statistical techniques are useful in the context of advanced iterative procedures involving artificial intelligence and elicited expert knowledge. For example, 'Knowledge Discovery from Data' is a set of procedures that includes neural networks and rule-based clustering techniques for the analysis of nonlinear, non-deterministic phenomena where the data gathered may be incomplete or imprecise as is typical in implementation sciences, health system research and policy [7,8].

The requisites of complex analysis under conditions of uncertainty should lead to an in-depth revision of the epistemology and taxonomy of scientific knowledge and the related methods of analysis of data, particularly in health care and health policy. 'Frame development' is at the heart of this re-conceptualization process, and thus 'framing scientific knowledge' (FSK) has to be formally defined, its different components described, and the boundaries with other types of research fields clearly delineated.

Methods

In February 2013, L.S.C. and J.S. started a multidisciplinary expert group called Dialogues On Complexity and Health Systems, at the University of Sydney, to advance the understanding of complexity issues in health sciences particularly in public health research. The group included international experts from different disciplines and backgrounds with an interest in complexity in four key areas: public health, primary care, disability and mental health. The discussion topic for 2013 was 'Frames in the context of current paradigms in public health'. The expert group followed an iterative process based on the review of documents that were discussed in monthly meetings registered by a rapporteur (SL/AF). This position paper discusses the creation of new scientific knowledge through FSK and the role of this research area in the knowledge base of health sciences.

In the first section of this review we elucidate why a new taxonomy of 'scientific knowledge' may be needed in public health, and why it should incorporate new types of studies such as FSK. Second, we describe the development of frames of scientific knowledge and differentiate it from other framing approaches (i.e. 'social frames'). Third we discuss the placement and role of FSK in relation to other types of 'scientific knowledge'. In the fourth section we present different types of FSK studies in health sciences and comment on their utility based mainly on previous research made by members of the group.

Complexity and the new taxonomy of scientific knowledge

In order to adapt our research methods to understand complexity in health sciences, an overall revision of the taxonomy of 'scientific knowledge' should be performed, as the existing typology of research studies was only suited for the stages of discovery and corroboration, but not for the stage of implementation or knowledge-to-action research [9–11] This taxonomy should incorporate new and updated formal definitions of the most relevant key concepts. It may go far beyond the current proposals to revise the taxonomy of disease [12] or other reviews of the scientific taxonomy to better accommodate qualitative research in health sciences [13]. This taxonomy should incorporate updated definitions of 'scientific knowledge', a better distinction between deductive and non-deductive 'scientific evidence', and the differentiation between the latter and 'elicited scientific knowledge', which comprises prior expert knowledge and users' experiences.

The existence of 'scientific knowledge' (knowledge acquired through the scientific methods¹) was denied by Karl Popper who espoused the concept of a 'scientific knowledge' to absolute truth as shown in the recently published notes of his seminar at Otago in 1945 [14]. However, 'absolute truth' as the ultimate epistemic goal of science is debatable. G. Schurz has defined the goal of scientific knowledge as finding 'true and content-rich statements' following five basic attributes or assumptions: minimal realism, fallibilism, objectivity, intersubjectivity (i.e. consensus by the scientific community) and logical clarity [11]. This epistemic goal is related to a series of methodological features or conditions including the search for hypothesis, which are 'as general and as content-rich as possible' and observations that are as many and as relevant as possible (Schurz, p. 26 [11]). If science is seen as a 'methodological unity' more than a system for identifying absolute truth, then its progression through generalizability of a content-rich and relevant knowledge base becomes its core element and the scientific goal could be redefined as a method for finding the best fit explanation to the current and new evidence and the best set of predictions of new events relating them.

Artificial intelligence [8], computer sciences and 'knowledge management' [15], and 'business intelligence' [16] have contributed to a new understanding and categorization of scientific knowledge in health system research by providing pragmatic definitions of data, information and knowledge that can readily be applied to the field of scientific knowledge (Table 1).

Under this perspective, scientific knowledge can be defined as a fluid mix of framed evidence and experience acquired by means of standardized methods of research following the principles of commensurability (definition of units of analysis that can be compared like-with-like), transparency for corroboration (including replicability and falsifiability) and transferability (including generalizability to broader contexts). It provides a framework for incorporating new information and experiences and for generating new research questions, causal explanations, empirical hypotheses and theories that allow for a better understanding and prediction of natural phenomena.

Scientific knowledge derived from data (evidence) and expertelicited knowledge are complementary but different components

¹ The scientific method in the natural sciences since the 17th century is defined as consisting of systematic observation, measurement, and experiment, and the formulation, testing, and modification of hypotheses. In particular, experiments must be precisely defined and circumstances controlled as to achieve repeatability by others. In addition, the entire process is fully documented, and all data are shared to allow scrutiny by other researchers. In the 19th century, a series of non-experimental methods such as consilience and abduction where incorporated to the scientific armamentarium, although its contribution is still being debated by the scientific community.

Table 1 Logical inferences, basic concepts and stages of scientific knowledge in health care research

