Working towards legitimacy in decision-making

On governing appropriate medicine use and reimbursement in health care

Maartje G.H. Niezen

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Colophon

Research conducted between September 2003 and October 2004 was funded by the Dutch Health Care Insurance Board (CVZ).

Research conducted between September 2005 and October 2007 was funded by the Netherlands Organisation for Scientific Research (NWO) under the Ethics, Research and Government programme (project 253-20-022).

Research conducted between July 2007 and October 2009 was funded by the Netherlands Organisation for Scientific Research (NWO) under the Network for Networks program (project 458-06-021).

Printing of this thesis was subsidized by the Department of Healthcare Policy and Management (iBMG) of the Erasmus University Rotterdam.

Printing and cover design by Ridderprint BV, Ridderkerk, the Netherlands
ISBN: 978-90-5335-551-0

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Werken naar legitimiteit van besluitvorming

Over het sturen van gepast gebruik en vergoeden van geneesmiddelen in de gezondheidszorg

Proefschrift

ter verkrijging van de graad van doctor aan de Erasmus Universiteit Rotterdam
op gezag van de rector magnificus Prof. dr. H.G. Schmidt
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
dinsdag 26 juni 2012 om 11.30 uur

door

Martina Geertruida Hester Niezen - van der Zwet

geboren te Leiden

Promotiecommissie

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Introduction

In the last three decades governmental policy in prioritization of medicines is increasingly legitimized through the scientization of the decision-making process on the one hand and a separation in policy production and policy execution on the other. The discourse on health care reimbursement decisions has likewise been dominated by increased rationalization and formalization of the decision-making process. Since the early 1990s the Dutch government and arm's length agencies have undertaken much effort to regulate pharmaceutical care, mainly by emphasizing the role evidence should have in decision-making on the appropriate use of medicines at all levels, from decisions on insurance schemes coverage to prescriptions at the point of care (Commissie Dunning 1991; Gezondheidsraad 1991; College voor zorgverzekeringen 2007). The Dutch government has developed a series of tools to promote rational prescribing – such as professional guidelines authorized by state agencies, real-time monitoring systems and the conditional reimbursement of medicines – aimed at improving the quality and efficiency of care, and enabling the control of pharmaceutical health care expenditure (College voor zorgverzekeringen 2005; Niezen et al. 2007).

Despite the rationalisation of decision-making, governmental policymakers still experience difficulties in explaining the foundations for their decisions. Moreover, the execution of the health regulations in daily practice appears to deviate substantially from the intended policy and its underlying principles (Niezen et al. 2007). The Dutch drug reimbursement system is based on a bureaucratic system logic; if rational decision criteria are used, consistent and legitimate decision-making has taken place. The definition of formulary lists (medicines eligible for funding) presumes that appropriate medicine use and reimbursement not only can be defined, but subsequently can be implemented in health care provision. Thus, when health care providers prescribe medicines according to the national formulary, appropriate drug use is warranted. However, there is a discrepancy between the decision-making process outcomes and actual practice of medicine prescription and reimbursement. This discrepancy points at potential legitimacy problems which require further research. What work practices can be observed that are supposed to lead to (more) legitimate decision-making? And, if legitimate decision-making can be observed, how does that wear off in clinical practice? Increasing the legitimacy of prioritization decisions might decrease the difference between policy and practice. Making use of a social scientific perspective this thesis analyses the (development of the) infrastructure of the Dutch drug reimbursement decision-making process and health care allocation instruments in order to gain insight in the practice of health care prioritization decision-making and the way this is legitimized.

Accounting for priority setting in health care

Since the late 1970s the governance of scarce resources in health care and in particular the regulation of medicine use and reimbursement has dominated many policy agenda's. Health care policymakers have been searching for ways to remain in control over health care expenditures to assure health systems' sustainability. Simultaneously policymakers have been searching for ways to guarantee the access to and quality of health systems (Gezondheidsraad 1991; Raad voor de Volksgezondheid en Zorg 2007a; Raad voor de Volksgezondheid en Zorg 2007b). Most western governments are responsible for assuring the provision of accountable and accurate health care (services) to their citizens; the 'right to health'. At the same time governmental decision-makers in the health care sector are confronted with the explosive growth of health care interventions, an ageing population combined with the increased public interest in health and well-being that comes with a strong economy. This creates a desire for more health care interventions than society may be prepared to pay for or is able to afford (Raad voor de Volksgezondheid en Zorg 2006). Subsequently, the policy agenda of health care is dominated by the question how one can meet this growing demand for health care with restricted means (Ministerie van Volksgezondheid Welzijn en Sport 1983).

The primary response of governmental regulators to deal with scarcity of health resources is resource allocation and prioritization. With resource allocation, governments try to ensure that resources available to health care are put to optimal use. The priorities for the allocation of scarce resources are set via principles, values and/or defining practices (Sabik & Lie 2008). However, while the need for rationing in health care systems is widely acknowledged, the way the priority setting process is managed is still much debated. The principles used in deciding on the prioritization and/or rationing of health care services may vary: "treating people equally, favouring the worst-off, maximising total benefits, and promoting and rewarding social usefulness" (Persad, Wertheimer & Emanuel 2009, p.423). Moreover, the (combination of) mechanisms and principles used also depend on the health systems in place (social health insurance, tax based health systems, voluntary or private health insurance) in the different countries. Despite the existence of these decision criteria and/or frameworks, shaping an accountable decision-making process remains problematic. The reimbursement choices made based on the current decision framework including prioritization criteria such as effectiveness, efficiency and necessity regularly cause controversies and sometimes even are judged as unfair by different stakeholders (Kirejczyk et al. 2003). Some examples are the (non) reimbursement of Viagra, IVF treatments or

the post-code prescribing of Herceptin (Stolk, Brouwer & Busschbach 2002; Borstkankervereniging Nederland 2005).

In Dutch benefit package management the use of scientific knowledge in the decision-making process and a rational decision framework have been considered important to account for appropriate reimbursement regulations. Especially in the field of pharmaceutical care rationalizing and formalizing decision-making has increased, likely because the pharmaceutical care sector is clearly delineated so that implementation of new steering mechanisms is relatively easy (Ngo et al. 2007). Decisions on pharmaceuticals should be rational, and based on scientific findings generated by 'neutral' specialists and research. Policymakers feel that adhering to the rules of science is a token of trustworthiness whereas basing decisions on consensus or individual judgment increases their arbitrariness (Dehue 2000; Dehue 2005). Increasingly, the process of decision-making is made transparent in order to make legitimate decisions. The quest for rationalized rationing thus has led to objectivity and transparency in decision-making procedures as its central values. The explication of the decision framework and the information used in the decision-making process is expected to provide legitimacy for the drug reimbursement decisions and related regulations. Subsequently, the regulations and policy tools are expected to be followed in clinical practice. Regulatory instruments such as guidelines and medical databases are supposed to stimulate and control established appropriate medicine use in medical practice. Governmental regulation of medicines in this way includes the task of overseeing medical practice.

Health technology assessment in current decision-making infrastructure

The current infrastructure of Dutch benefit package management bases its legitimacy on both scientific evidence (evidence based medicine) and transparency of the decision-making process (laid down in procedures and laws). Especially health technology assessment (HTA) has gained importance in the decision-making process for benefit package management. HTA can be defined as "a multidisciplinary field of policy analysis. It studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology" (International Network of Agencies for Health Technology Assessment (INAHTA) http://www.inahta.org/HTA./). Its use is widely accepted and stimulated within health care allocation decision-making (Banta and Jonsson 2009; Banta and Oortwijn 2000; Banta and Perry 1997). In a full HTA, health, (health) economic, social, legal, and ethical concerns are taken into account. However, when applied for resource allocation decision-making such as listing a drug on a national

formulary, the smaller definition of HTA, economic evaluation or cost-effectiveness analysis, is often used (Giacomini 1999; Lehoux & Blume 2000; Lehoux & Tailliez 2004; Lehoux 2006). In fact, HTA in the form of economic evaluations has become the golden standard within the medicine allocation decision-making, since it is seen as a bridge between the domains of science and (health care) policy. It provides scientific evidence, and therefore robust, rational and objective evidence into the decision-making process.

The use of HTA has not prevented criticisms on the current priority-setting infrastructure. Some known problems are related to the limits of health economics in the valuation of a health intervention: the uncertainty of information underlying economic calculation and the incompleteness of the economic model. Other problems relate to health economics as main source informing benefit package management, such as: lack of reflexivity and integration of other social, ethical, political aspects informing the worth of a health technology for society. Lastly, known problems concern the dissemination of benefit package management outcomes in medical practice.

The first criticism targets the assumption of unproblematic economic modelling in benefit package management and focuses on the uncertainty of information and lack of deliberate reflexivity in current evaluation of medicines. Ashmore, Mulkay and Pinch (1989) analysed the introduction of the Quality Adjusted Life Year (QALY) and argued that the economization of health care enabled health care to be thought of and talked about in economic terms and to become part of the economic debate in general as well as gain grounds for health economics as a separate scientific discipline. “The apparent promise of health economics, that a rational grasp of, and thereby “control” over, health-care decision-making is possible, is hard to resist” (Berg, Van der Grinten & Klazinga 2004, p.36). Yet, the calculations of QALYs and in specific the valuation of health conditions after intervention is not as simple and unproblematic as promised. Moreover, the economization of health care evaluation inhibits the development of sustainable reflexive practice in the form of e.g. dialogue (deliberate reflexivity) (Ashmore, Mulkay & Pinch 1989). Nevertheless, health economic modelling has become the universal standard of rationality in health decision-making and therefore also stands for accountability of priority setting decisions.

A second problem relates to the lack of integration of social, political, and ethical aspects of health technology into HTA. Lehoux and Blume (2000) explored the evaluation of the Cochleair implant – an electrode implanted surgically into the inner ear and designed to take over the task of a non-functioning cochlea – in order to gain insight in technological change and health technology assessment

practices. When the implementation practice was deemed appropriate and expanded to paediatric implementation based on health economic evaluation, protests arose mainly from the deaf community. Blume argues these continuous disputes could have been prevented if a socio-political perspective would have been included in the assessment of the cochlear implant (Blume 1997). However, in practice only little assessments embodied and took the concerns by the deaf community serious since these do not fit current assessment processes and arrangements. The neglect of the (socio-political) stakes in the controversy led to a situation in which traditional HTA proved insufficient to warrant the legitimacy of decisions on the value of a medical technology (Lehoux & Blume 2000).

Another acknowledged problem is the dissemination of HTA in clinical practice. Lehoux (2006) argues that current benefit package management infrastructure does not address how to promote the design of innovations that are likely to be more valuable than others. Whether the products of HTA, the recommendations of appropriate drug reimbursement and use, are disseminated depends on the network of providers, consumers, manufacturers and the habits, routines, established practices, expertise, rules and laws that regulate the relations and interactions (Lehoux 2006; Edquist & Johnson 1997). Yet, HTA as a means of implementing knowledge-based change within health care systems falls short. The linear, rationalistic process underlying the benefit package management fails to sufficiently take into account its environment; seeking dialogue with or consultation of the network, integrate related routines and regulation. It is exactly the understanding of the infrastructure of decision-making, its environment and regulatory mechanisms that may facilitate or impede the implementation of recommendations.

The Dutch government has struggled to cope with these problems of the drug reimbursement system. In the last decades the Dutch government has introduced and further defined decision criteria of the decision framework and improved the decision-making process, for example by introducing the requirement of pharmacoeconomic reports on a health technology (Commissie Dunning 1991). One of the main problems has been that despite the increasing number of economic evaluations of health technologies, their impact on policy decisions has been limited (Battista et al. 1994; Battista et al. 1999; Cookson & Maynard 2000; Stolk et al. 2005). The case of the reimbursement of sildenafil (Viagra®) is exemplary and depicts a discrepancy between the economic evaluation (a favourable cost-effectiveness outcome) and the actual resource allocation decision (exclusion from basic benefit package) (Stolk et al. 2005). Stolk et al. (2005) assume the discrepancy between evaluation and decision can be ascribed to insufficiently taking into account fairness concerns in economic modelling.

Subsequently, they argue, optimalization of priority setting requires balancing health economics (efficiency) and ethics (equity). Currently an equity adjustment procedure in economic evaluations is introduced in Dutch decision-making on the value of health technology. This equity adjustment ensures that "in priority decisions neither equity nor efficiency concerns are put aside but instead are treated in a systematic way" (Stolk 2005, p146). Another example of a solution to the problems of benefit package management has been the transformation of the Dutch health system into a regulated market allowing for the responsibility of stimulating appropriate medicine use and reimbursement to be partly transferred to Dutch health insurers. Conditional reimbursement of medicines is also one of the new ways in which the Dutch government tries to cope with the growing challenges. The conditional reimbursement of high cost medicines requires hospitals to develop databases on high cost medicines as a prerequisite for application for additional funding. Again, responsibility is shifted from government to other stakeholders. Despite these efforts to introduce new criteria to close the decision framework or optimize priority-setting regulations, the discrepancy between policy and practice remains.

Above mentioned problems and consequences of the benefit package infrastructure might even lead to doubting decisions and recommendations made, instead of accounting for its scientific rigor and legitimacy. The idea of listing medicines on a positive or negative reimbursement list depicts an 'in-or-out' bureaucratic system logic focussing on the outcomes of scientific research and the decision-making process. Moreover, accounting in the Netherlands is framed in terms of evidence based medicine and ethics (procedures and laws), and suggest particular activities to professionals in order to legitimize their activities (Pols 2004). Although such bureaucratic system logic allows for rationality in a complex situation and the promise of oversight, it is also based on uncertainty and ambiguity of underlying principles. Moreover, little attention has been paid to the management of diverging views about (the value of) health technology (Lehoux et al. 2005). For example, an institutional barrier may be that the health economists' perspective on rationalizing the use of (scarce) collective resources is often in contradiction with a clinical perspective giving priority to a patient's well-being. Subsequently, the regulation of appropriate medicine reimbursement and use based on HTA reports is scrutinized since the regulation does not fit (medical) practice.

Notion of infrastructures

Using the notion of infrastructure allows for gaining insight in the practice of health technology evaluation and its problems. The notion of infrastructure is commonly used in Science and Technology Studies (STS) exploring Large Technical Systems

in relation to design and use of computing and information technologies (Bowker 2005; Hine 1995; Hine 2006; Star 1995; Star & Ruhleder 1996). It reflects the structure upon which something else, in this case priority setting based on valorisation of health technology, rides or works taking into account its users, environment, dependencies, required skills, regulations etc. (Star & Bowker 2006). Star and Ruhleder (1996) have defined salient features of infrastructure in order to clarify the concept, amongst which: an infrastructure both shapes and is shaped by the conventions of practice, it is build on an installed base, an existing structure, and subsequently struggles with the inherent strengths and weaknesses of this base. And one of the most important features of infrastructure is that it only becomes visible upon breakdown.

The notion of infrastructure is used to understand the merits and failures of the benefit package management system in producing legitimacy for its decisions and recommendations. It is the infrastructural work in defining and maintaining units to measure, putting into place a set of agreements embodied in practices (e.g. coding the relationship between policy and professionals), which allows for priority setting and defining appropriate reimbursement and use of medicines. Thus, the benefit package management infrastructure embodies the processes of discussion, negotiation, and compilation that have gone into its creation; it involves technical decisions as well as political and ethical decisions (Bowker 1994; Hine 1995). The decision framework (decision criteria) as well as the consequences of these decisions can become irreversible, invisibly locked in the seemingly value neutral infrastructure. In this respect, an infrastructure can be jussive; it tells us what can be remembered and what not, what can be controlled and what not, what we can say and what not (Bowker 2005). Exploring the work practices in Dutch benefit package management allows for deconstructing the design of its infrastructure. The work practices embody the shaping character of the benefit package management system in for example the relation between policy and practice, the struggles with its own structure and potential ethical and political concerns regarding its legitimacy.

In line with a STS perspective the exploration of three case studies, resembling different solutions sought by Dutch government to deal with the problem of health technology evaluation, is not focussed on advocating or condemning accounting practices. Yet, the exploration focuses on studying the accounting systems as they function in practice (Berg 1997). Therefore it is not legitimate decision-making I am interested in, yet the work needed to legitimize decisions. The legitimacy of decisions is on the one hand procedural (consistent use of decision criteria, transparency in the decision-making process, etc.) and on the other hand social (what values or principles underlie the decision framework, what stakeholders

involved, what knowledge used, etc). Subsequently, the production of legitimacy is a dynamic process. The work of Boltanski and Thévenot (2006) provides insight in this dynamic process and the different ways actors legitimate their action of decision-making. Boltanski and Thévenot (2006) define a framework of different repertoires of justification that allows one to study how people justify their actions. In *Which road to follow? The Moral Complexity of an "Equipped" Humanity* Thevenot (2002) shows that the attribution of a worth and order with which values are attributed shapes (the outcome(s) of) decision-making processes and work practices. Moreover, the authors claim there are different orders of worth, which means there are different gradients of right and wrong that establish different versions of how the public good (such as health care) should be evaluated (Thevenot 2002; Boltanski & Thevenot 2006). In other words, there are different repertoires which should be taken into account when trying to legitimize a reimbursement decision. Moreover, the activity of making legitimate decisions can be seen as situational in different social styles and institutions. Whether the actions of regulators are considered legitimate is enclosed in the interplay between health regulators and their environment (Thevenot 2002). In this thesis, I explore the dynamic development of these worths in Dutch decision-making on drug reimbursement.