Basic concepts	Definition	Examples (diabetes)		
Logical reasoning				
Inference	Process of deriving logical conclusions from premises known or assumed to be true.	Observational studies		
Inductive Deductive	Inferences from specific instances to general conclusion or explanation. Inferences from general instances to a specific conclusion. Deduction is necessary inference as the certainty of the explanation can be derived from the certainty of the premises	Observational and ecological studies Experimental studies		
Abductive	Inference to the best explanation. It needs a prior knowledge base to select the best or the most plausible explanation	Clinical diagnosis, knowledge discovery from data Artificial intelligence and implementation		
Means-end inferences	Relates fundamental norms to the means to achieve a predetermined end. This requires experts to decide which is the best or most optimal mean from a set of alternatives to achieve the final goal.			
Data and information				
Scientific data	Facts and figures collected using standard assessment methods of research, which relay something specific, but which are not organized.	PG, BSL, HbA1c		
Scientific information	Categorized, calculated and condensed data using scientific analysis and visualization techniques.	Threshold values of PG BSL and HbA1c for the diagnosis and management of diabetes		
Types of scientific knowledge				
Scientific knowledge	A fluid mix of contextualized information (evidence), know-how and experience (expert knowledge) that allows for a better understanding and prediction of natural, psychological and social phenomena. It is acquired by means of standardized methods of research following the principles of commensurability, transparency for corroboration and transferability to broader contexts. Scientific knowledge should fulfil five basic assumptions: minimal realism, fallibilism, objectivity, intersubjectivity and logical clarity. It provides a framework for incorporating new information and experiences and for generating new research questions, hypotheses	Diagnostic criteria for diabetes; rationale for tight BSL/HbA1c control; treatments that minimize potential end-organ damage		
Scientific evidence	and theories. The part of scientific knowledge based on contextualized information from facts and data and which is analyzed using quantitative	Diabetes as a risk factor for myocardial infarct, stroke, peripheral vascular disease, retinopathy and nephropathy		
	approaches alone or combined with qualitative methods to generate inferences using mainly deductive reasoning, but also and non-deductive logical reasoning (induction and abduction)			
Scientific expert knowledge	A set of formalized know-how, understanding, experience and insight in a defined area of knowledge, which is informed, contextualized, stable, consistent and connected. It is elicited using qualitative approaches alone or combined with quantitative methods to generate means-end	Recommendations in clinical practice guidelines of diabetes [51]; consensus algorithm for initiation and adjustment of therapy for		
	interences and non-interential knowledge to complement evidence.	diabetes [73]		
Stages of scientific				
Discovery	Generation of new and relevant scientific evidence mainly using experimental approaches and deductive inference.	First RCT of a new therapy for diabetes (e.g. DPP-4 inhibitors) [74]		
Corroboration	Discovery can also be generated by consilience using inductive inference. Justification of the new scientific evidence by determining the degree of confirmation given the acceptability of observational data using logical induction. It requires transparency of prior information and uses quantitative techniques for ordering available evidence (e.g. meta-analysis), and qualitative techniques for reaching expert consensus (intersubjectivity)	Meta-analysis of available evidence (e.g. all studies on the benefits of DPP-4 inhibitors) [75]		
Implementation	Factual application of corroborated scientific knowledge to real-life practice and policy and to controversial cases. Under conditions of uncertainty and non-monotonicity it requires expert knowledge and incorporates abduction and means-end inferences logical reasoning.	Differences between evidence on efficiency from RCT and information from observational studies (e.g. effectiveness of DPP-4 inhibitors versus sulfonylureas in clinical practice) [76]		

These formal definitions are partly based on the unified approach to the philosophy of science [11] and the knowledge management approach [15]. BSL, blood sugar levels; DPP-4, dipeptidyl peptidase-4 inhibitor; HbA1c, glycated haemoglobin; PG, plasma glucose; RCT, randomized controlled trial.

of science and they should not be merged in a single unidimensional grading system of 'scientific quality' as was suggested in the 1990s when EBM was applied to the development of systematic reviews and practice guidelines. These two sources are combined in different ways to produce two major types of inference: the standard deductive reasoning derived mainly from quantitative experimental designs, and non-deductive reasoning derived from mixed quantitative and qualitative observational designs. The boundaries between deductive and non-deductive 'scientific evidence' are not always clear, as it happens with the boundaries between 'scientific evidence' and 'experiential scientific knowledge'. As a matter of fact, and contrary to the reductionist approach to science, prior expert knowledge is not a confounding factor to be controlled, but an essential part of non-deductive research of complex phenomena [3].

Three major types of non-deductive inference should be considered: induction, abduction and means-end inferences.

Induction

Induction was largely discarded as a process of scientific reasoning by Popper [14]. However the inductive research method incorporated into the consilience approach and based on different sources of observational data is now regarded as a relevant source of scientific evidence [17,18]. In the mid 1800s, William Whewell coined the term 'consilience' to name one of the tests of the inductive inference process of empirical science. According to Whewell, before an inference can be confirmed as an empirical 'truth', induction should accomplish three criteria: prediction ('our hypotheses ought to foretell phenomena which have not yet been observed'), consilience ('explain and determine cases of a kind different from those which were contemplated in the formation') and coherence, which is in itself an iterative process where hypotheses must 'become more coherent' over time. The consilience approach, which underlies the theory of evolution [19], was restated as a valid system to generate scientific evidence in complex domains by E.O. Wilson in the late 1990s [20]. Consilience [21] uses observational data from different sources as basic information for modelling phenomena that can generate predictions and incorporate prior expert knowledge to interpret the information and increase coherence in an iterative process to improve empirical hypotheses and to generate a theory. In summary, consilience and experimental approaches are complementary and use observational information in different ways to generate scientific evidence from data.

Abduction

Abduction, or inference to the best explanation, is another major type of logic reasoning together with deduction and induction. As with induction, and contrary to deduction, it is a non-necessary inference (i.e. the certainty of the explanation cannot be derived from the certainty of the premises), but it differs from induction in the need of a prior knowledge base to select the best or the most plausible explanation. Thus, a preliminary knowledge could be applied to a new single event to generate a prediction based on probability and/or plausibility. On the other hand, inference could base the generation of new knowledge only on the measurement and the evaluation of a set of events. Abduction was described as a relevant source of scientific reasoning for developing hypothesis and performing diagnosis in health sciences by Charles S. Peirce at the turn of the 20th century. After intense criticism in the following decades it was restated as a relevant source of scientific knowledge in complex areas [22], and is now extensively used in artificial intelligence. The incorporation of prior expert knowledge in the procedures of 'Knowledge Discovery from Data' [7], for complexity analysis is based on abduction.

Means-end inference

Means-end inferences relate fundamental norms to the means to achieve a predetermined end [11]. This requires experts to decide which is the best or most optimal mean from a set of alternatives to achieve the final goal. The means-end inferential reasoning is essential for artificial intelligence, policy planning and implementation sciences. It is required for the factual application of scientific knowledge previously gathered by discovery and corroboration to practical problems in the real world under conditions of uncertainty.

Figure 1 illustrates how deductive/experimental and nondeductive/modelling approaches do provide complementary sources of evidence-based knowledge, and how abductive reasoning could be related to them in generating causal hypothesis and in guiding assumptions in probabilistic models. These different approaches can be combined in hybrid designs and include expert knowledge in the quest to produce new scientific knowledge, a combination that is absolutely essential in implementation research. The new cross-design synthesis [23] and mixed designs studies [24] combine quantitative and qualitative techniques as well as deductive, inductive and means-end-derived elicited knowledge to represent and understand highly complex phenomena in health system research and policy, such as cost of illness studies [23], effectiveness of complex interventions [24], case-mix development and relative efficiency of catchment areas [7], or rapid synthesis to inform policy planning [25].