The Dutch benefit package management system and legitimate decision-making

In order to understand current benefit package management and the way decision-making on scarce health care resources is defined, the development of the design of this infrastructure is crucial. "Throughout the 1990s, a call for evidence based medicine and rational priority setting in health care contributed to defining the aims and means of HTA" (Lehoux & Blume 2000, p1085). HTA offered legitimacy for decisions, since it introduced systematically gathered, scientific evidence on the value of a health technology in the prioritization decision-making process. This introduction of evidence based medicine and evidence based policy in The Netherlands was boosted by the report of the Committee *Choices in Care* (Commissie Keuzen in de Zorg - also known as Committee Dunning) and The Health Council report "*Medisch handelen op een tweesprong*", both published in 1991 (Commissie Dunning 1991; Gezondheidsraad 1991). The public discussion of both reports facilitated the growing awareness that resources were not endlessly available and promoted the need for evidence based choices in health care. Both reports emphasize the need for evidence based medicine, for example making use of guideline development programs of the professional associations. The Committee Dunning argued in their report it was time to make choices based on a framework of four filters: necessity, efficacy, efficiency and 'own responsibility'.

Efficacy and efficiency were to be based on HTA studies and necessity and 'own responsibility' were thought to be based on normative reasoning. Of course, these Dutch reports are not unique. They depict a wider international trend for the need of rationalized rationing in health care and are shaped by and reflect on the ongoing HTA developments (Ashmore, Mulkay & Pinch 1989).

Whereas two decades ago legitimacy of policy (-making) was derived from the rationality of the priority setting system and its evidence based character, nowadays the process itself and its transparency have become more in focus for legitimate decision-making (Holm et al. 1998). In this development, the procedures for decision-making are made more transparent and the appraisal of collected evidence is increasingly explicit. This reflects a wider tendency in Dutch health care (and, more general, public policy) settings, in which transparency has become a dominant value in and of itself. The value transparency is embedded in market based governance (Bal 2008). Subsequently, within the timeframe of the research conducted for this thesis (2003-2009) the transition from state / corporate governance to market governance is visible in the policy measures and instruments used to monitor and control health care. In the transitory process from state controlled to a more market based mechanism governing health care, regulatory processes concerning health care reimbursement have been made more scientific and formal. Consequently, since 2000 the Dutch Health Care Insurance Board (CVZ) increasingly has stressed the importance of a more precise and objective construction of the decision-making system and its framework. Choices in health care should meet the requirements of being transparent, solid and judicial sustainable, preferably without affecting innovative developments (College voor zorgverzekeringen 2007).

Research questions

This thesis offers an analysis of several solutions searched for by Dutch health policymakers in order to complete and close the decision framework in the Netherlands as well as the new approaches taken in drug reimbursement decision-making processes. Exploration of the priority setting infrastructure in the pharmaceutical care sector is particularly relevant since this sector can be regarded as the frontrunner for new and innovative steering mechanisms in governing appropriate care. In order to gain insight in the different aspects of the work needed to legitimize decisions I specifically explore the (knowledge) practices in prioritization decision-making processes. The (development of) criteria of the decision framework, databases and related social processes are part of the work practice legitimizing priority setting decisions and embedded in the infrastructure (in

development) of benefit package management. The following research questions have guided my exploration of Dutch benefit package management.

- What work is conducted to legitimize decision-making regarding appropriate drug use and reimbursement?
- How does the decision-making infrastructure, such as the conditional reimbursement regulations and databases, govern appropriate drug use and reimbursement in (clinical) practice?
- What (new) forms of social relations, objectivity and knowledge does the benefit package management infrastructure produce, and how might this lead to new governing mechanisms of appropriate drug use and reimbursement?

Research method

The research in this thesis is based on the exploration of three case studies using mainly qualitative research methods. The three case studies allowed for the exploration of Dutch drug reimbursement processes and related policy tools to steer both policy and clinical practice. We were able to examine the process of governing appropriate drug reimbursement and use by introduction of 'new' policy measures and tools rather closely. This close examination was made possible by a research project commissioned by CVZ and two independent research projects funded by NWO on the introduction of budget impact as a rationing criterion and the use of databases as steering instruments. These research projects have included both quantitative and qualitative research methods as the projects were conducted in multi-disciplinary teams. However, I have concentrated on the qualitative part of the three research projects, making use of documentary and interview evidence as well as participative observation.

The study period (2003-2009) and the use of qualitative, semi-structured interviews have allowed for an iterative research process, in which new theoretical insights developed alongside the data analysis and writing of first results of the project. In total 86 interviews were conducted with 80 respondents from various practices and expertises; health insurers, Ministry of Health, medical specialists, pharmacists, pharmaceutical manufacturers (representatives), patient organizations, health economists, general practitioners, etc. Some respondents have been interviewed several times during the research period and with regard to different case studies. The major part of the interviews I conducted alone or in cooperation with my skilled colleagues of the different project teams. Some of the interviews were held by colleagues. All interviews were transcribed and coded (see the specifics in each of the chapters). Alongside the interviews I participated in and observed conferences

and meetings in which the drug reimbursement process, decisions and policy tools were discussed. Moreover, I have analyzed relevant literature and documents on drug reimbursement processes of specific medicines or medicine groups; growth hormone, clopidogrel, cholesterol lowering therapy, TNF-α blockers, thiazolidinediones, oncolytics (in specific Ibritumomab tiuxetan and Alemtuzumab). Because of the use of these different types of empirical data I was able to triangulate my findings.

The relatively long time span in which the study was performed allowed me to observe the various ways in which governmental decision-makers have tried to obtain authority as decision-makers and underwrite and improve the legitimacy of their decisions and decision-making processes. Although the active data-collection ended in 2009, activities thereafter related to drug decision-making have informed me when writing the papers for this thesis.

Case studies

The first case study explores conditional reimbursement of outpatient medicines as a new form of benefit package management. The conditional reimbursement regulation (Schedule 2 of Health Insurance Regulation[1]) makes the reimbursement of particular medicines conditional to specific criteria or rules. For example, the use of medicines is restricted to specific categories of patients (e.g. based on indications) and/or place in treatment lines (e.g. step-up treatment). By conditionally reimbursing specified drugs, CVZ expected to stimulate the appropriate use in practice supported by evidence based policy. In this particular case study we combined quantitative and qualitative research methods to analyze how conditional reimbursement instrument aimed for steering appropriate drug use and reimbursement and in what way this shaped clinical practice. The quantitative research focused on the volumes of drug use versus the expected volumes and the annual growth since admission on the conditional reimbursement regulation and should provide for a general idea on the functioning of the measure in daily practice. The qualitative research method involved 65 interviews and document analysis to gain insight in the stakeholders' perspectives on appropriate drug use and reimbursement in relation to the functioning of the conditional reimbursement policy tool in five specific cases; TNF-α blockers, clopidogrel, thiazolidinediones, growth hormone and cholesterol lowering therapy. In the interviews as well as in two focus group sessions, stakeholders were asked to reflect upon the found quantitative data regarding appropriate medicine use. This provides insight in the findings as well as underlying mechanisms of the conditional reimbursement policy instrument. Our exploration enabled us to gain insight in the way a policy tool was

[1] The Health Insurance Regulation regulates the execution of the Dutch Health Insurance Act (ZVW).

able to steer daily (clinical) practice as well as how various stakeholders used or work around the conditional reimbursed tool steering the appropriate reimbursement and use of medicines.

The second case study depicts the conventional way in dealing with the perverse consequences of current benefit package management infrastructure. The continuous discrepancies between the HTA outcomes and the actual resource allocation decision by the Ministry of Health requires for a refinement of the decision framework. Whereas the current Dutch decision framework explicitly entails the criteria of effectiveness, cost-effectiveness, and severity of illness, the role of budget impact remains less obvious despite the official request for budget impact estimates to inform the decision-makers in the decision-making process. We explored the role of budget impact as a decision criterion through a literature review and in addition conducted eleven semi-structured interviews with stakeholders. All stakeholders have expertise in or were involved in the Dutch drug reimbursement decision-making process. In the interviews we asked if budget impact should be an implicit or explicit rationing criterion and whether rationales for budget impact as a rationing criterion were available to (not) legitimate its use in the decision-making process. The rationales found in our literature review were used as an input for the discussion on legitimating rationales in the interviews. Exploring the possible addition of a criterion to the decision-making process or framework allowed for insight in the construction of evidence used in decision-making and gaining legitimacy of the decision-making process.

The third case study explores the PHAROS registry (on expensive oncolytics such as Ibritumomab tiuxetan and Alemtuzumab) and the way the PHAROS registry infrastructure allowed for the production and construction of new forms of knowledge, objectivity and social relations. In 2006 the conditional reimbursement regulation was extended from outpatient medicines (case study 1) to inpatient medicines through the High-Cost Medicines Regulation. Importantly, the High-Cost Medicines Regulation includes the prerequisite of evidence development on the effectiveness and cost-effectiveness of listed medicines in clinical practice. The evidence development based on data collection in databases such as the PHAROS registry was intended to inform and govern decision-making on the reimbursement of inpatient medicines as well as to promote their rational prescribing. Findings of this case study have been reported in comparison with earlier findings from the first case study on conditional reimbursement in specific the growth hormone database. Subsequently, I conducted ten semi-structured interviews in addition to the interviews of the first case study regarding growth hormone and/or the use of data collection informing policy. Furthermore I participated in and observed conferences and informal meetings, and I analyzed

minutes, email exchanges and policy documents including documents from archives of the main policy actor, CVZ.

Outline of the thesis

Chapter one focuses on the debate regarding the way the Dutch priority setting process is managed by addressing the cost problem and inequalities in treatment in the inpatient pharmaceutical care sector. While the need for rationing scarce resources is widely acknowledged, the way Dutch health regulators manage the expensive inpatient medicines costs is heavily debated. Governmental steering aims to solve this problem by regulating the (additional) financing of expensive inpatient medicines and transferring responsibility of equal access to care to health insurers and hospitals. Yet (medical) practice depicts the policy regulation as inadequate and potentially leading to legitimacy problems regarding the equal distribution of care. This chapter shows that despite the efforts of health regulators, the expensive medicines regulation did not have the desired effects. Can we expect economic modelling and refining the benefit package management system to solve the problems regarding the explosive growth of medicine costs and subsequently the necessary priority setting decisions? Or, is a reflection on the value of health and health technology required as well as the use of new mechanisms to steer appropriate drug use and reimbursement?

Chapter two examines how conditional reimbursement as a policy tool was developed to optimize the benefit package decision-making framework. Whereas in chapter one regulating additional funding for expensive inpatient medicines is meant to optimize priority-setting decision-making, the conditional reimbursement of outpatient medicines similarly intends to close the benefit package system. The refinement of the regulation of appropriate medicine use and reimbursement is based on HTA and allows for rationality in decision-making as well as the promise of control. In order to deal with the high cost of pharmaceuticals and simultaneously guarantee access to pharmaceutical care, health regulators focussed on using evidence based boundaries of appropriate medicine use and reimbursement in the form of formulating conditions regarding e.g. patient groups and health providers. Yet, does the conditional reimbursement tool actually govern appropriate drug use and reimbursement in (medical) practice? I analyze from a stakeholders' perspective whether the decision-making practices are found legitimate and how conditional reimbursement as a policy tool is or is not contributing to appropriate drug reimbursement and use.

In the previous chapters I examined how health regulators deal with the problem of defining and stimulating the appropriate use and reimbursement of medicines by

means of optimizing regulation and the conditional reimbursement policy tool. In chapter three I explore what kind of work is done to introduce a new decision criterion in the decision framework with the purpose of closing the (economic) model for priority setting in health care. A literature review focussing on the different possible rationales allowing for the use of budget impact as an explicit criterion in the decision framework was conducted. This review of possible rationales provided understanding in the work needed to legitimize a decision criterion and what the possible implications are for the decision framework and underlying rationales. Underlying assumption of the work to legitimize budget impact as a rationing criterion is that making implicit decision criteria such as budget impact explicit, contributes to the transparency of the decision-making process and therefore the accountability of the decision-makers. This literature review in combination with semi-structured interviews provides insight in whether adding a rationing criterion to the framework solves the benefit package management problem. Or, possibly leads to more complex decision-making and potentially decreases the legitimacy of priority setting decision-making.

The building of a benefit package management's infrastructure entails both shaping and being shaped by the conventions of practice. Chapter four explores and compares how two databases, the Growth Hormone Database and the PHAROS registry, were intended to be employed to control the use of growth hormone, Ibritumomab tiuxetan and Alemtuzumab. The outpatient conditional reimbursement regulation (chapter two) has been translated to the inpatient setting in specific high cost medicines such as oncolytics. The prerequisite of evidence building through data collection and subsequently outcomes research is assumed to contribute to the production of evidence informing both policy and clinical practice. In my exploration I examine how the work needed to collect the data in the databases and the interpretation of the data facilitated governing appropriate drug use and reimbursement. Moreover, I analyze how the databases enabled the production of new forms of knowledge and objectivity and subsequently reconfigured the relation between clinical and policy practice.

In chapter five, all three case studies are combined and re-examined, this time to study the action of legitimizing decisions. Analyzing the activity of 'making legitimate choices' in the three case studies provides insight in how legitimacy is constructed by health regulators and perceived by stakeholders. In the period 2003-2009 I observed how the various stakeholders approach the evaluation of medical technologies by CVZ, and subsequently the question whether the medical technology should be reimbursed or not. Again the question what work is conducted to legitimize decision-making regarding appropriate drug use and reimbursement is addressed. However, the solution is not sought in optimizing the

decision framework or health care regulation. Instead in this chapter the activity of making legitimate choices is analyzed from a more situational approach to regulatory behaviour; whether the actions of regulators are considered legitimate is enclosed in the interplay between the health regulators and their environment (Thevenot 2002). The evaluation of medicines can in its' strive for 'objectivity' not be seen separately from politics and morality. Subsequently, it might be worthwhile to explore what types of repertoires are used to evaluate a medical technology and how these repertoires are incorporated in the current drug reimbursement decision-making process.

In the final chapter, the discussion, I present my findings of the previous chapters in relation to the research questions as previously formulated. Next, I display a general discussion of the practical and theoretical consequences of the conclusions drawn in this thesis for understanding the action of legitimizing decision-making in Dutch drug policy. Furthermore, I reflect upon the chosen research methodology and argue for mixed methods research, especially in complex research arenas such as health care, which involves both moral and factual ambiguity. Lastly, I reflect upon the contribution of the social scientific discipline in the understanding of the construction of legitimate decision-making.

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Chapter One

Inequalities in oncology care: Economic consequences of high cost drugs

Based on: Maartje G.H. Niezen, Elly A. Stolk, Adri Steenhoek, Carin A. Uyl-De Groot. Inequalities in oncology care: Economic consequences of high cost drugs. *European Journal of Cancer* 42 (2006) p. 2887 –2892

Introduction

The expenditures for hospital drugs increase approximately 10% per year, and grow much faster than the hospital budget does. Between 1996 and 2000 the expenditures increased approximately 8% per year in the Netherlands. An even steeper upward trend is predicted for the future: a 20% yearly increase in expenditures for hospital drugs is considered plausible (Pharmo Instituut 2002). The introduction of new, expensive hospital drugs is causing this; examples are the oncolytics trastuzumab (Herceptin ®) and oxaliplatin (Eloxatin ®). To finance hospital care most countries apply the traditional system of fixed global budgets, or the more modern variant of allotted amounts at a specific diagnosis-based level (e.g. in prospective payment systems based on case mix). The costly drugs also have to be paid for out of these budgets. Hospitals or hospital departments thus have to find additional resources to purchase newly introduced expensive drugs. It is clear that expensive and innovative drugs exert a great pressure on the hospital pharmacy budget, or on the allotted amounts at the level of specific diagnoses. Examples of regional differences between and within countries in the use of these expensive cancer drugs show that inequalities are increasing and that hospitals are no longer able to pay for these expenses from the allotted budgets (Borstkankervereniging Nederland 2005; Wilking and Jönsson 2005; Groot 2006). The question therefore is whether we can expect hospital managers to deal adequately with this problem, or whether the financing system forces them to make impossible choices.

This chapter argues that today's governmental policies do not adequately handle the unsustainable and exponential growth of expensive drugs such as oncolytics. In the majority of western countries, hospital finance has been based on global budgets to stimulate more effective provision of care (also called 'technical efficiency'). This strategy shifted a social problem to hospitals, but with good reason: the perceived overcapacity in the health care system. The advantage of this budgeting system is that it offers hospitals an incentive for efficiency, and enables managers to make decisions on structural issues that have greatly improved technical efficiency of the health care system. For example, efficiency of hospitals can be improved by reducing staff size, reducing the number of hospital beds, or by cutbacks in the number of casualty departments. In the Netherlands, this financing system has been operational for more than two decades now. As a consequence, room for improvement of technical efficiency is decreasing. Hence the chance increases that health care goals will no longer be met if no other policies are applied. For that reason, we cannot just depend on the hospitals to deal with the budget pressure exerted by expensive drugs. Sooner or later it will

become a social problem again; a financial problem, a quality problem, or an ethical problem related to increasing treatment inequalities.

This chapter discusses some of the current policy strategies to deal with this problem, as well as their limitations as they occur in the Netherlands. Importantly, this chapter will try to map the contours of the current problem and its possible solutions and will not offer solutions.

Expenditures for hospital drugs

Drugs dispensed in hospitals are part of the entitlement to hospital care, which is financed out of a global budget (see section Dutch policy). Looking at Figure 1.1, it becomes clear that this budgeting system is problematic for the financing of hospital drugs.

Figure 1.1 Hospital drugs: development in volume and expenditures since 1991 (1991 = 100%)

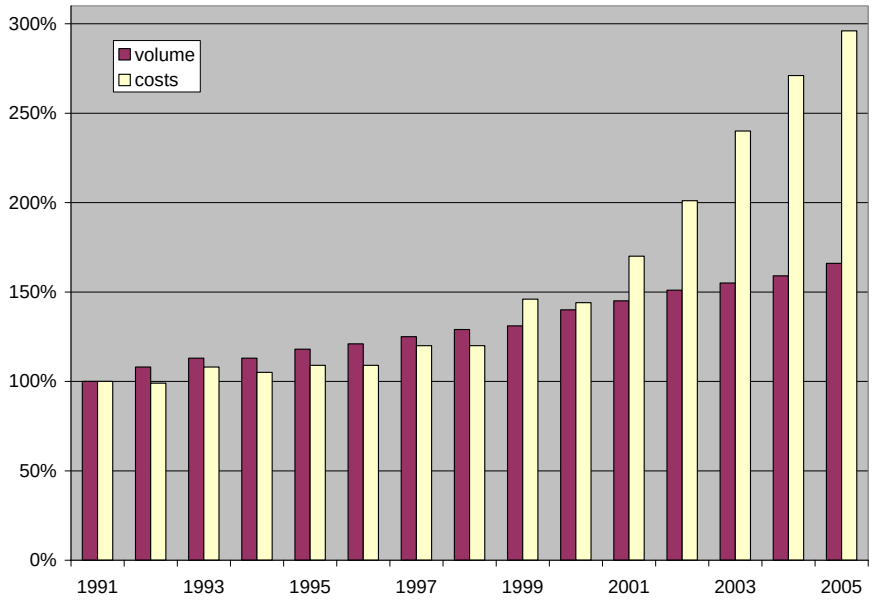
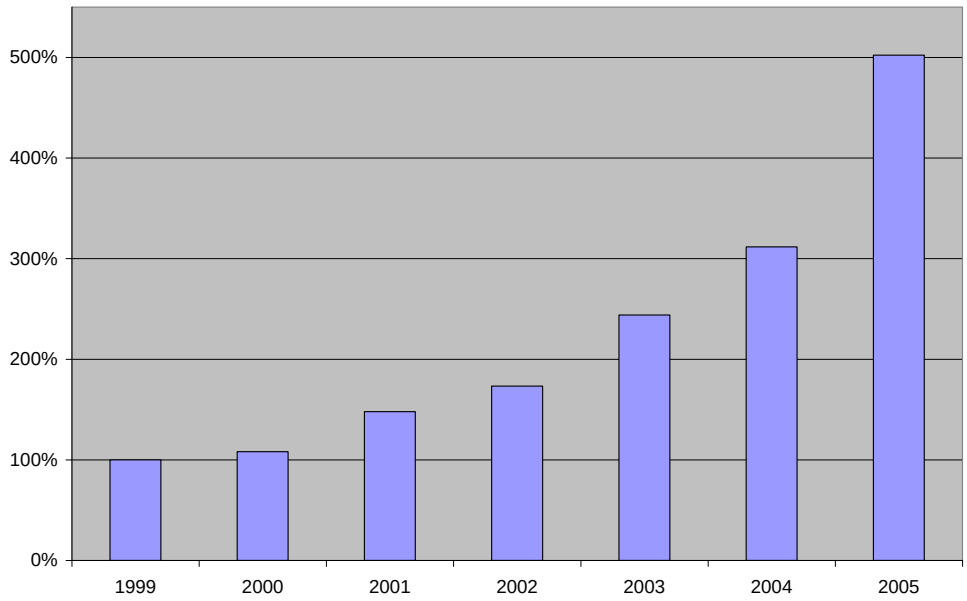


Figure 1.1 depicts the development in volume of and expenditures for hospital drugs over the last 15 years in one (anonymous) Dutch, non-university teaching, regional hospital (about 900 beds). The figure shows a sustainable yearly growth rate of about 5% in the volume of hospital drug use, which is more or less in line with the rate of the allowed annual growth of hospital expenditures in the same period. However, the cost of hospital drugs grow about twice as fast, increasing

300% over 15 years and 150% in the last 5 years. The growth rate of drug costs is thus outpacing the growth of the hospital budget.

The growth of expenditures for hospital drugs can be largely attributed to the introduction of new drugs that are very costly. Indeed, the percentage the hospital budget spent on new and expensive drugs increased from 6.2% in 1996 to 11.7% in 2000 (Pharmo Instituut 2002). Especially for this group of drugs, the financing is perceived as problematic as it leads to large variation in the availability of certain expensive drugs across hospitals and to referral of 'expensive' patients to specialised centres, which are then confronted with much higher patient costs than other regional hospitals (something that the central budgeting system does not automatically control for). Since 1996, the costs for so-called 'expensive drugs' have increased 500%. In Figure 1.2 the purchasing data of the expensive medicines according to the Regulation Expensive Medicines of the hospital pharmacy are depicted (for the same anonymous hospital as mentioned before).

Figure 1.2 Development in total expenditures for expensive drugs* since 1999 (1999 = 100%)



* Expensive drugs are those drugs that have been listed on the 'Regulation Expensive Medicines' since 2002.

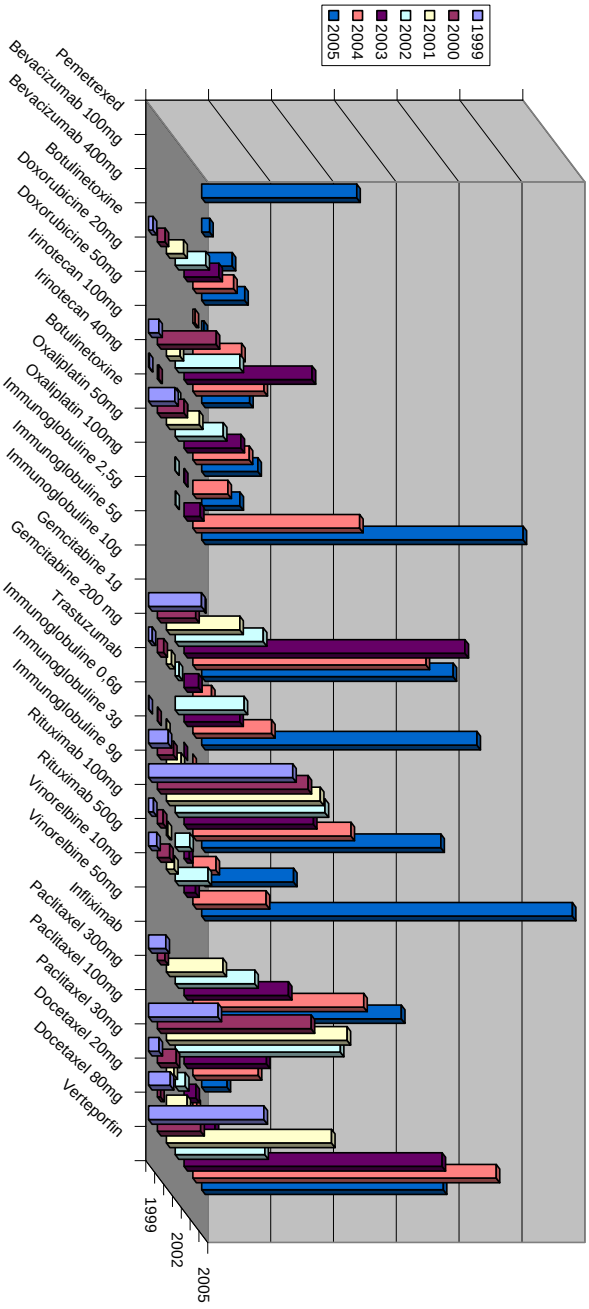
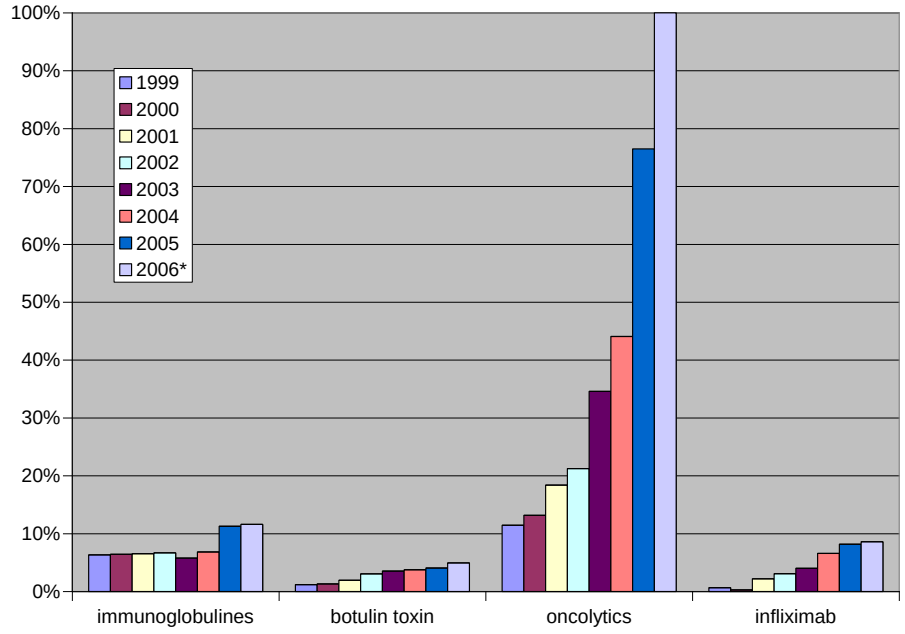


Figure 1.3 Relative expenditure levels for expensive drugs by year and product

A large share of these costs relate to few drugs. The introduction of some oncolytics (e.g. cytostatics and monoclonal antibodies) has especially contributed to the growth in expenditures (see Figures 1.3 and 1.4). The introduction of the first few expensive drugs mid-nineties was then heavily debated. For example, when paclitaxel (Taxol ®) was registered, the debate about the high costs was very intense. Taxoids were considered to be not cost-effective, but the general opinion was that hospitals could not withhold this therapy from severely ill patients only because of a cost-argument. The government even decided to additionally subsidize the costs of taxoids' treatment. The taxoids' case seems to have created a precedent. First, the introduction of even more expensive oncolytics in later years did not lead to public debate about their financial implications. Secondly, the possibilities to receive additional resources for provision of high cost treatments were expanded (see Section Dutch Policy).

Figure 1.4 Relative expenditure levels for expensive drugs by year and drug group



Dutch policy

Until 2005 hospitals received a lump sum budget annually. This budget was determined by the National Health Tariffs Authority (CTG). This hospital budget had to finance all provided care and cover all other expenses. A similar system applies in many western countries (Swartenbroekx et al. 2005). A new financing

system was introduced based on the modern belief that health care can be managed more efficiently when the system offers hospitals incentives for competition and patients more freedom of choice (Ministerie van Volksgezondheid Welzijn en Sport 2001). As of January 1, 2005, hospital care is financed using diagnosis and treatment combinations (diagnose behandeling combinaties – DBCs). A DBC defines all hospital and medical specialist activities and services arising from the demand for care by a patient consulting a specialist in a hospital. This new financing system, based on case-mix, introduces more transparently defined hospital products covered by prices reflecting costs. Because of this direct link between provided care and available resources, it may become easier to prevent discrepancies between budget and expenditures. However, we should not expect a resolution of the current budgetary problems caused by high cost hospital drugs on a short notice. The DBC finance system applies only to 10% of hospital expenditures. For other expenditures the traditional budgeting system still applies. The percentage of expenditures covered in the DBC system will likely be expanded over the following years, but at the time of writing it is not known if or how this will include costs of hospital drugs. The reason is that not all hospitals can deliver sufficiently detailed costs data to attribute the costs of hospital drugs to different DBCs. Moreover, the dynamics of the hospital formulary may require more flexibility than the DBC system can offer.

Recognising the problem of financing expensive drugs like oncolytics and the increasing risk of practice variation in hospital care, the Dutch government implemented a law that forced health insurers to contribute to the costs of some expensive drugs in 2002 (Nederlandse Zorgautoriteit 2006). For all drugs listed on the ‘Regulation Expensive Medicines’ separate reimbursement should be offered. Until 2005 hospitals had to pay between 25% and 100% of expenditures (Swartenbroekx et al. 2005); the reimbursement percentage was variable and was determined after negotiation with insurers. In 2006 the reimbursement rate was fixed at 80%. Reimbursement for the expensive drugs is limited to specific (sub) indications and conditions. The minister of Health decides on these conditions based on an advisory report drafted by the Commission Pharmaceutical Care (CFH) of the Dutch Health Care Insurance Board (CVZ) which assesses the drugs for their therapeutic value. Drugs are included on the list when the prognosis is that they will consume at least 0,5% of the total pharmaceutical expenses of hospitals. By March 2006 sixteen drugs were listed (see Table 1.1, oncolytics in bold). Three years after listing a decision will be made about the continuation of the subsidy based on a cost-effectiveness analysis using daily practice data collected in these three years. If the cost-effectiveness ratio is favourable, the temporary measure will become permanent. If negative, the medicine is removed from the list and is no longer eligible for additional subsidy.

Table 1.1 Drugs included on the Regulation Expensive Medicines, March 2006

– Docetaxel	– **Trastuzumab**
– Irinotecan	– Botulinetoxine
– Gemcitabine	– Verteporfin
– Oxaliplatin	**– Doxorubicine liposomal**
– Paclitaxel	**– Vinorelbine**
– Rituximab	**– Bevacizumab**
– Infliximab	**– Pemetrexed**
– Immunoglobine IV	**– Bortezomib**

In spite of the additional funds for expensive drugs, their expenditures still increase rapidly. Obviously, the measure has not fully resolved the problem. Unless the reimbursement rate is set at 100% it is unlikely that treatment inequalities can be prevented.

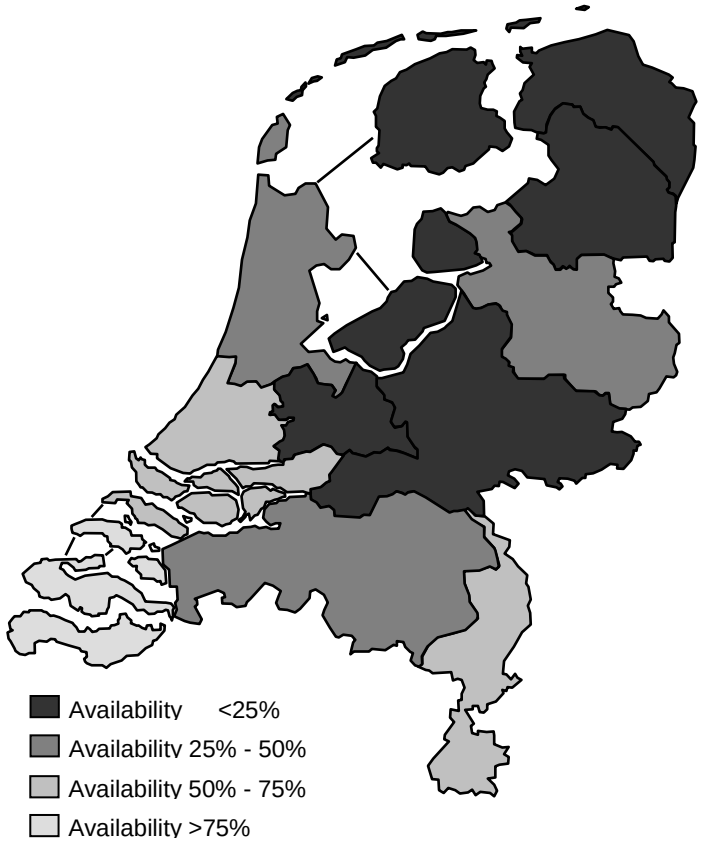
Problems

Because of the central budget an artificial scarcity was created which aimed to improve a technical efficiency. Hospitals were stimulated to cut redundant costs. Fact is, however, that possibilities for shifting budgets vary across hospitals, e.g. small hospitals typically have less room to manoeuvre than large hospitals, so they may seek other solutions. One of the easiest ways to resolve the problem is simply not to purchase expensive products and to refer patients to other hospitals. Therefore, the budgeting mechanism created a large variation in the availability of certain expensive drugs across hospitals. This, in turn, resulted in a disproportionate stream of 'expensive' patients to specialised centres. These specialised centres were thus confronted with a disproportionately high cost of specific drugs, so that their scarcity problem became more pronounced and they were disadvantaged vis-à-vis other hospitals. In these circumstances it is not surprising that some patients do not receive the care they are entitled to. A recent study into the use of trastuzumab (Herceptin ®) shows that this drug is not as often prescribed as was expected on the basis of clinical guidelines and demographic data (Borstkankervereniging Nederland. 2005). The differences across regions are pronounced, as is depicted in Figure 1.5. Policies have thus not been able to prevent postcode prescribing.