Prior expert knowledge (including experts' implicit or tacit knowledge) should not be regarded as a source of bias, but as a highly relevant component of the scientific knowledge base that has to be formalized and incorporated into the data analysis process. Expert knowledge should also be differentiated from expert 'opinion'. The former refers to formalized expert knowledge that is available for peer review and that follows the social criterion of demarcation that allows for the distinction of scientific knowledge from other types of knowledge (such as religion or ethics) [11,26], while opinions do not fulfil this criterion even when provided by experts.

In order to formalize and to incorporate prior expert knowledge to the analysis of data, a number of standard procedures have been suggested. For example the expert-based cooperative analysis uses an iterative process where the information from every stage of the data analysis is presented to the experts. They interpret it and generate implicit knowledge that is then formalized and incorporated as rules in the model for a consecutive analysis [7]. Rapid synthesis and translation process using the exchange model of knowledge transfer in the context of the interactive system framework is another example that combines systematic reviews and prior expert knowledge to guide health policy. This approach has



Figure 1 Relationship of framing of scientific knowledge with other types of studies in the context of the main types of logical reasoning (deductive, inductive, abductive and means-end inferences), and the different stages of scientific knowledge (discovery, corroboration and implementation).

been used for policy planning in the prevention of violence in the United States [25].

Differences between social framing and FSK

Framing theory, developed in social science research in the late 1960s [27], aimed to explain the relationship between a person's opinions and attitudes with his underlying belief systems, and its role in individual behaviours, preferences and choices. In the social sciences context, a frame is defined as a communication system that 'organizes everyday reality by providing meaning to an unfolding strip of events and promoting particular definitions and interpretations' [28]. It includes the set of dimensions that affects an individual's evaluation and influences his overall opinion and so could be termed 'the frame of thought' of that individual. Framing has also been defined as a dynamic process 'by which people develop a particular conceptualization of an issue or reorient their thinking about an issue' [28]. Different types of social frames have been described: episodic, thematic, conflict and strategic frames.

'Social framing' is widely used in politics and social sciences and has contributed to a better understanding of irrational choices,

ed to a better understanding of irrationa

the use of metaphors and moral intuitions [29]. Cognitive framing may also include the study of cognitive dissonance in social psychology [30], the development of mind schemes and schema therapy in psychology [31], and decision making in preference assessment and health economics [32]. These approaches converge on the neural theory of cognition and language [33].

In the medical context, social framing has been applied to understand clinical decision making, especially in the bias resulting from positive and negative frames of treatment choices [34].

The general concepts underlying 'social framing theory' can also be used to understand the development of scientific frames. Notably the social and policy literature distinguishes between mass public opinions, which are the main research focus of social framing, and 'high-quality expert opinions'. The latter are produced by scholars and are 'stable, consistent, informed, and connected' [28]. These scholar opinions are not merely judgments, they convey actual explicit expert knowledge and constitute the basis for the development of scientific frames and therefore ought to be differentiated from the 'set of beliefs' that experts also hold about a scientific subject.

FSK is a distinct type of expert-driven personal-based research methodology. Scientific frames are explicit, formal, standardized

Table 2	Framing scientific	knowledge (FSK):	definition and	preliminary	typology in	health care	e and public health	1 policy
---------	--------------------	------------------	----------------	-------------	-------------	-------------	---------------------	----------

Framing studies					
Aim	The main purpose of FSK is to contribute to the formulation of research questions, to understand and to represent complex phenomena and to guide decision making under conditions of uncertainty and insufficient evidence. FSK studies generate formal scientific frames that could be used to analyse and to interpret complexity in health sciences, particularly in public and health systems research.				
Definition	A group of studies mainly based on of 'prior expert knowledge' specifically aimed at generating formal scientific frames				
Attributes	Studies of FSK are explicit, specific, standardized, innovative, based on the available evidence and agreed upon by a group of experts (ideally the scientific community on the specific area) following a method that can be reproduced by other groups				
Exclusion	FSK should be differentiated from studies of 'social framing' that study the means by which people develop a particular conceptualization of an issue or reorient their thinking about an issue. Social framing is used in health sciences to understand clinical decision making and to describe the biases resulting from specific ways of framing in clinical practice, clinical reasoning, user choices, care decision making, research design, and in the interpretation of research results				
Preliminary typology	Scientific declarations and frameworks				
	Scientific position papers				
	Expert-based clinical recommendations (as opposed to clearly defined evidence base guidelines)				
	Scientific conceptual maps				
	Classifications				
	Framing health atlases (as opposed to ecological atlases)				
	Framing Col and Bol as opposed to Col and Bol studies using ecological and population-based approaches)				

Bol, burden-of-illness; Col, cost-of-illness.

and based on the available evidence that has been agreed by a group of experts, ideally the scientific community. This consensus or 'agreement of many mutually independent and competent researchers' is called by Schurz 'intersubjectivity', and it is one of the five attributes of scientific knowledge (see Table 1) [11]. These are useful tools to arrange the related knowledge base and to achieve a common understanding. Scientific frames are also purposeful and support decision making in public health.

In summary, the theory of framing can be used in two very different ways in health sciences: (1) to describe and understand the biases resulting from specific ways of framing in clinical practice, clinical reasoning, user choices, care decision making, research design and in the interpretation and implementation of research results; and (2) to generate formal scientific frames that could be used to analyse and to interpret complexity in health sciences, particularly in public and health systems research. In order to avoid any terminological confusion we differentiate here between 'social frames' and 'frames of scientific knowledge'. We use the later term to describe the standardized process of frame development in sciences. This does not mean that social framing is not scientific, it only indicates that the purpose of FSK is to provide explicit and scientifically based frames for the advancement of knowledge while social framing analyses the effects of belief systems on human behaviour using scientific methods (see Table 2).

Differences between FSK and other types of scientific knowledge

Figure 1 provides a representation of FSK and other types of scientific studies and its relation to different kinds of logical reasoning and stages of the development of scientific knowledge.

In one way or another every scientific research involves framing, but there is a relatively small number of studies that are only aimed at developing scientific frames and do not have other objectives. Scientific frames should be regarded as part of the (personal/subjective/expert) component of scientific knowledge and can be elicited either by qualitative research methods alone or using hybrid qualitative-quantitative designs. In any case, scientific frames define a type of prior expert knowledge and should be clearly differentiated from 'research methodology-inferred scientific evidence' (see Table 1). A taxonomy of scientific knowledge would be inconsistent if using the term 'qualitative evidence' to refer prior expert knowledge.

Elicited expert knowledge should also be distinguished from experience-driven qualitative knowledge (e.g. a narrative of coping with disease by a patient). While experiential knowledge can be a one-shot learning event, 'expertise' or 'expert knowledge' is acquired through long-term training. Although other definitions can be used, an 'expert' has been typically defined as a professional with more than 10 000 hours of practice in its given area of expertise [35]. Scientific frames can incorporate experiential knowledge, but cannot rely only on it.

It is important to note that framing is a type of expert-driven research. Even though qualitative studies include framing, many expert-based studies are not limited to it. On the other hand, frame development necessarily requires expert consensus, hence the frames developed by individual experts or small groups should be considered as a preliminary category of scientific knowledge, until they are formally accepted by a broader scientific group and fulfil Schurz's intersubjectivity assumption [11].

Towards a typology of framing studies in health care

In 2010, M.B. Valloton highlighted the importance of not only guidelines, but also 'codes, conventions, and declarations' in health decision making and advanced a preliminary classification

of these types of studies [36]. He also described the confusion in the conceptualization and use of these documents in the health sector. Framing studies contribute to formulate research questions, to understand complex phenomena and to guide decision making under conditions of uncertainty and insufficient knowledge. The background for a preliminary typology of scientific framing studies in the context of healthcare and health policy is provided in Table 2 and each type is now further described in detail.

Declarations, frameworks and related scientific documents

Expert-based formal declarations, charters, consensus statements and action plans constitute a major tool for framing new areas of knowledge and for health policy implementation. Some are produced by international organizations such as the Jakarta Declaration on Leading Health Promotion into the 21st century [37]; others are produced by major professional organizations such as the 1963 World Medical Association Declaration of Helsinki [38]. The latter is a rare exception to the dearth of transparency in their development procedures and the lack of studies on their impact assessment.

Unfortunately, there is a lack of consensus on how a framing declaration in health care should be produced, structured, published, disseminated, revised and assessed. As a result, declarations developed using structured qualitative designs coexist with 'informal expert group statements' in a category of 'undefined scientific knowledge'. Even when declarations appear rigorously compiled, the methods of their development are generally missing from the document (i.e. the qualitative design followed for its development, process, calendar, minutes and other related documents). All statements should be published together with explanatory documents that provide the foundations and the rationale for these major statements, recommendations or calls for action. The huge disparity in the quality of declarations contributes to a lack of understanding of their scientific value, which may explain the difficulty in publishing them in scientific journals.

The declarations on 'Bridging and Knowledge Transfer between Disabilities and Ageing' [39,40] provide an example of the inherent difficulties encountered for drawing a line between formal 'frame declarations' and other pre-scientific 'statements'. The framing declarations on 'Bridging and Knowledge Transfer' were produced by an expert group using a year-long iterative procedure of reading, rewriting and finally gaining approval by experts convening at scientific conferences. All the material accompanying the documents was published in an open-access scientific journal [41].

Health charts are major visualization tools that provide summaries of scientific knowledge and that require expert knowledge in the selection and representation of the underlying 'evidence' and other sources of relevant information. They are major implementation tools, but they are rarely regarded as an object of scientific development and monitoring (e.g. throughout impact analysis). Only health charts that actually contribute to a new understanding of a specific area should be included in this group. Those charts that reproduce and simplify the existing scientific frame for specific target groups without any new contribution over the previous state of the art should not be included here. In 2011, the International Diabetes Federation (IDF) published the IDF's Diabetes Roadmap [42]. This framing kit included a Diabetes Chart, the International Charter of Rights and Responsibilities of People with Diabetes, a series of policy briefings, the Call to Action on Diabetes, and the IDF Advocacy Briefing for the 2011 Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Noncommunicable Diseases. The IDF Roadmap constitutes an example of new frameworks toolkits that cover different facets of care complexity in chronic conditions.

Position papers and related scientific documents

Scientific position papers often provide a consensus on the state of the art in a given area of knowledge as agreed upon by a formal group of experts. On other occasions, position papers are explanatory documents that complement a declaration or another brief framing document. The policy briefings of the IDF Roadmap could be included under this category [42]. Similarly, the Barcelona Declaration on 'Bridging Knowledge in Long-term Care and Support' [39] was published together with a series of related position and complementary papers, and so was the Call for Action published 3 years later on the same topic (Toronto Declaration on 'Bridging Knowledge, Policy and Practice in Aging and Disability') [40,41,43–45].

There may be overlaps between position papers and practice guidelines when referring to clinical interventions. A major difference between scientific position papers and guidelines is the level of contribution of the results of the systematic review and the expert consensus to the final document. As an example of this problem, the 'Guide to Prescribing Psychotropic Medication for the Management of Problem Behaviours in Adults with Intellectual Disabilities' produced by the Section of Intellectual Disabilities of the World Psychiatry Association [46] was really a position paper as it was based mainly on consensus agreement, even though the developers took a previous systematic review of the literature into account. The accompanying paper to the recommendations made by the Intellectual Developmental Disorders Working Group to the International Classification of Diseases and Related Health Problems (ICD) 11th edition Advisory Committee on Mental Disorders constitutes another example of this type of framing documents [47].