In the Netherlands, hospital treatment qualifies for reimbursement if that particular treatment is considered 'usual care' for that specific patient group. In the trastuzumab case, patients thus may not get the treatment they are entitled to, which is undesirable and even against the law. The previously mentioned

'Regulation Expensive Medicines' aimed to ensure that patients can validate their entitlements. The example shows that this regulation does not have the desired effects. This was to be expected. The Regulation describes the conditions under which a hospital receives extra budget (80% of the total costs) for expensive drugs. Nevertheless, the hospitals still have to cover 20% of the costs. This may seem a relatively small amount, but declining possibilities to cut in other hospital expenditures makes it a large financial gap to bridge. The Dutch Federation of Hospitals estimates the cost increase caused by new expensive drugs to be €200 million for 2006 (NVZ vereniging van ziekenhuizen 2006). To indicate what the consequences are, let's say that an average hospital is confronted with a €2 million cost increase. If the hospital has to finance this from its own resources, it could imply that about 45 people lose their jobs. However, this is not a sustainable solution, since hospitals already have a shortage in personnel.

Figure 1.5 Estimated availability of trastuzumab (Herceptin ®) in Dutch regions*



* Figure reproduced from Borstkankervereniging Nederland (2005).

Likely, the financing of hospital drugs will become even more problematic in the future. Clinicians expect a continued increase of average drug prices. A reason is that drugs become more expensive because of new production technologies, e.g. biotechnology. What is more, the new drugs often target relatively small patient subgroups, creating a downward pressure on revenues and hence an upward effect on prices. Trastuzumab is an example of this new group of so-called personalised drugs; it is only effective in women with breast cancer who have an amplified HER2/neu gene (Joensuu et al. 2006). More and more of such products are registered, so that average drug price increases. The threshold of 0,5% gets more difficult to reach. Since the total budget does not sufficiently increase to compensate for inflation and innovation, the Regulation Expensive Medicines does not improve financial viability of hospitals. From that point of view, the Regulation primarily offers a solution for practice variance in the treatment with (listed) expensive drugs, but this may come at the cost of increasing practice variance in other treatment areas. The reason is that now a part of the budget is earmarked as the Regulation explicitly states, what care should be delivered. Moreover, it does not indicate how priorities should be set in the allocation of remaining resources.

Future directions

To solve current problems, changes to the financing system of hospitals are required: we need to search for a new balance between central budgeting and fee-for-service financing. The introduction of a case-mix financing system may help to resolve the problems, especially when this system is expanded to all hospital care and to include expenditures for hospital drugs. An implication of this policy change, however, is that the system loses incentives for technical efficiency, because this case-mix system is in theory open-ended. Typically, control over the total level of expenditures in open-ended financing systems is maintained through tighter control of the benefit package. This means that more emphasis is put on productive efficiency, and that more outcomes research is performed to make sure that the use of health care technologies at the practice level is evidence based. In many countries, reimbursement decisions of outpatient medication are made at the national level, based on evaluations of (cost)-effectiveness. In contrast, local hospitals are responsible for meeting the health care needs of their populations, but they are free to make decisions concerning the use of new technologies. It is not exactly known how these local managers decide on the content of the hospital formularies. Do they consider therapeutic value? Do they consider cost? Do the new drugs meet the expectations in daily practice? And when are costs considered to be too high? There is increasing awareness that more openness in the decision-making process is required. If we expect all patients to receive high quality care, all hospitals would have to answer such questions in a similar way. Also the

recognition that some of the newly implemented interventions proved not effective in retrospect has increased awareness of the need for more scientific evidence before introduction of new health technologies into hospital care. In improving the decision-making process the government should play a role. It would be helpful if they promote research into efficient use of resources in hospitals by evaluating new and existing services from medical, economic and ethical point of view and establish organisational structures for dissemination of the results to local decision-makers. In that respect it is a good development that Dutch policymakers recently accepted some responsibility for the promotion of evidence based decision-making regarding hospital treatments. This becomes apparent from the change in the policy rule for expensive drugs stating that three years after listing, the medicine should be re-assessed to see if the drug meets its expectations and to decide if the particular drug still deserves its place in the Regulation.

The question remains whether this type of outcomes research really solves the problem? Perhaps we should not expect too much. If outcomes research shows that a medicine meets all common requirements for effectiveness and cost-effectiveness, it does not necessarily mean that the hospitals or Dutch government are able to fund this medicine. Demonstrating which drugs represent added value for each additional euro spent, outcomes research can be used to prioritise which drugs are in- or excluded from the hospital formularies. But it does not solve the problem that it may not be affordable to fund every medicine that meets all requirements for effectiveness and cost-effectiveness. The introduction of new (cost-effective) drugs means that health outcomes can be improved at reasonable cost, but it also means that total resource consumption has to increase. There is no guarantee that the hospital is able to meet the additional resource requirements (Sendi et al. 2003). What is required to make the system work is certain flexibility of the total budget or of the applied assessment criteria.

The question then is not just whether or not a hospital is able to use its pharmaceutical budget as efficient as possible, but also if the total budget for health care is used in an optimal way. A comprehensive approach would include transparency of resource use and outcomes for the entire hospital and also in other health care sectors, and the flexibility to reallocate available budgets. In the end, this approach may allow for comparisons to be made between expenditures for health care and other public goods (e.g. education), so that benefits associated with possible expansions can be related to the question whether or not the health care budget should be increased to meet the health needs of the population.

Discussion

The social problem of expensive drugs is new and enormous in the Netherlands, and likely also in other western countries. If the current policy is not changed, the 16 medicines now classified as 'expensive' will cost approximately up to €600 million in about 5 years. This amount is comparable with the current turnover of all drugs in all hospitals (Steenhoek & Rutten 2005). This is not just a problem of hospitals, sooner or later it will become a social problem again. Governments should intervene before the problem gets out of control, as a financial problem, a quality problem, or an ethical problem related to increasing treatment inequalities. This paper has pictured the development of the problem and identified fundamental issues that need to be resolved. Will budget impact be allowed to overrule cost-effectiveness? And, does this give legitimacy problems? These questions are a signal that reflection on the value of health is necessary and the available budgets have to be reconsidered. These questions quickly need answers, because of the enormous speed with which the cost explosion is developing. Since many expensive drugs are used especially in the field of oncology, the current lack of political action is worrisome. The transparency of its high expenditures may make this field vulnerable to budget cuts (Van Bochove 2006). On the other hand, the severity of many types of cancer also stimulates discussion about fairness. Hopefully oncologists will be able to use this discussion to their advantage and stimulate a public debate about the real issue that system changes are needed to guarantee that patients get the treatment they need.

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Chapter Two

Conditional reimbursement within the Dutch drug policy

Based on: Maartje Niezen, Antoinette de Bont, Elly Stolk, Arthur Eyck, Louis Niessen, Herman Stoevelaar. Conditional reimbursement within the Dutch drug policy. *Health Policy* 84 (2007) p. 39–50. Elsevier Ireland Ltd.

Introduction

While the benefit package for pharmaceutical care in Dutch health care has been defined at the national level, most decisions on the actual provision of pharmaceutical care are made in the doctor's office. There is growing recognition that these bedside decisions do not necessarily reflect the same values that guided the delineation of the benefit package. For example, in 1991 the Health Council noted that some therapies were routinely performed, despite a lack of proven effectiveness (Gezondheidsraad 1991). The council concluded that doctors might sometimes lack the specific knowledge that is required to make optimal decisions. Against this background, the government has developed a series of tools that promote rational prescribing, aiming to improve the quality and efficiency of care, and enabling the control of pharmaceutical health care expenditures. Note; the two objectives, improving quality and efficiency, and trying to contain costs, are not easy to incorporate in one measure as they have a tendency to contradict each other.

Recently, the policy of conditional reimbursement has received increasing attention. Policymakers may influence medical decisions through guideline development, installation of expert committees, record keeping of treatments provided, and financial incentives (e.g. to promote prescription of generic drugs) (Stolk & Poleij 2005). In comparison with the aforementioned policy measures, conditional reimbursement influences prescribing behaviour using more compelling means, potentially giving the government a higher level of control. Because a tension may exist between this policy objective and the views of the medical community, the effectiveness of conditional reimbursement in influencing medical practice is not self-evident. To determine the future scope for policy interventions using conditional reimbursement, we evaluated several Dutch experiences with conditional reimbursement until now.

The goal of conditional reimbursement is to promote effective and efficient use of certain pharmaceuticals (College voor zorgverzekeringen 2005). For this purpose, reimbursement of a service is made conditional to specific criteria or rules. For example, the application of a drug may be restricted to specific categories of patients, prescriptions may only be provided by authorized physicians, or prior authorization must be obtained from the health insurance company. Mostly, conditions apply to those drugs that are considered expensive and/or have a risk of inappropriate use (Van Oostenbruggen et al. 2005); conditions are then defined to limit off-label drug use and promote drug use for indications where effectiveness has been established. Spontaneous expansion of use of these medicines is not

allowed, so that a consolidating effect on volumes of use is expected. All drugs, to which these conditions apply, are included in the so-called Health Insurance Fund (Provision of Pharmaceuticals Regulation Schedule 2, in Dutch 'Regeling Farmaceutische Hulp 1996' (RFH 1996) Bijlage 2). Criteria for inclusion are: high costs, risk of inappropriate use, or the need for specific expertise in order to ensure appropriate patient selection.

In other countries, such as Finland, Germany, and the United Kingdom, similar policy-instruments are used, albeit that these countries have different health care systems (Kooijman 2003; Marx 2000; Raftery 2001; Vuorenkoski, Toiviainen & Hemminki 2003). The 'Anlage 4 der Arzneimittel Richtlinien' (AMR) regulates the prescription of particular types of medication in Germany (Marx 2000). In the UK, all drugs with conditional reimbursement are added to 'Schedule 11 of the National Health Service (General Medical Services) Regulations 1992'. Additionally, the NICE technology appraisals may restrict drug use to specific patient groups (Raftery 2001). In Finland, there are three reimbursement categories: limited, special (75 percent), and complete (100 percent), where conditions apply to the higher reimbursement categories (Vuorenkoski, Toiviainen & Hemminki 2003). Obviously, differences may exist between the country specific regulations. But, there are also many similarities in applying the principle of conditional reimbursement. The drugs that are conditionally reimbursed in the Netherlands are often reimbursed under conditions in other countries too; moreover, the types of conditions for reimbursement are often alike (Niezen et al. 2004).

Apparently, conditional reimbursement is regarded as an important policy tool to promote the appropriate use of medicines. However, evidence about its effectiveness in daily practice is limited. Therefore, the Dutch Health Care Insurance Board commissioned a study to evaluate the effectiveness of conditional reimbursement as a means to stimulate appropriate drug use, and to identify potential issues for improvement.

The Dutch conditional reimbursement policy

In the Netherlands, pharmaceuticals do not automatically qualify for reimbursement. The Minister of Health decides whether or not a drug will be reimbursed, based on advice of the Commission for Pharmaceutical Care (CFH) of the Health Care Insurance Board (CVZ) about the therapeutic value, efficacy and cost-consequences of a drug (Stolk and Poleij 2005; Van Oostenbruggen et al. 2005; College voor zorgverzekeringen 2000a). When included in one of two so-called 'positive lists' (Schedules 1A and 1B of the RFH 1996), medications are reimbursed. Schedule 1A consists of clusters of similar medications, with a

reimbursement limit for each of these clusters. Schedule 1B contains non-substitutable medications for which no price limit is set. If conditions are to be met for reimbursement, the medicines are listed in Schedule 2. While the CFH advises the Minister of Health about Schedule 1A and 1B, the CVZ directorate advises about Schedule 2. Because conditional reimbursement is, in The Netherlands at least, related to policy issues (e.g. possible risk for inappropriate use), policymakers, rather than pharmaceutical experts, give advice on the content of the conditions. After the conditions are formulated, revision is only possible when pharmaceutical companies formally request the Ministry of Health for widening of indications or admittance of new indications based on new scientific evidence, or when the Ministry of Health (sometimes based on CVZ advices) regards this necessary.

The conditions that are used can be divided into the four categories listed below. Mostly, the restriction of the indication is combined with one or two other types of conditions for reimbursement. These (combinations of) conditions should prevent off-label drug use and promote both effective and efficient therapy and the quality of care:

- Restrictions of the indication.
  Indications can be restricted to specific categories of patients, such as: children born after a pregnancy of 32 weeks or less (palivizumab) or social health insured, diagnosed with diabetes mellitus type 2, insufficiently responding to monotherapy (rosiglitazone and pioglitazone).
- Referral to professional guidelines.
  The conditions can refer to the professional guidelines of a specialist group prescribing the medication, or a protocol specifically written for the treatment, e.g. growth hormone-prescribing must accord to the 'Protocol use of growth hormone'. The guidelines vary from evidence based to consensus based.
- Prescribing only by treating specialist and/or specific demands on the requested expertise of the prescribing physician or the treating facility.
  Sometimes prescriptions may only be provided by authorized physicians, as is the case for antiretroviral medicines—the drug may only be prescribed by a treating internist or paediatrician, who is tied to an HIV-treating (sub) centre laid down by the Minister of Health.
- Prior authorization must be obtained from the health insurance company.
  Until 2006, medical advisors of health insurance companies assessed the prior authorization requests for reimbursement of drugs such as glatiramer. As of January 2006, however, this category no longer exists since a new regulation has been introduced; the 'Regulation Health Care Insurance'

(Ministerie van Volksgezondheid Welzijn en Sport 2005). Health care insurers are now free to reimburse after prior authorization whenever they think it is appropriate, as long as this is announced in their statute.

In August 2003, the Schedule 2 conditions applied to 37 (groups of) medications. During the research period (August 2003-September 2004) the number of medications included in Schedule 2 increased to 40. Eighteen changes were made, varying from administrative corrections to changes of indications, and also the addition of new drugs to already existing or new categories (Niezen et al. 2004). Examples of these changes are: the addition of new indications in the condition for etanercept (March 1, 2004 and April 1, 2004) and the addition of a new medicine, galantamine, to the rivastigmine group (November 11, 2003). Although Schedule 2 has contained up to 47 (groups of) medications (December 2005) the list now contains 42 drugs/groups (August 2006).

Methods

To evaluate whether or not the conditional reimbursement policy promotes appropriate drug use, ideally, one would collect data about drug use in the situation with, and the situation without, conditional reimbursement policy. Unfortunately, conditions are only specified when a drug enters the benefit package; hence, no data are available about the situation in which no conditional reimbursement policy exists. A direct cause-effect relation cannot be established; therefore, it is not possible to see how much conditional reimbursement policy affects prescribing behaviour and drug costs. We can, however, evaluate whether or not the desired effects (appropriate drug use following the requirements for reimbursement) are attained. Hereafter, this form of appropriate drug use will be defined as ‘authorized use’ whereas ‘appropriate use’ will be the desired use according to clinicians.

We took a two-tiered approach to the investigation of the effects of the conditional reimbursement regime. First, we collected macro-level data on the volumes of drug use. The purpose was to explore whether the volume of drug use was at the expected level, in order to get a general idea of the overall functioning of the conditional reimbursement measure. Deviations from expectations may have indicated poor functioning of the measure. Next, we analysed the macro-level data using two indicators: the number of users in the years following introduction of the drug, and the annual growth. To analyse annual growth we analysed trends in the volumes of use of all conditionally reimbursed drugs, starting with the year the drug entered the market (data 1994-2002). The macro-level data were obtained from the so-called ‘GIP-database’, a registry of reimbursement data held by CVZ for 7.5 million insured people who are representative for the entire Dutch population.

Second, we gathered micro-level data for five selected cases, as it was not a priori clear that inferences can legitimately be made from macro-data investigation alone, because there may also be other explanations of its outcomes than inappropriate or unauthorized use. The micro-level data were expected to provide insight into what fraction of individual prescriptions actually met the conditional reimbursement requirements. Moreover, by means of interviews (N= 65) and document analysis, the micro-level data were interpreted and the stakeholders' perspectives on the functioning of the policy measure were obtained.

The five selected cases were: TNF-α blockers, clopidogrel, thiazolidinediones, growth hormone and cholesterol lowering therapy. The case selection was based on the diversity principle; we purposively selected cases for which the data (macro-level and interview-data) indicated proper functioning of the regime or poor functioning, as to gain the best understanding of the factors that promote or inhibit effectiveness of the conditional reimbursement policy. Moreover, the selection covered all types of potential conditions related to reimbursement. We collected micro-level data on drug prescriptions and the background characteristics of receiving patients from different databases. Consulted databases were: the GIP-database[1] (Health Care Insurance Board) for the TNF-α blockers and thiazolidinediones, the National Growth Hormone Database[2] (Dutch Growth Foundation-National Registration for Growth Hormone, the Integrated Primary Care Information (IPCI)-database[3] (Erasmus MC) for the statins (cholesterol lowering therapy) (Vlug et al. 1999) and the Pharmo-database[4] (PHARMO, Institute for Drug Outcome Research) for clopidogrel. Using these data, we analysed what fraction of individual prescriptions actually met the conditions. The analyses differed by case, depending on the specific conditions for reimbursement[5]. For example, if reimbursement was limited to certain indications, we gathered data to confirm the indication. If the condition specified that a step-up therapeutic pathway should be followed, we analysed whether patients had received the specified therapies prior to use of the listed drug (see Box 2.A). However, with these types of analyses and databases under treatment is difficult to detect. Per case, the micro-level data were collected from the database best suited to give information about the authorized use and appropriateness of the individual prescriptions.