Expert-based recommendations in clinical guidelines

Although there is an extensive literature on clinical guidelines and its quality (e.g. Appraisal of Guidelines, Research and Evaluation-II [48]), there is not a clear distinction between 'evidence-based' clinical guidelines where recommendations are mostly derived from the systematic literature review, and 'expertbased' clinical guidelines where recommendations principally reflect prior expert knowledge, and thus could be more accurately regarded as framing documents. McAlister and colleagues [49] have pointed out that 'treatment recommendations for the same condition from different guideline bodies often disagree, even when the same randomized controlled trial (RCT) evidence is cited'. In their review of cardiovascular risk management recommendations of nine guidelines, they found that 55% of these recommendations were not based on 'high-quality' evidence [49]. It is interesting to note that AGREE-II requires a thorough explanation of the method used for reaching consensus on every recommendation (Delphi panel, Glaser technique, etc) although this is rarely mentioned in the final documents. Recently Lenzer et al [50], have produced a declaration on the relevance of conflict of interest in the development of guidelines, but surprisingly no indications were made with regard to the method for reaching consensus and the transparency of the process (e.g. available minutes, voting procedures, etc.). The lack of a proper distinction between 'evidence-based' guidelines and the framing of 'expertbase' guidelines and their recommendations may contribute to the difficulty in assessing the implementation of these tools [51].

Conceptual maps

Conceptual maps are visualization tools that could provide a qualitative or quantitative representation of the relationship among different domains of a category or within classification systems. They are useful to order and understand the tacit knowledge that different stakeholders draw upon when collaborating on a complex objective such as understanding the main functions for priority setting in a health system [52].

Health classification systems

Health classifications are another type of framing document developed mainly from prior expert knowledge. Even where strong evidence exists, a major contribution from experts is required to compile groupings and meta-categories of diseases and syndromes. As an example, the decision whether dementia should be coded as a chapter of psychiatry or neurology requires expert judgement regardless of our underlying understanding of the pathophysiology of the diseases grouped under this meta-category. A clear example of the complexity of expert decision making is the ongoing debate on the definition and placement of 'intellectual disability' or 'intellectual developmental disorder' (formerly called 'mental retardation') in the family of classifications of the World Health Organization-International Classification of Functioning (WHO-ICF). A number of international organizations state that it is a disability and therefore it should be coded at the ICF [53]. Others advocate that it is a meta-syndrome and should be coded at ICD [54]. A third approach considers that a dual approach should be followed as this is a complex construct with different disease, health and social perspectives and characteristics. Hence, it should be coded in both classification systems and the two terms should reflect the different contexts [47].

A clear example of the relevance of classification systems as framing documents is provided by the WHO ICF. Its conceptual frame has had a huge impact in shaping our current understanding of human functioning and its related research [55].

Surprisingly, the requirements for clinical guidelines to provide a thorough explanation of the methods used to reach consensus is rarely evident in the development of the main international classification systems. Problems in the development and use of Diagnostic and Statistical Manual of Mental Disorders 5th edition illustrates this fact [56]. It is important that proper qualitative methods are followed to develop international classifications, and that the minutes, interim reports, voting procedures and any other relevant document related to their development are publicly available. Only then can classification systems be understood as proper scientific framing documents. In the future, this could allow for a better understanding of classifications pertaining to the scientific framing group where the qualitative procedures for reaching consensus are clearly stated.

Framing health atlases

In recent years, health atlases have become a major tool for policy decision making. However, major differences appear in the methods followed to compile the information provided in these atlases and the overall validity of the results presented. While some atlases are limited to register information collected by local experts and could be clearly typified as frames of scientific knowledge (e.g. 'WHO Atlases of Mental Health and of Resources in Intellectual Disabilities' [57,58]), others atlases provide a thorough analysis of service provision, availability, capacity and use at different levels of organization (e.g. local, regional and national) following ecological approaches [59,60]. While the WHO atlases only provide indicative information, the national and regional atlases gather bottom-up information and provide actual observational evidence usable for policy planning. As in other cases described earlier, two different categories of health atlases could be identified: framing atlases based mainly on expert knowledge and atlases based on local evidence.

Framing studies of 'cost-of-illness' (Col) and 'burden-of-illness' (Bol)

In spite of their huge impact on policy and research, very little effort has been expanded to adequately classify CoI and BoI studies [61]. As a consequence, studies that would better fit into the category of FSK are mixed up with others that, although following hybrid or mixed approaches, would better fit within the framework of scientific evidence.

The lack of a typology that could be applied to differentiate the studies of elicited knowledge (FSK) from ecological evidencebased studies has a huge impact on current scientific knowledge. On the one hand, the whole area of CoI and BoI is discredited as lacking sufficient scientific grounding [62], on the other framing of CoI and BoI have been massively quoted and broadly used as 'hard evidence' for guiding resource allocation and for priority setting.

Our own experience in both types of research clearly differentiates between knowledge on the CoI obtained from framing studies where the main source of information is elicited expert knowledge based on literature reviews [63,64], and actual CoI studies based on a cross-design synthesis of multiple sources of information, secondary analysis of all available data bases, surveys and epidemiological studies where prior expert knowledge provides an essential, but complementary role [23,65]. The same happens to BoI studies, where at present, framing studies [66] coexist at the same level of 'evidence' as ecological and population-based studies [67] because of the lack of an adequate taxonomy of these two types of research.

The case of the 'Global Burden of Disease' (GBD) study series deserves particular attention. Since its first publication in 1996 to

its last edition [68], the GBD series have had a major impact on global health policy and the papers produced by the GBD group have been published in top-ranking journals, even though GBD may not fit the requirements that editors and reviewers of these journals may request from other expert-driven studies regarded as qualitative designs. This has caused an international debate on the methods and the actual scientific value of the GBD [69]). As an example, GBD experts opted for including as 'disability' any significant impairment either short or long term, regardless of the fact that other formal definitions have been produced by WHO that include levels of severity and allow for a better categorization [70]. As a result, the relative impact of long-term severe impairment (e.g. intellectual disability) is decreased in relation to other conditions with lower impairment, but high prevalence (e.g. depression), in spite of its lifelong consequences and high direct and indirect costs [71]. The intensity of this debate would probably slow down if GBD and other related studies could be classified as FSK. In that case the 'Burden of Diseases Study' could be regarded as relevant knowledge to approach a highly complex issue in public health and policy, but never as actual evidence to guide local resource allocation.

The list of scientific framing studies can be expanded further. For example clinical-guided reviews (rapid synthesis, critical reviews), indicator sets and cards, and any collaborative textbook where a formal iterative review and discussion process is followed could all be included in this new category.