[1] http://www.gipdatabank.nl
[2] http://www.groeistichting.nl
[3] http://www.ipci.nl
[4] http://www.pharmo.nl
[5] Moreover, the analyses also differed as the databases covered data of prescribed use (Pharmo, IPCI), reimbursed use (GIP) and a combination of both (National Registration Growth Hormone).

To explain why and when over- or under-consumption occurred, we performed stakeholder analysis for the five selected cases. The purpose of this approach was to obtain specific information about what kind of requirements are more or less effective, and the circumstances under which conditional reimbursement policy is likely to be more or less effective. Where applicable, the preliminary results from the quantitative analysis were discussed during the interviews. We analysed the stakeholders' perspectives on the conditional reimbursement policy using document analysis and in depth-interviews, focusing on the conditional reimbursement policy in general (N= 12) and its consequences for the five selected cases more specifically (N= 53). Most of the documents analysed were obtained from the archive of CVZ (among which pharmacotherapeutic- and CFH-reports and correspondence with the pharmaceutical industry, patient interest groups and specialists), and the library of the Ministry of Health. Two interviewers, MN and AE, held all the interviews. Each stakeholder group was represented with at least four respondents.

Results

Expected versus observed use of medications

Table 2.1 shows the figures on expected versus observed use of medications for which a conditional reimbursement regimen applied. In 19 cases it is impossible to say whether or not the observed use is at the expected level, because no figures on expected use were provided by the CFH (most likely due to a lack of epidemiological data)[6]. In five cases, actual use was substantially higher than expected (e.g. no. 10, 20 and 29), while in six other cases the observed volumes were much lower than the estimates of the CFH (e.g. no. 15, 26 and 28). From a comparison of these absolute numbers it is thus hard to conclude whether or not the conditional reimbursement policy has a consolidating effect on drug use.

[6] Projections are mostly based on data given by the pharmaceutical company and available data in their own GIPdatabank

Table 2.1 Expected versus observed use 1999-2002

Schedule 2		Expected users		Observed users (N)				Relative change user population (1999=100%)
		N[a]	Year[b]	1999	2000	2001	2002	
1.	Rubella vaccine			203	164	120	148	-27%
2.	D(K)TP-vaccine			178	131	173	158	-11%
3.	Hepatitis B vaccine			7381	7878	6047	5622	-24%
4.	Pneumococcal vaccine			1924	2124	1917	2210	15%
5.	Heamophilius Influenzae B vaccine			347	404	449	578	67%
6.	R-DNA-interferon			4462	5156	5449	5809	30%
7.	Growth hormone			2053	2268	2446	2606	27%
8.	Antiretroviral drugs			13095	14603	15942	16850	29%
9.	Epoetins			3822	5516	7789	11006	188%
10.	Cholesterol lowering therapy	380000-630000	2000	612255	682281	773771	844872	38%
11.	Recombinant interleukine2			45	38	13	35	-22%
13[c]	Granulocyte (Macrophage) Colony Stimulating Factors			2572	609	2970	3243	26%
14.	Acetylcysteines			104774	116359	96881	90425	-14%
15.	Alglucerase, imiglucerase	100-200	2003	46	46	46	47	2%
16.	Rabies vaccine			74	106	141	129	74%
17.	Gabapentin, lamotrigine, levetiracetam, topiramate	1750	2000	7709	15478	31259	46018	497%
18.	Mycophenolate mofetil		2000	1514	2027	2377	2778	83%
19.	Rivastigmine	8750	1998	913	1454	2072	2796	-100%
20.	Apraclonidine,dorzolamide, latanoprost	39.000-85.000	1999	45449	64936	77074	95038	109%
21.	OTC-drugs			1568	2254	2646	3755	139%
22.	Hepatitis A vaccine			2848670	1591322	1528993	1555154	-45%
23.	Palivizumab	1300	1999	-	1109	1469	1520	37%
24.	Montelukast		2000	-	5555	19610	24325	338%
25.	Clopidogrel	61269-79616	2003	134	3747	16550	34244	-74%
26.	Etanercept	2170-4340	2000	10	181	630	874	8640%

Table 2.1 Expected versus observed use 1999-2002 (continued)

Schedule 2		Expected users		Observed users (N)				Relative change user population (1999=100%)
		N[a]	Year[b]	1999	2000	2001	2002	
27.	Modafinil	640-1600	2000	-	30	493	1033	-97%
28.	Becaplermin	1134-7560	2000	-	2	447	352	17500%
29.	Rosiglitazone, pioglitazone	1675	2003	-	-	7690	18416	139%
31.	Glatiramer		2001	-	-	-	314	n.a.
32.	Linezolid	300	2002	-	-	-	37	n.a.
33.	Anakinra		2002	-	-	-	210	n.a.
34.	Epoprostenol	90	2002	-	-	-	-	n.a.
35.	Bosentan	90	2002	-	-	-	-	n.a.
36.	Tacrolimus	58443-147081	2003	-	-	-	-	n.a.
37.	Miglustat	7	2003	-	-	-	-	n.a.

[a] The estimates were derived from published advices of the Commission for Pharmaceutical Care (CFH) of the Health Care Insurance Board, who estimated the budget impact of funding new and innovative drugs that could be admitted into the benefit package through Schedule 1B (since 1996). The estimates only are available as of 1996. If a drug entered the benefit package before 1996, no estimates are available unless recalculations have been made. For rivastigmine and cholesterol lowering therapy estimates were derived from other sources (Ziekenfondsraad 1998; Gezondheidsraad 2000).

[b] In some cases the numbers are based on recalculations, e.g. when conditions were adjusted. Therefore the year for which estimated numbers are available, can differ from the year of initial introduction in the benefit package.

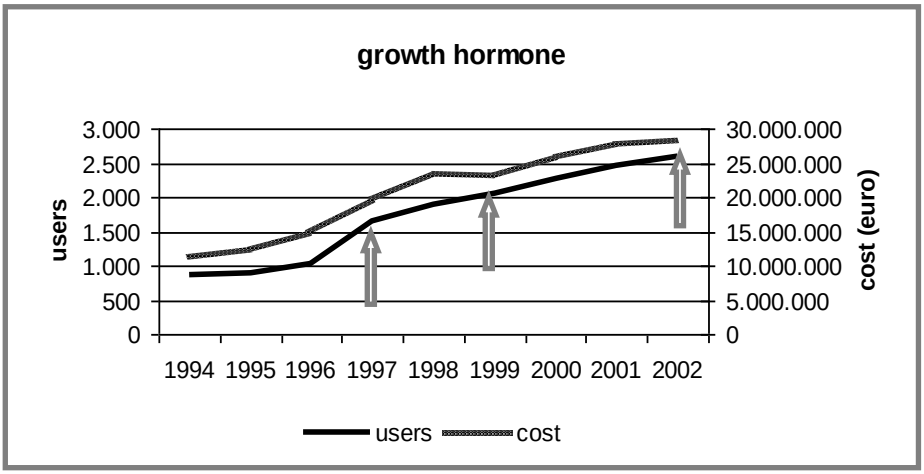
[c] Number 12, total parenteral feeding, is not included in this study.

Annual growth and policy effects

If pharmaceutical use had stabilized over the years, we may assume that there was a consolidating effect of the conditional reimbursement-instrument. This seems to be the case for only six drugs (excluding vaccines). On the other hand, a continuously strong increase in the number of users may point at a failing regimen, and that pattern is also found for six medicines/groups (e.g. statins (cholesterol lowering drugs), epoetins and antiglaucoma medicines). Nevertheless, it still is possible that the requirements are met as other factors and also the type of condition can influence the interpretation of the outcomes, e.g. guideline conditions may be met while substantial growth rates are observed. The other medicines were recently introduced (TNF-α blockers, clopidogrel and thiazolidinediones), such that diffusion and dissemination effects hamper interpretation of the time series data.

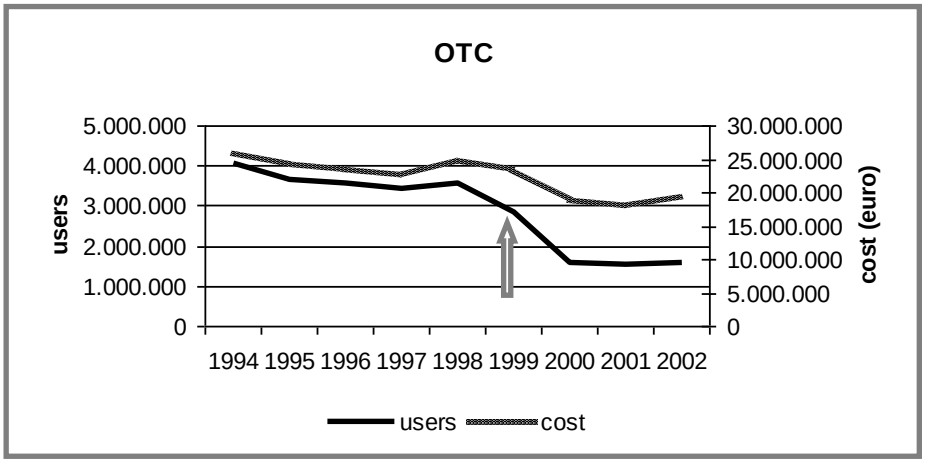
For some drugs, the conditional reimbursement policy changed during the observation period, allowing us to observe possible cause-effect relations. Figures 2.1–2.3 show how the policy change probably affected the use of the growth hormone, OTC drugs and cholesterol lowering therapy. The arrows mark the moments when the policy changed. In each case there is a change in the number of users. These three cases suggest that conditional reimbursement may be an effective policy tool to steer drug use. However, the question remains to what extent the cases are typical for the conditional reimbursement measure.

Figure 2.1 Growth hormone



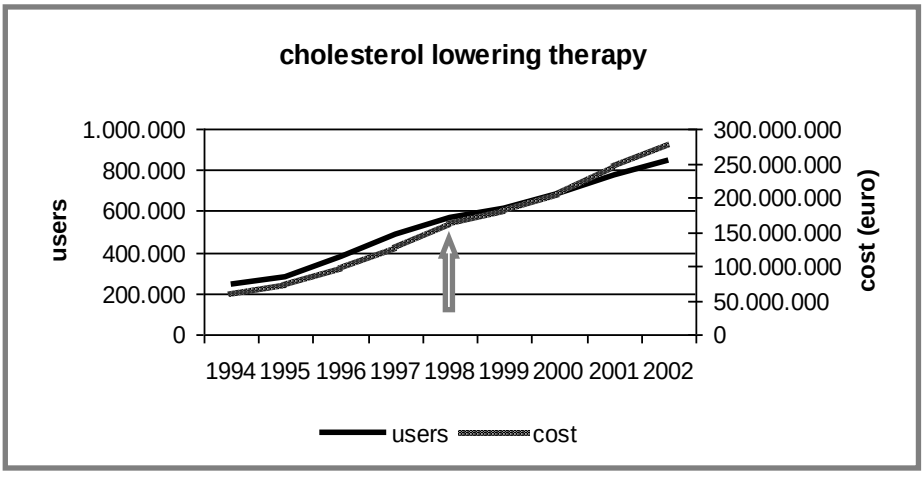
The restrictions for reimbursement of the growth hormone changed on several occasions, each time broadening the indications (Ziekenfondsraad 1997, 1999; College voor zorgverzekeringen 1999). Various changes in the reimbursement regimen (indicated by the arrows in Figure 2.1), also point at an increase in the medication use.

Figure 2.2 OTC



In 1999 the conditional reimbursement policy regarding OTC-drugs was radically changed (Rikken and Eijgelshoven 2000). A new measure determined that the OTC-drugs would only be reimbursed for the chronically ill. This is clearly shown in Figure 2.2; the number of users is halved although the mean number of DDDs per user is increased, resulting in only a marginal cost reduction.

Figure 2.3 Cholesterol lowering therapy



The arrow indicates the introduction of a new guideline for statins into clinical practice in 1998 by The Dutch Institute for Health care Improvement (CBO) (Centraal Begeleidingsorgaan voor de Intercollegiale toetsing 1998). Figure 2.3

shows that since 1998 the drug use pattern has changed, however the restrictions related to reimbursement were not altered. Therefore the time series analysis indicates a possible unauthorized use of the statins according to the conditional reimbursement policy.

Case studies

The micro-level data for the five case studies clopidogrel, thiazolidinediones, statins, TNF-α blockers and growth hormone is summarized in Table 2.2.

Table 2.2 Inappropriate use according to Schedule 2-measure and professional guidelines

Drug	Indication area	Unauthorized use (against Schedule 2)	Inappropriate use (against professional guidelines)
Clopidogrel[a]	Recent ischemic stroke, myocardial infarction, peripheral arterial disease	13%	7%
Clopidogrel[a]	Acute coronary syndrome without ST-elevation	24%	Under-use
Clopidogrel[a]	Percutaneous trans-luminal coronary angioplasty	29%	Under-use
Etanercept[b]	Rheumatic disease	15%	2%
Growth hormone[c]	Faltering growth	12%	4%
Thiazolidinediones[d]	Diabetes control	17%	0%
Statins[d]	Hypercholesterolemia	94%	8%

[a] Pharmo-database.
[b] GIP-database.
[c] LRG-database.
[d] IPCI-database.

Clopidogrel

In the case of clopidogrel, the low adherence to policy guidelines has been the subject of heavy debate. For three indications (Table 2.2), clopidogrel is not reimbursed according to the conditions for reimbursement in 13%, 24% and 29% of the cases, respectively. Based on emerging scientific evidence, however, physicians considered its use appropriate for a number of indications not listed in Schedule 2, and adapted their guidelines accordingly. Over the past few years clinical guidelines were regularly updated when more patient groups, for which

effectiveness of clopidogrel was demonstrated in clinical studies, were identified. When following these guidelines, only 7% might be prescribed inappropriately, and even more prescriptions should have been written since under-use has been detected according to clinicians and patient representatives. Policymakers, however, had not updated the conditions since the first inclusion of the drug in Schedule 2, and did not allow reimbursement of its use in these new identified subgroups. They argued that extended reimbursement was not feasible, because the new indications for clopidogrel were not registered; neither by a national procedure (Medicines Evaluation Board), nor at a European level (European Medicines Agency). The pharmaceutical industry and some specialists however, claimed that the exclusion of these indications was based on implicit cost-arguments. Accordingly, many respondents mentioned that the revision procedure for clopidogrel, as well as of other drugs, is not very transparent, and is often accompanied by procedural mistakes.

Thiazolidinediones

According to the conditional reimbursement instrument 17% of the drug prescriptions of thiazolidinediones should not have been reimbursed. This is why the adherence to the regimen became, just like in the clopidogrel case, the subject of debate. The high percentage of unauthorized use results from application of thiazolidinediones for indications not yet listed on Schedule 2. Moreover, the Schedule 2 conditions reflect a step-up treatment pathway, while more and more clinicians seem to believe that a step-down approach may be more beneficial to patients. Thus, where policymakers insist that, under these circumstances, policy guidelines should prevail, it became apparent that the professionals have another view on the appropriate treatment of patients with diabetes.

Statins

In the case of cholesterol lowering therapy, it appeared that 94% of the prescriptions were not according to the Schedule 2 requirements. However, when compared with the latest European guideline (Mantel-Teeuwisse et al. 2004) only 8% is ‘inappropriately’ prescribed. Again, the problem of discrepancies between professional norms and policy restrictions seems to apply. In this case, however, another problem also becomes apparent. Health insurers generally believed that statins should be dropped from Schedule 2. The underlying idea is that monitoring the appropriate application of this drug in clinical practice is rather problematic. Additionally, they argued that the administrative costs of monitoring certainly would exceed its potential savings. They found that the assessment of the appropriate reimbursement of statins is difficult because of the large population, and the requested data to check whether a patient meets the requirements are not easy to collect. The Schedule 2 indication requires, for example, that a patient should have

been on a diet for at least 6 months without result prior to prescription. In addition, the patient must suffer from a heritable hypercholesterolemia or have a cholesterol level ≥8 mmol/l and at least one additional risk factor (e.g. diabetes mellitus). Nevertheless, policymakers found the Schedule 2 listing of cholesterol lowering therapy still useful, because it is a sign to physicians and health insurers that careful prescription is required. Moreover, policymakers consider listing important as it provides a legal basis for intervention, regardless of the extent of successful implementation in daily practice.

TNF-α blockers

For etanercept, the figures presented in Table 2.2 suggest unauthorized use, with up to 15% of users for whom the specified step-up treatment pattern was apparently not followed. Legitimacy and desirability of the conditions were not an issue, though, because the unauthorized use could, for the most part, be justified. When etanercept was introduced, there were insufficient supplies to treat all patients, and specific selection rules were applied. A national board was established to evaluate each request for this expensive drug. When supply increased, permission was extended to the initial user group, meaning that they were relieved from the obligation of proving having met all indication criteria. The timely discussions between CVZ and the members of the central assessment committee contributed to the efficient functioning of the restrictions, though the adjustments of the restrictions were not established as quickly as in the case of the growth hormone. In addition, the health insurers were also represented in the committee, keeping the connection between policy and practice very tight.