Conclusions

This paper delineates a framework, typology and case examples of a new class of scientific studies: FSKs, which play an increasing role in the analysis of complexity in health care and policy. This grouping of studies can be defined, classified and differentiated from non-scientific frames related to science, as they use expert knowledge and qualitative approaches in their development. Its categorization may allow for a better distinction between evidence-based studies and studies mainly based in elicited expert knowledge in areas such as health economics and health geography. In addition, they provide a better research framework for declarations, clinical practice recommendations, health classifications and other scientific documents, where the methods used are not formally described in the majority of cases. The development of this typology will allow for a differentiation of FSK from non-scientific frames related to science, as FSK use expert knowledge and qualitative approaches in the development of declarations, classifications and health charts, among others.

The development of a new category of studies specifically aimed at framing scientific knowledge should be part of a broader and pressing endeavour: the need for a new taxonomy of scientific knowledge that better fits the complexities in health care practice and policy. The typology of FSK cannot be understood without this broader context. At the bulk of this new approach is the fact that scientific knowledge is a type of knowledge that is generated by standardized methods characterized by the principles of commensurability, transparency for corroboration (including falsifiability) and generalizability. These characteristics distinguish scientific knowledge from other types of knowledge enquiries. Other approaches to standardized and systematic research, such as in the business and military sectors, do not submit themselves to transparency for corroboration and do not follow the assumption of intersubjectivity. In these two cases, the 'truth' is tested not by peer-reviews and corroboration, but through competition. On the contrary, scientific research is characterized by transparency as the ultimate goal of the 'competing' groups is to share their 'derived form of knowledge' for rejection or corroboration.

Within the agreed paradigm, at every given stage, scientific knowledge can be as far from truth as lay opinion. However scientific knowledge differs from other approaches in its capacity to refute itself over time and to advance in the progressive understanding and better representation of reality. The final pursuit of the scientific knowledge is not truth in itself as Popper stated, but to rise above falsehood. An equivalence could be drawn between the concept of comparative and progressive global justice formulated by Amartya Sen [72], and the progression of scientific knowledge as it has been formulated here. Both are engaged in 'the task of advancing rather than perfecting', and both can be differentiated from the search of the ideal, either being 'perfect justice' or 'absolute truth'.

Acknowledgements

This review paper is the result of the discussions made by the multidisciplinary expert group Dialogues on Complexity and Health Systems, to advance the understanding of complexity issues in health care research and policy held at the Menzies Centre for Health Policy and the Mental Health Policy Unit, Brain and Mind Research Institute, University of Sydney. Other participants at some of the sessions of the group were Abdolvahab Baghbanian, Di O'Halloran and Andrew Wilson. We also thank the students of the Unit of Study HSBH3005 'Evidence-based Healthcare', Faculty of Health Sciences, University of Sydney, 2013, for their critical contribution to this debate.

References

- Savigny, D. & Adam, T. (2009) Systems Thinking for Health Systems Strengthening. Geneva: World Health Organization.
- Sturmberg, J. P., O'Halloran, D. M. & Martin, C. M. (2012) Understanding health system reform – a complex adaptive systems perspective. *Journal of Evaluation in Clinical Practice*, 18, 202–208.
- Salvador-Carulla, L., Garcia-Alonso, C., Gibert, K. & Vazquez-Bourgon, J. (2013) Incorporating local information and prior expert knowledge to evidence-informed mental health system research. In Improving Mental Health Care: The Global Challenge (eds G. Thornicroft & D. Goldberg), pp. 209–228. Chichester: John Willey & Sons.
- Oxford Centre for Evidence-Based Medicine (2009) Levels of Evidence. Available at: http://www.cebm.net/?o=1025 (last accessed 27 June 2014).
- Bate, P., Fulop, N., Øvretveit, J. & Dixon-Woods, M. (2014) Perspectives on Context. London: Health Foundation.
- Lewin, S., Oxman, A. D., Lavis, J. N., Fretheim, A., Garcia Marti, S. & Munabi-Babigumira, S. (2009) SUPPORT tools for evidenceinformed policymaking in health 11: finding and using evidence about local conditions. *Health Research Policy and System*, 7 (1), S11. doi: 10.1186/1478-4505-7-S1-S11.

- Gibert, K., Garcia-Alonso, C. & Salvador-Carulla, L. (2010) Integrating clinicians, knowledge and data: expert-based cooperative analysis in healthcare decision support. *Health Research Policy and System*, 8, 28. doi: 10.1186/1478-4505-8-28.
- Gibert, K., Valls, A. & Batet, M. (2013) Introducing semantic variables in mixed distance measures: impact on hierarchical clustering. *Knowledge and Information Systems*, 40, 559–593.
- Wilson, K. M., Brady, T. J., Lesesne, C. & NCCDPHP Work Group on Translation (2011) An organizing framework for translation in public health: the Knowledge to Action Framework. *Preventing Chronic Diseases*. Available at: http://www.cdc.gov/pcd/issues/2011/mar/ 10_0012.htm (last accessed 21 October 2014).
- Rabin, B. A., Purcell, P., Naveed, S., Moser, R. P., Henton, M. D., Proctor, E. K., Brownson, R. C. & Glasgow, R. E. (2012) Advancing the application, quality and harmonization of implementation science measures. *Implementation Science*, 7, 119. doi: 10.1186/1748-5908-7-119.
- 11. Schurz, G. (2014) Philosophy of Science: A Unified Approach. New York: Routledge.
- Desmond-Hellmann, S. (2012) Toward precision medicine: a new social contract? *Science Translational Medicine*, 4, 129ed123.
- Crowe, M. & Sheppard, L. (2010) Invited editorial: qualitative and quantitative research designs are more similar than different. *The Internet Journal of Allied Health Sciences and Practice*. Available at: http://ijahsp.nova.edu/articles/Vol8Num4/crowe_8_4_.htm (last accessed 21 October 2014).
- Popper, K. (2012) Principles of scientific method. New Zealand Science Review, 29, 16–25.
- 15. Davenport, T. H. & Prusak, L. (2000) Working Knowledge. Boston: Harward Business School Press.
- Watson, H. (2009) Tutorial: business intelligence past, present, and future. *Communications of the Association for Information Systems*. Available at: http://aisel.aisnet.org/cais/vol25/iss1/39/ (last accessed 21 October 2014).
- Wilson, E. O. (2001) How to unify knowledge keynote address. Unity of Knowledge: The Convergence of Natural and Human Science, 935, 12–17.
- Rand, K. L. & Ilardi, S. S. (2005) Toward a consilient science of psychology. *Journal of Clinical Psychology*, 61, 7–20.
- Snyder, L. J. (2006) Reforming Philosophy: A Victorian Debate on Science and Society. Chicago and London: University of Chicago Press.
- Wilson, E. O. (1998) Consilience among the great branches of learning. *Daedalus*, 127, 131–149.
- Emery, R. (2003) Could a 'philosophical fitness landscape' foster Wilsonian consilience in biosystems debates? *Bio Systems*, 72, 217–227.
- Haig, B. D. (2009) Inference to the best explanation: a neglected approach to theory appraisal in psychology. *American Journal of Psychology*, 122, 219–234.
- Bendeck, M., Serrano-Blanco, A., Garcia-Alonso, C., Bonet, P., Jorda, E., Sabes-Figuera, R., Salvador-Carulla, L. & COSTDEP Group (2013) An integrative cross-design synthesis approach to estimate the cost of illness: an applied case to the cost of depression in Catalonia. *Journal of Mental Health*, 22, 135–154.
- Bellon, J. A., Conejo-Ceron, S., Moreno-Peral, P., *et al.* (2013) Preventing the onset of major depression based on the level and profile of risk of primary care attendees: protocol of a cluster randomised trial (the predictD-CCRT study). *BMC Psychiatry*, 13, 171.
- Thigpen, S., Puddy, R. W., Singer, H. H. & Hall, D. M. (2012) Moving knowledge into action: developing the rapid synthesis and translation process within the interactive systems framework. *American Journal* of Community Psychology, 50, 285–294.
- Pennock, R. T. (2011) Can't philosophers tell the difference between science and religion?: demarcation revisited. *Synthese*, 178, 177–206.