Growth hormone

Twelve percent of the prescriptions can be classified as ‘unauthorized’. However, in some cases of growth hormone use, the diagnosis of growth hormone deficiency was evident, so that the clinical requirements in the consensus criteria of the ‘Protocol use of growth hormone’ were not collected (4%). The label ‘unauthorized’, therefore, does not really apply for these prescriptions as they do meet the content of the requirements. Both policymakers and health insurers agreed that the conditional reimbursement of the growth hormone contributed to its effective and appropriate use. According to the interviewees, the national (uniform) assessment was the main reason why the conditional reimbursement policy functioned properly, like in the TNF-α blockers case.

Common issues

Most stakeholders in the clopidogrel, statins and thiazolidinediones case studies shared the opinion that the required conditions were not functioning well. Actors in

the field of health care and health insurers considered the system to be too inflexible to allow timely adjustment to emerging scientific and clinical insights. They argued that a periodic review was missing. According to the practising physicians, drug prescription beyond the authorized indications, as listed in Schedule 2, is very common in the cases of clopidogrel, thiazolidinediones and cholesterol lowering therapy. They mentioned that the strict application of the reimbursement rules conflicts with the latest professional guidelines (Table 2.2). The figures may also give reason for concern, as they show that the health insurers do and/or cannot (always) force adherence to the regime. Health insurers claim that – because of new and widening indications – they are losing control of authorized prescription and related reimbursement. Some of them have been able to improve their grip on conditional reimbursement (e.g. by checking their registered data or implementing compulsory authorization requests), but this applies to only a minority of health insurers. This development was considered problematic by health care providers, who fear for inequalities in the delivery of health care.

Whereas the cases mentioned above show the different problems of conditional reimbursement, the stakeholders in the growth hormone and TNF-α blockers cases seem to cope effectively with the conditional reimbursement measure. The health insurers were satisfied with the national assessment committees, because these generally led to clear, feasible and manageable conditions. The committees were constituted by order of CVZ and, instead of the individual health insurers, centrally assessed the claims for reimbursement of the medications in a uniform way, using objective criteria[7]. Unauthorized drug use is therefore not very likely to occur. This way of decision-making was considered very positive by not only the health insurers, but also by the specialists and patient representatives. Whereas health insurers appreciated its uniformity and the use of strict criteria, the specialists were pleased with a certain degree of flexibility and discretionary space for exceptional cases, and the patient representatives felt they were done justice because of the presence of specialists in the assessment committees. Overall, the different stakeholders felt their voices were heard. Moreover, the growth hormone case shows a dynamic conditional reimbursement policy, in which scientific developments, professionals' views and policy considerations are in a continuous process of interaction.

[7] The individual central assessment committee for TNF-α blockers (2004) and growth hormone (2005) have been abolished and subsequently integrated in the National Evaluation of Applications of Drugs (Landelijke Beoordeling van Aanvragen Geneesmiddelen (LABAG), http://www.labag.nl) financed by the Dutch health insurers. The assessment of difficult cases still includes the expertise of (mostly the same) specialists.

During the interviews, the stakeholders generally agreed with the policy objectives of the conditional reimbursement instrument. However, they expressed not being satisfied with the decision-making procedures for considering the inclusion of drugs in Schedule 2, the definition of the conditions, and (lack of) adjustments. Moreover, they tended to disagree with policymakers about the interpretation of evaluation outcomes. On the one hand, policymakers tend to evaluate the outcomes from a rather 'mechanical' perspective, focusing on merely the compliance with reimbursement rules. Clinicians, on the other hand, evaluate the outcomes from a broader perspective. From their viewpoint, the policy is expected to be implemented in accordance with general criteria for reimbursement, clinical objectives and available medical evidence. As knowledge and expertise are continuously shifting, clinicians advocate a dynamic view when interpreting the policy outcomes. Generally, the policy guidelines restrict use to a smaller group of patients than professional clinical guidelines do. This is partly due to the fact that conditions are not always revised when the body of clinical evidence grows. Obviously, the consequence is that the two parties heavily disagree about the extent of inappropriate or unauthorized prescribing (see Table 2.2).

Discussion

From our study, we can conclude that the policy of conditional reimbursement is currently not as effective and efficient as was expected by policymakers. Analysis of expected versus observed volumes points at substantial unauthorized drug use in a number of cases. These findings were confirmed in five case studies that also suggested that adherence to professional clinical guidelines is higher than to restrictions related to conditional reimbursement. Interview data showed that conditional reimbursement generally is considered as a valuable instrument for improving the quality and efficiency of pharmaceutical care. However, respondents also identified a number of problems related to the policy measure's effectiveness, mainly concerning the communication of the conditional reimbursement regulation and the cooperation within its affected arena. The underlying bottlenecks of these identified problems; transparency, legitimacy, feasibility and commitment on the part of the stakeholders, should be dealt with for a successful implementation of the conditional reimbursement policy.

All respondents mentioned the lack of good and timely cooperation between policymakers and health insurers, medical specialists, patient organisations, and pharmaceutical industry. This lack of cooperation leads to a lot of 'noise' and delay in the communication. Under the current regime, this leads to a polarizing attitude among the different stakeholders. Practising physicians blamed health insurers for their policy regarding the reimbursement of certain drugs, but often proved to be

unaware of the fact that insurers merely execute a national policy. This lack of knowledge often results in a negative spiral of misunderstanding and miscommunication. Failing communication may be illustrated by the fact that many of the interviewed physicians and pharmacists were unaware of the additional conditions applying to statins and the thiazolidinediones. Also, both policymakers and specialists hold on to their definition of 'appropriate use', without communicating which definition should be used and why or how.

Actors in the field of health care expressed the opinion that the processes of selecting drugs for conditional reimbursement and defining the corresponding criteria were not transparent and ambiguous. The pharmaceutical industry and health insurers criticized the policy for a lack of transparency and accountability. The pharmaceutical industry questioned the consistency of decision criteria (e.g. clopidogrel) and thus its legitimacy. Therefore, they asked for the possibility to participate in the decision-making process. Also, representatives of patient organisations and physicians shared these concerns because inequalities in treatment regimes that are not evidence based are considered to be unjustifiable. In their view, a more consistent application of the regulation would increase its understanding and acceptance. Health insurers stressed the importance of their involvement in the decision-making process about conditional reimbursement, in order to improve the feasibility of the restrictions in daily practice. For example, central assessment committees proved to be efficient for some drugs, whereas authorization by the patient's health insurer, though potentially effective, was considered to be too time-consuming, very elaborative, and sometimes seen as interfering with the professional autonomy of physicians (e.g. cholesterol lowering therapy).

CVZ is the key stakeholder in the conditional reimbursement policy, and is responsible for its implementation in daily practice. However, the success of the policy is highly dependent on the commitment and cooperation of health insurers, medical professionals, patient organisations, and the pharmaceutical industry. This means that CVZ has to balance between policy goals set at a national level, and the feasibility of the policy measures in daily practice. From this perspective, CVZ first needs to improve its own commitment and display its pro-active involvement. In addition, they should improve the transparency, legitimacy, and feasibility of the system and enhance the commitment of other stakeholders. Improving regulations 'on paper' does not easily solve the lack of transparency. To improve the transparency of the measure, CVZ should take into account the different interests and goals of the stakeholders. Subsequently, CVZ should translate its own target into practical goals that are understood and can be implemented by the other stakeholders. Improving the legitimacy does not only mean the involvement of

stakeholders in the decision-making process, but also means giving the stakeholders enough space to adapt the regulations in such a way that these are optimally feasible in practice. In addition, feasibility problems may be anticipated by increasing the understanding on the part of CVZ of the organisational processes used in daily practice.

A transparent conditional reimbursement policy can only be reached when clear tasks are defined and all stakeholders know their responsibilities. The policy would benefit from a central and stimulating position of CVZ during the preparation, implementation and carrying out of the measure, with maximum involvement of other stakeholders. Intensive interaction between the different parties is needed to share experiences in the field of appropriate drug use, knowledge about recent scientific developments and available data on the appropriate use of medications. This knowledge can be used to continuously and timely update the conditional reimbursement regulations. National policymakers also should communicate more clearly towards the health insurers and field actors. The conditional reimbursement policy requires a pro-active attitude of the policymakers concerned. Good information at the beginning of the policy chain prevents problems later on. This pro-active attitude can be realized by improving the quality and accessibility of information, and by making the policy process more open for intermediate discussion.

Conclusion

Conditional reimbursement can be an effective and efficient tool for enhancing appropriate drug use. However, its implementation is hampered by a lack of transparency of the system, doubts about the instrument's legitimacy, blindness to feasibility, and a low commitment amongst medical specialists and pharmacists. Our analysis of the conditional reimbursement in Dutch pharmaceutical policy shows that controlling and sanctioning did not contribute much to its effect. Instead, its effect hinges on the way prescribing conditions are developed and especially on how these conditions changed the relations between clinical and policy practices. Rather than monitoring, it is the extension and involvement of the actors, their objectives and their mutual relationships that seemed to affect the clinical practice of drug prescriptions. Therefore bottlenecks should be simultaneously handled in close collaboration with the principal stakeholders, acknowledging the mutual dependency that exists between the various parties. Thus, taking into account the characteristics of the actors, their objectives and the relationships between them, seems to be a promising direction for the further development and use of the conditional reimbursement measure.

Box 2.A. The conditional reimbursement regime for five cases on 1 January 2004

Medicine	Conditional reimbursement regime	Testing authorized use
Clopidogrel	Only for an insured who, after a myocardial infarction or ischemic cerebrovascular accident or with a peripheral arterial disease, cannot be treated with acetylsalicylic acid because of hypersensitivity for acetylsalicylic acid or has another absolute contra indication for acetylsalicylic acid	Population: All patients who had received clopidogrel within one month after admission to the hospital for a cardiovascular event; Analysis: We examined medical records to confirm appropriateness of clopidogrel use given the diagnosed cardiovascular event; Database: Pharmo
Rosiglitazone and pioglitazone	Only for an insured suffering of diabetes mellitus type 2 who insufficiently responds to mono therapy with a sulfonylurea derivative and has contra indications or intolerance for metformin	Population: everyone who used thiazolidinediones at least once between 2001 and 2003; Analysis: we traced their medical treatment history to see if the specified step-up therapeutic pathway was followed; Database: GIP.
Etanercept[a]	Only for an insured with active rheumatic arthritis and an insufficient response to or intolerance for disease modifying antirheumatic drugs (DMARDs), including at least methotrexate except when methotrexate is contraindicated. The insured is only eligible for reimbursement when s/he is treated following clinical guidelines, by a specialist, and use of etanercept was authorized by the insurer	Population: everyone who used etanercept at least once between 2000 and 2003; Analysis: we traced their medical treatment history see if the specified step-up therapeutic pathway was followed; Database: GIP.
Growth hormone[b]	Only for an insured with growth hormone deficiency, who has not yet reached 18 years of age, the medicine is prescribed by an internist according to the 'Protocol use of growth hormone', each time for maximal one year, with prior authorization of the health insurance company; The protocol specifies how the diagnosis of growth hormone deficiency should be confirmed. It also specifies an effectiveness criterion (minimally expected growth in cm).	Patients: patients younger than 18 years of age, who started or continued growth hormone treatment between 1998-2002; Analysis: We examined their medical data included in the registry to see if the diagnosis was confirmed and if effect of growth hormone on growth met requirements; Database: National Growth Hormone Registry.

Box 2.A. The conditional reimbursement regime for five cases on 1 January 2004 (continued)

Medicine	Conditional reimbursement regime	Testing authorized use
Cholesterol lowering drugs	Only for an insured: suffering from familial hypercholesterolemia with a strongly increased chance of suffering from atherosclerotic cardiovascular disease as a consequence of a cholesterol level ≥ 8 mmol/l with at least one, or as a consequence of a cholesterol level 6 mmol/l at least two of the following additional risk factors: coronary artery hart diseases (CAHD) in the anamnesis; a family anamnesis of CAHD; diabetes mellitus; hypertension; and over 6 months a diet was not effective	Patients: all persons whose general practitioner initiated cholesterol-lowering therapy with statins in 2002 or 2003; Analysis: we examined their medical data to confirm the diagnosis of familial hypercholesterolemia, or the cholesterol levels and co-morbidity. We did not investigate if people had been on a diet; Database: IPCI.

[a] Presented are the conditions for reimbursement of etanercept in adults with Rheumatoid arthritis. The conditional reimbursement scheme further specifies when patients with juvenile arthritis, ankylosing spondylitis, and psoriatic arthritis are eligible for reimbursement of etanercept.

[b] Presented are the conditions for reimbursement of growth hormone in children with growth hormone deficiency. The conditional reimbursement scheme further specifies when patients with Turner syndrome and Prader-Willi syndrome are eligible for reimbursement of growth hormone.

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Chapter Three

Finding legitimacy for the role of budget impact in drug reimbursement decisions

Based on: Maartje G. H. Niezen, Antoinette de Bont, Jan J. V. Busschbach, Joshua P. Cohen, Elly A. Stolk. Finding legitimacy for the role of budget impact in drug reimbursement decisions. *International Journal of Technology Assessment in Health Care*, 25:1 (2009), 49-55. Cambridge University Press.

Introduction

It is widely acknowledged that effectiveness, cost-effectiveness, and severity of illness play or should play a role in drug reimbursement decisions (Briggs & Gray 2000; Drummond, Jonsson & Rutten 1997; Stolk, Brouwer & Busschbach 2002; Van Oostenbruggen et al. 2005). Lesser consensus can be found for the role of budget impact as an additional decision criterion. Especially health economists argue that the budget impact argument undermines cost-effective allocations, and therefore leads to suboptimal distributions of health in the populations (Niezen et al. 2004; Trueman, Drummond & Hutton 2001; Van Luijn 1999). Nevertheless, given increasingly stringent budget constraints, policymakers have a need to know what the impact of any new technology will be on their limited budget. Budget impact analyses provide such information (Mauskopf 2005, 1998; Neumann 2007). Budget impact refers to "the total costs that drug reimbursement and use entail with respect to one part of the health care system, pharmaceutical care, or the entire health care system, taking into account the possible reallocation of resources across budgets or sectors of the health care system" (Cohen, Stolk & Niezen 2007, p728). If, on the basis of cost-effectiveness information, a positive reimbursement decision is suggested, budget impact addresses the question of what amount of resources would be needed to implement the decision. For reimbursement purposes, several national health technology assessment agencies, including the Health Care Insurance Board in the Netherlands (CVZ) and the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, already require that drug manufacturers submit both cost-effectiveness and budget impact analyses of newly approved pharmaceuticals (Mauskopf 1998).

Advocates of the budget impact criterion point out that cost-effectiveness analysis fails to meet the needs of policymakers, whose overriding concern is not so much the cost-effectiveness of the interventions, but their budget constraints (Trueman, Drummond & Hutton 2001). Cost-effectiveness analysis does not address affordability. This is especially a problem when resource requirements for the funding of new technologies are relatively large. The precise role of budget impact and its rationale in drug reimbursement decisions have not been made clear in the literature. Whereas a small number of studies have addressed descriptions of methods for conducting budget impact analysis (Mauskopf 2005; Mauskopf et al. 2007; Orlewska and Mierzejewski 2004; Trueman, Drummond & Hutton 2001), the literature on drug reimbursement decisions is still dominated by formal cost-effectiveness and severity of illness-analyses. This may be due to the fact that budget impact is not perceived as a legitimate decision criterion, as it lacks scientific rigor; meaning rational use of evidence based, and explicit knowledge

(Bal and Lindeloof 2005). In this study, we outline current policy practices in which budget impact plays a role in drug reimbursement decisions. Next, we provide a synopsis of results gathered from interviews with eleven key stakeholders involved in drug reimbursement decisions in the Netherlands. Subsequently, we examine possible rationales underlying the use of budget impact as a decision criterion for resource allocation. In doing so, we hope to provide more explicit knowledge for the use of the budget impact as an argument for allocation in health care.

Method

Our initial examination of the role of budget impact as a decision criterion consisted of a literature search in PubMed covering the period 1990-2007. Instead of using Mesh or Emtree terms, we used more specific (combinations of) keywords; 'budget(ary) impact,' 'affordability,' 'drug reimbursement and budget impact / affordability,' and 'drug reimbursement and rationing / prioritization.' In addition, we used a snowball method to generate references starting with the milestone articles by Trueman, Drummond & Hutton (2001) and Mauskopf (2005). We supplemented the literature review by conducting semi-structured interviews with eleven key stakeholders involved in drug reimbursement decisions in the Netherlands (see Tables 3.1 and 3.2).

Table 3.1 Background of interview respondents

Organization	Employment	(N)
Ministry of Health	Policy associate Drugs and Medical Technology	2
Health care Insurance Board (CVZ)	Policy associate benefit package decisions	2
	CEO	1
Dutch organization for innovative drugs (Nefarma)*	Policy associate drug reimbursement	2
UMC St Radboud, Department of Epidemiology, Biostatistics and Health technology assessment	Health economist / scientific researcher	1
Canisius-Wilhelmina Hospital	CEO	1
The NVZ Dutch Hospitals Association	Policy advisor health care	1
Erasmus MC, Institute of Health Policy and Management	Professor in 'Societal aspects of hospital drug policy' and also a hospital pharmacist	1

* An umbrella organization for the Dutch innovative pharmaceutical industry

Table 3.2 Topic list semi-structured interviews

- How do you define budget impact?
- What is the relevance of budget impact as a criterion in drug reimbursement decision-making?
- When is budget impact used as a decision criterion?
- In what decision-process (e.g. budget re-allocation, admission to the benefit package, etc.)
- When is budget impact used in the drug reimbursement decision-making process?
- Is budget impact's use formally acknowledged (official reports on budget impact similar to cost-effectiveness and severity of illness)
- Is budget impact mere addition to cost-effectiveness information or can it trump cost-effectiveness and severity of illness arguments too?
- Can you name specific drug types (e.g. orphan drugs, drugs for life-style conditions) for which budget impact is most likely to play a role?
- Do you know of specific cases in which budget impact played an important role?
- What motives or argumentations are there to use budget impact as a decision criterion in resource allocation?
- Have you used budget impact analyses to guide your decisions?
- If yes, what was your motivation to do so?

The interviewees were selected on the basis of their involvement in reimbursement decisions of pharmaceuticals in which budget impact had been a major discussion point. The interviews were recorded and converted to transcripts, which have been hand coded to analyze the content of the interviews. The codes were discussed among the researchers (code words were, e.g., budget impact/costs, cost-effectiveness, objective/scientific rationing, uncertainty, opportunity costs, and equality) (Green & Thorogood 2004).

Current practice

Use of budget impact is very much a reality in current health care decision-making; policymakers use budget impact as a decision criterion in certain instances. Results from a multinomial modelling of NICE decision-making, for example, showed that interventions with a high budget impact were more likely to be recommended for conditional reimbursement and use, that is, *with restrictions*, holding clinical- and cost-effectiveness, as well as other considerations constant. The model showed that "[t]he potential budget impact [. . .] was significantly higher for those interventions that were recommended for restricted use than those recommended for routine use, without restrictions" (Dakin, Devlin & Odeyemi 2006, p358).

In the Netherlands, it appears that budget impact also played a significant role in a number of drug reimbursement decisions (Niezen et al. 2007). Some examples are the reimbursement decisions for clopidogrel, trastuzumab, and the entire class of statins. In 1999, CVZ advised the Ministry of Health to admit clopidogrel for all approved indications to the health benefit package, on the grounds of its favourable clinical- and cost-effectiveness profiles. However, because of its relatively high cost compared with existing therapy (acetylsalicylic acid), combined with the potential for substantial off-label use, CVZ recommended severe restrictions on the use of clopidogrel. Despite CVZ's recommendations, the Ministry of Health decided not to reimburse clopidogrel at all, citing budget limitations (Eijgelshoven et al. 2003; Niezen et al. 2004; Van Luijn 1999). Subsequent to the Ministry's decision, a successful legal challenge by the drug manufacture obliged the Ministry of Health to reimburse clopidogrel for all approved indications. Nevertheless, the Ministry has not reimbursed new indications for clopidogrel, and continues to place severe restrictions on its reimbursement and use. Again, the Ministry refers to high budget impact, due to the potential for substantial off label use in a large patient population (Amerongen 2003; Eijgelshoven et al. 2003). The Ministry of Health expressed similar concerns about the reimbursement of statins (Niezen et al. 2007). The large pool of potential users of statins suggests that a positive reimbursement decision would exert significant upward pressure on pharmacy expenditures. This reasoning led to the Ministry's decision to place conditions on the reimbursement of statins (Hoedemaekers & Oortwijn 2003).

Although reimbursement of statins for specific subpopulations may be explained by stratified cost-effectiveness analyses (across sub-populations), Niezen et al. (2007) show that strictly prescribing in accordance with the conditions of reimbursement imposed on statins entails under-treatment, according to the (evidence based) professional guidelines. This example demonstrates that budget impact likely played a role. A third example, the in-patient cancer drug trastuzumab (breast cancer), is generally seen as cost-effective. The drug's budget impact is high, owing to its relative high price per patient and the relatively high volume of breast cancer patients who would be considered eligible for its use. Recent research demonstrates that trastuzumab was unevenly distributed among patients in The Netherlands (Borstkankervereniging Nederland 2005). Although hospitals received additional funding for trastuzumab, the cost of the drug grew much faster than the assigned budget, causing great pressure on the hospital pharmaceutical budget (Niezen et al. 2006). Evidently, unequal access was caused in part by the 'intolerably' high impact unrestricted reimbursement has on the local budget of certain hospitals.

Interviews

Most interviewed policymakers confirmed that budget impact did play a role in certain specific cases, such as clopidogrel and sildenafil. Budget impact becomes a more important factor when the uncertainty regarding other criteria, such as cost-effectiveness and severity of illness is high. However, the interviewed policymakers could not explain how the budget impact criterion precisely interacts with effectiveness, cost-effectiveness, and severity of illness. The respondents confirmed that budget impact played a role, but that its role was intuitive or based on a 'gut feeling' (Respondent VIII, 2006). The most common reply was that "it depends on the other case specific factors". Moreover, policymakers did not provide a concrete definition of what is meant by budget impact and what budget impact analyses specifically assess.

> *I do not know the term budget impact very well, thus my understanding of it would depend on the context in which I encountered it, and not as part of my understanding of health economics. (Respondent X, 2006)*

The lack of clarity surrounding the concept 'budget impact' does not appear to hamper its use.

> *The higher the budget impact, the more therapeutic value there must be and efficiency determines the outcome, just because the effect on the budget is bigger. As uncertainty [regarding an intervention's effectiveness] increases, one could choose to be more reserved in deciding to fund. Nevertheless, patients' interests and therapeutic value are the focus of interest, also for the Minister [of Health]. Only, the Minister is also responsible for not exceeding growth targets and thus will be more critical. (Respondent IX, 2006)*

Policymakers have little incentive for formally discussing their concerns regarding the impact of reimbursement decisions on the (pharmacy) budget. Since reasonable arguments supporting the use of budget impact are lacking or not (yet) formulated, policymakers typically concentrate on using arguments of effectiveness, cost-effectiveness and severity of illness. Thus, policymakers rely on and interpret the available scientific, technical, and clinical data, contained in evidence based 'cost-effectiveness analyses' or 'health technology assessments.' Such analyses offer them the supposed promise of a rational grasp of, and concomitant 'control' over, health care decision-making (Bal and Lindeloof 2005; Berg, Van der Grinten & Klazinga 2004). Consequently, policymakers often rely only on information gathered from cost-effectiveness analyses to justify their decisions, instead of explaining how budget impact had an effect on the decision.

> *Because we really think it is important to maintain efficacy and therapeutic value, because yes. . . that forms the core of the decisions that we make. So that cost or what you call budget impact, that is at the bottom of the list. (Respondent VIII, 2006)*

> *Actually, we do not like the cost discussion. Because, indeed, in the case of clopidogrel, yes, we are not going to formally acknowledge it [cost or budget impact led to the decision]. And in the case of sildenafil, well, it felt more normal; you could explain more easily that we do not pay for erection disorders and that type of stuff. Yet, clopidogrel is sometimes a life-saving medication, although it is only so for one in a hundred users. But you do not want to go into a cost discussion. (Respondent VIII, 2006)*

The citations above show how uncomfortable policymakers are with formally acknowledging that budget impact plays a role in reimbursement decisions. Implicitly, budget impact already seems to have a place in priority setting, although explicitly budget impact seldom is used as an argument for denying a drug reimbursement outright or imposing conditions on its reimbursement, given that it appears to lack scientific rigor or a rationale.

Rationales in favour of the budget impact criterion

Although the respondents did not give explicit rationales for budget impact, literature does show some rationales that justify budget impact's use as a rationing criterion. These rationales comprise the opportunity costs of reimbursement decisions, the fact that each decision involves gains and losses that are evaluated differently, uncertainty and equal opportunity.

Opportunity costs

One of the main arguments in favour of using budget impact analyses found in the literature, is a deficiency in common cost-effectiveness analyses; opportunity costs are disregarded (Birch & Gafni 2006; Cohen, Stolk & Niezen 2007; Gafni et al. 2007; Harris 2001; Sendi, Gafni & Birch 2005, 2002; Sendi & Briggs 2001). Expansion of the benefit package will typically be considered when a drug has a favourable incremental cost-effectiveness ratio (ICER), suggesting that incremental health gains are worth the incremental costs. Most of the recently developed drugs, though, have positive cost-effectiveness ratios. Consequently, a positive reimbursement decision for a new intervention suggests the need to expand the budget for health care, or some of the existing benefits in the benefit package would have to be eliminated, to fund the new intervention. Whichever solution one chooses, there is an opportunity cost involved that must be considered. The opportunity cost of a positive reimbursement decision increases with the size of a

drug's budget impact. One will have to sacrifice increasing amounts – there is less to spend on other public programs or existing health benefits - to fund the new drug. The higher the opportunity cost, the more one has to sacrifice, the less likely it will be for a drug to be reimbursed.

Moreover, the opportunity cost argument necessitates a re-evaluation of the justification of the value of the incremental ICER thresholds and their use in decision-making (Gafni & Birch 2006; Sendi, Gafni & Birch 2002; Sendi & Briggs 2001). Health care payers operating within a constrained budget may deny reimbursement of new medical technologies with a high budget impact, because funding these interventions would lower the lambda (λ), or threshold ICER, which is equal to the ICER of the last program selected for reimbursement before the budget is exhausted. In other words, λ reflects the opportunity cost of marginal health care resources, or benefits foregone of the last unit of health care resources spent (Birch & Gafni 2006; Gafni & Birch 2006; Gafni et al. 2007; Sendi, Gafni & Birch 2005). A lower λ could mean that other pharmaceuticals, already in the benefits package, would no longer meet the threshold. However, because not all cost-effectiveness ratios of treatments included in the current benefit package are known, neither is λ known. Accordingly, Gafni & Birch (2006) suggest that policymakers require actual information on the opportunity costs of marginal resources. A possible approach to priority setting combining information on (opportunity) costs, cost-effectiveness, and health related benefits of drugs, is program budgeting and marginal analysis (PBMA). "PBMA addresses allocative efficiency by providing a systematic framework for maximizing health related benefits for a given budget considering both the outcomes from, and costs of providing, a range of services" (Peacock 1998, p.2).

Loss aversion; endowment effects

Policymakers may be more reluctant to exclude than to include drugs from the collectively funded benefits package. A shared feeling among policymakers we interviewed is that taking something away from patients that works and with which they are already familiar, outweighs the benefit of adding something new. This rationale is closely tied to opportunity costs. However, in this case, it directly concerns what happens when a treatment is eliminated from the benefit package. It reflects the people's tendency to prefer avoiding losses to acquiring gains. Budget impact makes it possible to consider the actual felt loss, the endowment effect, in rationing decisions. The higher the budget impact, the more one has to sacrifice, the more loss is felt by health insurance payers and patients and less likely the decision is accepted. To illustrate, a person who loses $100 will lose more satisfaction than another person will gain satisfaction from a $100 windfall. In turn,

there is a discrepancy between an individual's maximum willingness to pay for a good and the minimum compensation demanded to give up the good. There are several explanations for this phenomenon, described by Dupont & Lee (2002) including the 'endowment effect' which captures the overvaluation of a good that is in already in one's possession; the 'status quo bias' which describes the preference to remain in a current state; and 'prospect theory' where losses impact the agent's utility more than gains of the same magnitude (Dupont & Lee 2002; Kahneman & Tversky 1979). The inherent difficulty of having to exclude treatments from the current benefit package is increased by the fact that policymakers also have to choose which interventions to eliminate. However, they have no list of interventions which are ranked on unfavourable (cost-) effectiveness. Consequently, they have to justify their choices to society, and may fear the public backlash that may ensue as happened in the Netherlands concerning the IVF reimbursement policy (Ministerie van Volksgezondheid 2006). An additional complication is that society interpreted the social health insurance package as a 'social contract' which cannot just be broken from one side (Anand & Dolan 2005).

Uncertainty

A third rationale for considering budget impact in resource allocation decisions is uncertainty. Invariably, there is uncertainty about the actual cost-effectiveness of new health interventions (Harris et al. 2001). Likewise, in health care finance, the budget implications of expansion of the benefit package are usually uncertain, due to the fact that at the time of launch little is known about the extent to which a drug will be used (Niezen et al. 2007). It is simply hard to estimate the size of the user population. Will a newly approved drug only be used by those who suffer severely from a particular condition, or will it also be used by those who have a milder form of the condition? Similarly, a newly launched drug may experience a broadening of indications through off-label use, further increasing uncertainty (Al, Feenstra & Hout 2005). Programs may therefore require more resources than initially budgeted. In case reimbursement results in budget overspend, or when large deficits loom, uncertainty is a particularly acute problem. Uncertainty may explain why small-scale programs are often favoured over large-scale programs (Harris et al. 2001). Policymakers have to adhere to strict budgets and therefore must consider opportunity cost. Typically, the potential for large deficits increases with the size of the patient population. Hence, policymakers prefer to diversify their 'investments', which leads to an improved handling of uncertainty regarding unexpected costs, and a concomitant reduction in the risk of overspending (Sendi, Al & Rutten 2004). Thus, a large budget relates to more uncertainty and an increased need in a more precise budget impact analysis.

Equal opportunity

Budget impact may also play a role in reimbursement decisions as a way to preserve equal opportunity. Policymakers appear to allocate resources to all people who suffer from a disease, irrespectively of the (cost-) effectiveness of treatment. This reflects a viewpoint of justice, that is, that people favour an equal distribution of health resources regardless of each person's potential to benefit from those resources. This concern with equality works two ways: it explains the tendency to reimburse ineffective treatments for rare diseases or small groups, and also the tendency not to reimburse certain treatments with high budget impact (Ubel et al. 1996). For example, there are orphan drugs with unfavourable cost per QALY ratios, which are funded nevertheless, for example, imiglucerase and laronidase (McCabe, Claxton & Tsuchiya 2005). Positive decisions to fund orphans appeal to the fact that the number of patients taking each orphan drug is very small, therefore the budget impact is limited (Cohen, Stolk & Niezen 2007). When all orphan diseases are taken together, however, it is estimated that 1 in 12 people in Europe have a rare disease. This is a fairly large group to make exceptions for (Cohen, Stolk & Niezen 2008). There are also instances in which costly, yet cost-effective medical interventions, would consume more resources than available, if given to all eligible patients. Consequently subsidized access to the intervention cannot be guaranteed to all patients. In such circumstances, "people [appear to] place greater importance on equity than is reflected by cost-effectiveness analysis" (Ubel et al. 1996, p.1174) and would therefore rather choose a less cost-effective intervention available to all, than a very cost-effective intervention for some. Budget impact analysis can then be used to assess whether it is affordable to offer the cost-effective intervention to the entire patient population so that equal opportunity can be guaranteed, or whether instead a less cost-effective intervention can be offered to the entire population. Similarly, the rationale of equal opportunity explains why policymakers might prefer to preserve resources rather than spending most of it at once.

Policy implications

Budget impact, we demonstrate in this article, plays a role in drug reimbursement decisions. Also, we demonstrated, Dutch policymakers do not easily admit that they consider budget impact. In fact, policymakers are reluctant to explicitly use budget impact as a formal criterion. Therefore, this study is relevant for policymakers who, to remain accountable by the public at large, are confronted with a transparency requirement.

This study identified four rationales for considering the budget impact of new drugs when a decision needs to be made about reimbursement. The first rationale is opportunity costs: a positive reimbursement decision for a new intervention suggests the need to expand the budget for health care, or to eliminate existing benefits to fund the new intervention. Whichever solution one chooses, there is an opportunity cost involved that must be considered. The second rationale relates to loss aversion: people may be generally unwilling to eliminate funding for existing benefits in favour of a new intervention. Budget impact considers the felt loss by assessing the amount of resources needed to make free. Third, budget impact is considered in relation to decision uncertainty. Fourth, people seem to favour an equal distribution of health resources regardless of each person's potential to benefit from those resources, reflecting equal opportunity concerns. These four theoretical rationales indicate budget impact's relevance in reimbursement decisions.

Economic consequences of positive reimbursement decisions, we argue, are not sufficiently explored when only cost-effectiveness of a new product is considered and not its budget impact. Therefore the question is how to integrate budget impact into a framework for reimbursement decisions that is based on cost-effectiveness. The application of cost-effectiveness is not as simple and straightforward as it is often advocated, due to inflexible budgets, risk of overspending, and political pressures. For example, budget impact can trump the cost-effectiveness argument. An unfavourable ICER for a pharmaceutical treatment is less relevant to the policymaker when the total budget impact is low. Conversely, an adequate ICER can be trumped when the budget impact is high. However, what levels of budget impact and cost-effectiveness warrant such tradeoffs? We need to identify conditions under which a decision-maker can comfortably withhold or initiate treatment, and can be assured of a tolerable balance between the conflicting concerns. If guidance is lacking, the cost-effectiveness criterion cannot be put to its full potential, consistency of decision-making is at risk, and decision-makers will be vulnerable and exposed. Therefore, we need an open discussion to define what is acceptable or unacceptable. Such a discussion should also shed light on the motives for considering budget impact, because we need to acknowledge the fact that budget impact and cost-effectiveness analyses can be assessments based on different distributional and egalitarian rationales, namely equal opportunity and maximizing health. If budget impact is considered mainly because of the equal opportunity rationale, it is considered fair to ensure treatment for all patient groups, irrespective of the total health outcomes achieved. In other words, this particular rationale for budget impact calls into question if it is fair to allocate resources on the basis of a utilitarian principle; the equal opportunity rationale reflects that people may also strive for resource allocation fairness by some form of procedural justice

that ensures availability of treatment for all. Implications for the decision-making framework will then go beyond the need to facilitate application of cost-effectiveness, and require rethinking of the basis for resource allocation decisions.