- Goffman, E. (1974) Frame Analysis: An Essay on the Organization of Experience. Cambridge, MA: Harvard University Press.
- Chong, D. & Druckman, J. N. (2007) Framing theory. Annual Review of Political Science, 10, 103–126.
- McAdams, D. P., Albaugh, M., Farber, E., Daniels, J., Logan, R. L. & Olson, B. (2008) Family metaphors and moral intuitions: how conservatives and liberals narrate their lives. *Journal of Personality and Social Psychology*, 95, 978–990.
- Festinger, L. (1962) Cognitive dissonance. *Scientific American*, 207, 93–104.
- Kellogg, S. H. & Young, J. E. (2006) Schema therapy for borderline personality disorder. *Journal of Clinical Psychology*, 62, 445–458.
- Tversky, A. & Kahneman, D. (1981) The framing of decisions and the psychology of choice. *Science*, 211, 453–458.
- Lakoff, G. (2012) Explaining embodied cognition results. *Topics in Cognitive Science*, 4, 773–785.
- Gong, J., Zhang, Y., Yang, Z., Huang, Y., Feng, J. & Zhang, W. (2013) The framing effect in medical decision-making: a review of the literature. *Psychology Health Medicine*, 18, 645–653.
- Ericsson, K. A., Krampe, R., Tesch-Romer, C. (1993) The role of deliberate practice in the acquisition and maintenance of expert performance. *Psyhcological Review*, 100, 363–406.
- Vallotton, M. B. (2010) Council for international organizations of medical sciences perspectives: protecting persons through international ethics guidelines. *International Journal of Integrated Care*, 10, e008.
- World Health Organisation (WHO) (1997) Jakarta Declaration on Leading Health Promotion into the 21st Century. Jakarta: World Health Organisation.
- World Medical Association (WHO) (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA: The Journal of the American Medical Association*, 310, 2191–2194.
- Salvador-Carulla, L., Balot, J., Weber, G., *et al.* (2009) The Barcelona declaration on bridging knowledge in long-term care and support. Barcelona (Spain), March 7, 2009. *International Journal of Integrated Care*, 9, e179.
- Bickenbach, J., Bigby, C., Salvador-Carulla, L., Heller, T., Leonardi, M., Leroy, B., Mendez, J., Putnam, M. & Spindel, A. (2012) The Toronto declaration on bridging knowledge, policy and practice in aging and disability: Toronto, Canada, March 30, 2012. *International Journal of Integrated Care*, 12, e205.
- Salvador-Carulla, L., Putnam, M., Bigby, C. & Heller, T. (2012) Advancing a research agenda for bridging ageing and disability. *International Journal of Integrated Care*, 12, e204.
- International Diabetes Federation (IDF) (2011) IDF's Daibetes Roadmap for the UN High-Level Summit on NCDs. Brussels: International Diabetes Federation.
- Naidoo, V., Putnam, M. & Spindel, A. (2012) Key focal areas for bridging the fields of aging and disability: findings from the growing older with a disability conference. *International Journal of Integrated Care*, 12, e201.
- Spindel, A., Campbell, M. & Mendez, J. (2012) Bringing stakeholders together across ageing and disability: GOWD conference series. *International Journal of Integrated Care*, 12, e202.
- Leonardi, M., Bickenbach, J. & LeRoy, B. (2012) International initiatives on bridging knowledge, policy and practice. *International Journal of Integrated Care*, 12, e203.
- 46. Deb, S., Kwok, H., Bertelli, M., Salvador-Carulla, L., Bradley, E., Torr, J., Barnhill, J. & Guideline Development Group of the, W. P. A. Section on Psychiatry of Intellectual Disability (2009) International guide to prescribing psychotropic medication for the management of problem behaviours in adults with intellectual disabilities. *World Psychiatry*, 8, 181–186.

- 47. Salvador-Carulla, L., Reed, G. M., Vaez-Azizi, L. M., et al. (2011) Intellectual developmental disorders: towards a new name, definition and framework for 'mental retardation/intellectual disability' in ICD-11. World Psychiatry, 10, 175–180.
- Makarski, J. & Brouwers, M. C. (2014) The AGREE enterprise: a decade of advancing clinical practice guidelines. *Implementation Science*, 9, 103. doi: 10.1186/s13012-014-0103-2.
- McAlister, F. A., van Diepen, S., Padwal, R. S., Johnson, J. A. & Majumdar, S. R. (2007) How evidence-based are the recommendations in evidence-based guidelines? *PLoS Medicine*, 4, 1325–1332.
- Lenzer, J., Hoffman, J. R., Furberg, C. D., Ioannidis, J. P. & Guideline Panel Review Working Group (2013) Ensuring the integrity of clinical practice guidelines: a tool for protecting patients. *British Medical Journal*, 347, f5535.
- Colagiuri, R. (2009) Implementing evidence based guidelines: unlocking the secrets. *Diabetes Research and Clinical Practice*, 85, 117– 118.
- Gonzalez-Block, M. A., Rouvier, M., Becerril, V. & Sesia, P. (2011) Mapping of health system functions to strengthen priority programs. The case of maternal health in Mexico. *BMC Public Health*, 11, 164.
- Schalock, R. L. & Luckasson, R. (2013) What's at stake in the lives of people with intellectual disability? Part I: the power of naming, defining, diagnosing, classifying, and planning supports. *Intellectual and Developmental Disabilities*, 51, 86–93.
- Salvador-Carulla, L. & Bertelli, M. (2008) 'Mental retardation' or 'intellectual disability': time for a conceptual change. *Psychopathol*ogy, 41, 10–16.
- Madden, R., Ferreira, M., Einfeld, S., Emerson, E., Manga, R., Refshauge, K. & Llewellyn, G. (2012) New directions in health care and disability: the need for a shared understanding of human functioning. *Australian and New Zealand Journal of Public Health*, 36, 458– 461.
- 56. Moller, H. J., Bandelow, B., Bauer, M., et al. (2014) DSM-5 reviewed from different angles: goal attainment, rationality, use of evidence, consequences-part 1: general aspects and paradigmatic discussion of depressive disorders. *European Archives of Psychiatry and Clinical Neuroscience* doi: 10.1007/s00406-014-0520-x.
- World Health Organization (WHO) (2007) Atlas: Global Resources for Persons with Intellectual Disabilities 2007. Geneva: World Health Organization.
- World Health Organization (WHO) (2011) WHO Mental Health Atlas 2011. Geneva: World Health Organization.
- 59. Fernandez, A., Salinas-Perez, J. A., Gutierrez-Colosia, M. R., Prat-Pubill, B., Serrano-Blanco, A., Molina, C., Jorda, E., Garcia-Alonso, C. & Salvador-Carulla, L., on behalf of the GEOSCAT-SM group (2014) Use of an integrated atlas of mental health care for evidence informed policy in Catalonia (Spain). *Epidemiology and Psychiatric Sciences* doi: 10.1017/S2045796014000511.
- 60. Salvador-Carulla, L., Martinez-Leal, R., Poole, M., Salinas-Perez, J. A., Tamarit, J., Garcia-Ibanez, J., Almenara-Barrios, J. & Alvarez-Galvez, J. (2013) Perspectives: the mental health care gap in intellectual disabilities in Spain: impact analysis and knowledge-to-action plan. *Journal of Mental Health Policy and Economics*, 16, 131–141.
- 61. Salvador-Carulla, L. & Hernandez-Pena, P. (2011) Economic context analysis in mental health care. Usability of health financing and cost of

illness studies for international comparisons. *Epidemiology and Psychiatric Sciences*, 20, 19–27.

- 62. World Health Organization (WHO) (2009) WHO Guide to Identifying the Economic Consequences of Disease and Injury. Geneva: Department of Health Systems Financing, World Health Organization.
- Gustavsson, A., Svensson, M., Jacobi, F., et al. (2011) Cost of disorders of the brain in Europe 2010. European Neuropsychopharmacology, 21, 718–779.
- Pares-Badell, O., Barbaglia, G., Jerinic, P., Gustavsson, A., Salvador-Carulla, L. & Alonso, J. (2014) Cost of disorders of the brain in Spain. *PLoS ONE*, 9, e105471.
- Salvador-Carulla, L., Bendeck, M., Fernandez, A., Alberti, C., Sabes-Figuera, R., Molina, C. & Knapp, M. (2011) Costs of depression in Catalonia (Spain). *Journal of Affective Disorders*, 32, 130– 138.
- Wittchen, H. U., Jacobi, F., Rehm, J., *et al.* (2011) The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European Neuropsychopharmacology*, 21, 655–679.
- Sabes-Figuera, R., Knapp, M., Bendeck, M., Mompart-Penina, A. & Salvador-Carulla, L. (2012) The local burden of emotional disorders. An analysis based on a large health survey in Catalonia (Spain). *Gaceta Sanitaria*, 26, 24–29.
- Murray, C. J., Ezzati, M., Flaxman, A. D., *et al.* (2012) GBD 2010: a multi-investigator collaboration for global comparative descriptive epidemiology. *Lancet*, 380, 2055–2058.
- Nord, E. (2013) Disability weights in the Global Burden of Disease 2010: unclear meaning and overstatement of international agreement. *Health Policy*, 111, 99–104.
- World Health Organization (WHO) (2001) International Classification of Functioning, Disability and Health (ICF). Geneva: World Health Organization.
- Doran, C. M., Einfeld, S. L., Madden, R. H., Otim, M., Horstead, S. K., Ellis, L. A. & Emerson, E. (2012) How much does intellectual disability really cost? First estimates for Australia. *Journal of Intellectual & Developmental Disability*, 37, 42–49.
- 72. Sen, A. (2010) The Idea of Justice. London: Penguin Books.
- 73. Nathan, D., Buse, J. B., Davidson, M. B., Ferrannini, E., Holman, R. R., Sherwin, R. & Zinman, B. (2009) Medical management of hyper-glycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy A consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia*, 52, 17–30.
- Pratley, R. E., Jauffret-Kamel, S., Galbreath, E. & Holmes, D. (2006) Twelve-week monotherapy with the DPP-4 inhibitor vildagliptin improves glycemic control in subjects with type 2 diabetes. *Hormone* and Metabolic Research, 38, 423–428.
- Monami, M., Dicembrini, I., Martelli, D. & Mannucci, E. (2011) Safety of dipeptidyl peptidase-4 inhibitors: a meta-analysis of randomized clinical trials. *Current Medical Research and Opinion*, 27, 57–64.
- Ahren, B., Mathieu, C., Bader, G., Schweizer, A. & Foley, J. E. (2014) Efficacy of vildagliptin versus sulfonylureas as add-on therapy to metformin: comparison of results from randomised controlled and observational studies. *Diabetologia*, 57, 1304–1307.