Policymakers walk a fine line between increased transparency and increased efficiency; between specifying which criteria are used and how they should be used in explicit, evidence based assessments, and providing information within a reasonable time-frame taking into account an implicit "societal correction" on the technical assessments to guarantee decisions are fair (Braat, Van Rijen & Ottes 2007). Inevitably, certain decision factors remain implicit, partly because policymakers lack the time to reflect thoroughly on the decisions that they believe are sound, and also because they do not want to expose themselves to criticism from the public at large. Nevertheless, as we and others have shown, when put to the test of accountability, policymakers fail on account of their inadequate attempts to explain certain key policy decisions (Ham & Coulter 2001). In this study, we have demonstrated that budget impact can and should be openly discussed as a legitimate criterion in the context of drug reimbursement decisions. Open discussion of budget impact's role will enhance policymakers' accountability.

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Chapter Four

Reconfiguring policy and clinical practice: How databases have transformed the regulation of pharmaceutical care?

Based on: Maartje G.H. Niezen, Roland Bal, Antoinette de Bont. Reconfiguring Policy and Clinical Practice: How Databases Have Transformed the Regulation of Pharmaceutical Care? Accepted for publication in *Science Technology & Human Values*.

Introduction

Health policy is saturated in information technologies (Fox, Ward, & O'Rourke 2006; Roos, Menec, & Currie 2004). Paper-based records and scattered databases have been replaced by electronic records, data warehouses, and national population-based registries (Bowker 2005; De Mul, Adams, & de Bont 2009). As more and more clinical data are stored electronically, efforts to accumulate and organize it have increased. Furthermore, since it is now available in relatively easily accessible forms, clinical data have become both an object (something to be managed) and an instrument (something to manage with) and thus vital to a range of clinical, organizational, and governmental practices (Freeman 2002).

The aim of this chapter is to understand if and how the efforts to accumulate and organize clinical data and the increasing use of databases[1] in clinical, research, and policy practices have transformed the regulation of clinical practices. Data infrastructures such as databases mediate between clinical practitioners and regulators; the same data retrieved from clinical practice are used in clinical and policy practices and affects both. Databases can, first, facilitate self-regulation and quality assurance by national professional bodies, thereby allowing regulatory authority to be delegated to clinical practices (de Bont, Stoevelaar, & Bal 2007). They can also act as instruments of oversight. Data retrieved from local clinical practices can be stored externally in distant databases, which policymakers use for regulatory purposes (de Mul, Adams, & de Bont 2009; Waring 2007; Orr 2009). With access to detailed clinical data, policymakers believe they can impose order on clinical practice. For instance, health care policymakers can use clinical data to decide which therapies for which individuals should be reimbursed by health insurers.

This chapter's focus lies on how databases shape and are shaped by clinical and policy practices. Our empirical material derives from a study of the regulated use of pharmaceuticals in the Netherlands. Since late 1990s, the Dutch government has supported the development of clinical databases in order to gain insight and simultaneously construct evidence of the effectiveness of some expensive medicines in daily practice. In 2001, the Growth Hormone (GH) Database was the first clinical database employed to control the use of an outpatient drug. Similar databases have been developed for five outpatient medicines considered

[1] The concept 'databases' in this article can be seen as a synonym for 'data registries'. Whereas in the field of outcome research one prefers to speak of data registries, we have chosen to use the concept of 'databases' as used within Science and Technology Studies. It refers to the infrastructure allowing for the collection and processing of data as well as the data stored in these databases.

expensive at the time: antiretroviral therapy, paclitaxel, Interferon Beta, imiglucerase, and tumor necrosis factor-alpha (TNF-a) blockers[2]. In 2006, this form of regulation was extended to inpatient medicines. The Population-Based Haematological Registry for Observational Studies (PHAROS) is one of the first registries monitoring inpatient medicine use. The registry collects population-based data of especially new and costly treatments of three major haemato-oncological diseases, non-Hodgkin's lymphoma, chronic lymphocytic leukaemia, and multiple myeloma in daily practice. In this chapter, we reconstruct the employment of the GH Database and PHAROS registry.

The setup of the chapter is as follows. In the next section, we introduce the work of Beaulieu, Keating & Cambrosio, and Hine about the employment of databases. Their work provides a perspective to understand if and how the use of databases reconfigures the relation between clinical and policy practices (Keating & Cambrosio 2004; Hine 2006; Beaulieu 2001). Instead of studying the contribution of information to science, policy, or practice, these studies focus on how technologies take part in and contribute to forming policy practices. As Keating and Cambrosio (2007) have described, science depends upon regulations, especially in fields where evidence is collected collaboratively -such as in pharmaceutical research and other fields in biomedicine (Keating & Cambrosio 2007). In these settings, 'regulatory work' as embodied in the information infrastructures becomes a constitutive component of clinical work (Cambrosio et al. 2006; Keating & Cambrosio 2007). In the Regulatory Work in Clinical Practice section, we reconstruct the regulatory work that was needed for the collective production of data. Moreover, we explore the use of internal clinical practice regulation for external oversight. In the Collective Internal Regulation and External Supervision section, we aim to understand how the way 'evidence' or what is considered 'objective data' is constructed, may lead to new forms of regulating medicines. We explore whether and how these new forms of regulation in clinical practice changed the relation between clinical and policy practice. In our discussion, we summarize our findings and argue that databases not only have transformed the regulation of clinical practice but also have reconfigured and complicated the relation between policy and clinical practice too.

[2] For the treatment of HIV (antiretroviral therapy), lung, ovarian, breast cancer, head and neck cancer, advanced forms of Kaposi's sarcoma and the prevention of restenosis (Paclitaxel), multiple sclerosis (Interferon Beta), Gaucher's disease (imiglucerase) and rheumatic arthritis, Crohn's disease, psoriasis and colitis ulcerosa (TNF-α blockers), respectively.

Regulatory work and objectivity

In this section, we take a closer look at the notion of objectivity to understand the intermediate role of databases between internal and external regulation of clinical practice. In her study on the Human Brain Project, Beaulieu (2001, 2004) shows how repositories shape and are shaped by a particular notion of objectivity—digital objectivity (Beaulieu 2004; Beaulieu 2001). Digital objectivity refers to a mechanism for the production and validation of knowledge (pooling data) making use of quantification, standardization, and automation, and a search for bypassing human judgment. According to Beaulieu (2001), digital technologies such as cameras, scanners, and computer technologies provide interfaces which prescribe or regulate how to work and handle data methodologically since they standardize and automate work practices. Subsequently, digital technology has led to the introduction of new elements of control and restraint. The digital atlas is not only a research tool combining and integrating the various versions of the brain produced by the different disciplines in neuroscience; it also is built up into data sets that have a normative potential. For example, the individual scan which varies from the norm is marked on a brain map (Beaulieu 2001).

Cambrosio et al. (2006) take a next step in the construction of what is considered ''objective.'' By studying the collective production of evidence in biomedicine, they introduced the notion of ''regulatory objectivity'' (Cambrosio et al. 2006). The term regulatory objectivity refers to ''a new form of objectivity (. . .) that generates conventions and norms through concerted programs of action based on the use of a variety of systems for the collective production of evidence'' (Cambrosio et al. 2009, p.654). The authors demonstrate that the work of biomedicine practitioners in the laboratory and the clinic depends upon a network of conventions that must be considered to conduct a single measure or to make a certain diagnosis. The conventions range from sometimes tacit and unintentional to formal modalities (Cambrosio et al. 2006, 2009). According to Cambrosio et al. (2006), regulatory objectivity thus ''turns the focus away from objects toward collective forms of expertise combining people (clinicians, researchers, administrators, patients, etc.) and objects (entities, instruments, tools, techniques, etc.) connected by specific coordination regimens'' (Cambrosio et al. 2006, p.194).

Digital and regulatory objectivity are distinct from other notions of objectivity, such as mechanical objectivity (Porter 1992, 1995), because of their unprecedented levels of reflexivity (Cambrosio et al. 2006; Keating & Cambrosio 2009). This reflexivity points at the deliberate and conscious formation of internal consensus on how to proceed objectively as part of the continual and endogenous development of regulation within (clinical) practice. Within the framework of regulatory objectivity,

the process of reaching consensus is as important as the object of the resulting convention (Cambrosio et al. 2006). Medical professionals organized in groups across hospitals / institutions (and different from the professional associations) make collective agreements. These agreements, which are seen as the current state of evidence, are transformed into guidelines or standards. However, new scientific findings or new configurations of practices may open up the conventions previously taken for granted; the evidentiary hierarchies start changing and previously established agreements on the 'evidence' are reopened (Thevenot 2009). The regulatory objectivity framework revolves around the configuration of shared rules of action in the submission, definition, and collective investigation of 'uncertainty' (Cambrosio et al. 2009). The temporary agreements needed for internal regulation are under constant scrutiny and actors involved in the consensus process raise doubts about the reached 'conventionality' based on, for example, ongoing research. It is exactly this uncertainty of the 'conventionality' that glues the collective together and contributes to the dynamic and reflexive character of the process (Moreira, May, & Bond 2009; Rabeharisoa & Bourret 2009). In the following sections, we analyze the development of databases for the regulation of expensive medicines in the Netherlands to come to an understanding how such dynamic reflexive processes affect clinical and policy practices.

Regulatory work in clinical practice

Since the early 1990s, the Dutch government and its relatively autonomous agencies have undertaken much effort to regulate pharmaceutical care stringently, mainly by emphasizing the role evidence should have in decision making on the appropriate use of drugs at all levels, from decisions on insurance schemes coverage to prescriptions at the point of care (College voor Zorgverzekeringen 2007; Commissie Dunning 1991; Gezondheidsraad 1991). The Dutch government has developed a series of tools to promote rational prescribing—such as professional guidelines authorized by state agencies, real-time monitoring systems, and expert committees that must authorize prescriptions -aimed at improving the quality and efficiency of care, and enabling the control of pharmaceutical health care expenditure (College voor Zorgverzekeringen 2005; Niezen et al. 2007). One specific measure is the conditional reimbursement regulation (Schedule 2 of Health Insurance Regulation[3]) which makes the reimbursement of particular medicines conditional to specific criteria or rules. For example, the use of medicines is restricted to specific categories of patients (e.g., based on indications) and/or place in treatment lines (e.g., step-up treatment).

[3] The Health Insurance Regulation regulates the execution of the Dutch Health Insurance Act (ZVW).

Emphasizing the need for evidence-based policy allowed for the redefinition of 'appropriate use' of medicines in terms of diagnosis, cost-effectiveness, and effectiveness as happening within clinical practice. This redefinition enabled decision-makers to request data from clinical practice in the first place. Moreover, the new notion of appropriate use seems to have legitimized the regulation in the view of decision-makers; it makes it more logical to keep track of a pharmaceutical's cost and effectiveness in clinical practice and to connect its additional funding to the delivered cost- and pharmaceutical effectiveness of care or categorization of diagnosis.

In this section, we take a closer look at the regulatory work in clinical practice and the use of internal clinical practice regulation for external oversight. We base our research findings on an exploration of two databases in the Netherlands: the GH Database and the PHAROS registry (on expensive oncolytics such as Ibritumomab tiuxetan and Alemtuzumab). We conducted individual interviews (N = 61) and focus group interviews (N = 5) to collect data on the two databases in the period 2003-2009. The respondents were decision-makers, health managers from the pharmaceutical industry, as well as health insurers, academic researchers, and medical professionals. We audiotaped and transcribed verbatim the interviews as well as the focus group sessions. In addition, we observed conferences and informal meetings, and analyzed minutes, e-mail exchanges, and policy documents including documents from archives of the main policy actor, the Health Care Insurance Board (College voor zorgverzekeringen, CVZ).

Regulating growth hormone

In 1998 it became possible to produce GH outside the human body. As a result, GH turned from a scarce drug into an expensive drug. Subsequently, policymakers requested GH monitoring. Not only because the treatment is expensive (€23,000 per treatment per year in 2004), but also because the number of treatments could increase. GH treatment is indicated foremost for children with growth hormone deficiency (GHD), whose bodies do not produce sufficient GH (somatotropin) levels which results in growth failure. The treatment, however, could be broadened to other indications than GHD.

In an attempt to control costs, a clinical guideline focusing on the diagnostic criteria to determine GHD was authorized by CVZ. Since health insurers are only allowed to cover GH treatment if patients are diagnosed and treated according to this authorized guideline, the diagnostic criteria derived from clinical research and experience (the professionals' guideline) became a policy tool. Additionally, clinicians were obliged to lodge patient data in a national GH Database (a former

multicenter trial database) including laboratory test results, dosage, and possible tumours, managed by the National Registration of Growth Hormone (Landelijke Registratie Groeihormoonbehandeling, LRG).

The GH database shows how data registration represents a mechanism for the production and validation of knowledge.

> *Respondent 1: Here it [GH registration] is a combination of prevention of excessive use of an expensive medicine with the simultaneous collection of an amount of knowledge on such a medicine [GH] which is also useful, and which can diminish its use in the future. For example, now we see that the dosages go down. (Medical professional, 2003)*

Regulation of appropriate medicine use, thus, required pooling data from individual patient records into a national database, and subsequently allowed for gaining knowledge on GH dosages. Moreover, lodging patient data in the GH database required the quantification and standardization of clinical practice. Previous diagnostic criteria were transformed into numerical thresholds, determining the different patient categories by severity and likelihood of GHD (Table 4.1).

Table 4.1 Patient categories by severity of growth hormone deficiency and likelihood of growth hormone deficiency

Patient category	Technical description	Likelihood of diagnosis GH deficiency
Category 1	Very low maximum GH level (<5 mE/l) and very low IGF-1 or IGFBP3 <P3	Certain
Category 2	GH peak value < 10 mE/l en IGF-I of IGFBP3 <P50.	Almost certain
Category 3	Combination of GH peak value < 10 mE/l and IGF-I of IGFBP3 > P50 Or: GH peak value 20-30 mE/l and IGF-I of IGFBP3 <P50	Probably partial deficiency
Category 4	GH peak value 20-30 mE/l and IGF-I of IGFBP3 <P3	Possibly partial deficiency
Category 5	GH peak value 20-30 mE/l and IGF-I or IGFBP3 between P3 and P50.	Low probability
Category 6	GH peak value > 20 mE/l and IGF-I or IGFBP3 >P50	Unlikely
Category 7	GH peak value > 30 mE/l and IGF-I or IGFBP3 <P3	Probable Laron-type dwarfism

Source: (Ziekenfondsraad 1997)

The registration of data on GH diagnoses and prescription in a database not only allowed for the production and validation of knowledge, it also introduced an element of control. The obligation of data lodging made it possible to control the diagnosis and reimbursement of GH treatment. The patient record changed from 'notes' on a patient's condition to 'obligatory fields' to fill in. Only when all the boxes are checked, and the diagnosis is made according to the predefined categories, will a patient receive pharmaceutical treatment with GH. Patients placed in categories 1-4 in Table 4.1 should be treated with GH, and their treatment is eligible for reimbursement (Ziekenfondsraad 1997). A specialists' forum should make the decision for patients in category 5, as the diagnosis of GH deficiency is less certain for these patients. All requests for treating patients in categories 6 and 7 should be rejected. With data retrieved from the patient records it becomes possible to check whether patients treated with GH are classified in categories 1–5 and that none of the patients receiving GH are actually in categories 6 and 7 (see Table 4.1).

> *Respondent 2: . . . I mean, nowadays it is so easy . . . It goes into the computer and then you can work on, look at and do things with [the data] . . . ehm, I think that is the right thing to do since each clinic only has a limited amount of patients. Therefore we don't know how patients are treated in The Netherlands overall, or how we perform as paediatricians, for example, in growth hormone treatments. (Medical professional, 2004)*

The formalization of clinical (research) practices has brought database use into the decision-making process and has enabled the development of monitoring functions within medical practice that were formerly located in the realm of policy. The database forms part of the work needed to 'objectify' clinical work.

Regulating oncolytics

In 2006, conditional reimbursement regulation was extended from outpatient medicines to inpatient medicines through the High-Cost Medicines Policy Regulation (Beleidsregel Dure Geneesmiddelen, BDG[4]). The BDG regulates the additional funding of hospitals for expensive medicines. Importantly, this regulation includes evidence development on the effectiveness and cost-effectiveness of listed medicines in clinical practice after market approval. The BDG was installed to speed up the introduction of new inpatient medicines. New treatments for patients with haematological malignancies are constantly introduced, and are also subject to ongoing adaptations (e.g., different doses, introduction at other treatment stages

[4] The High-cost Medicines Policy Regulation (Beleidsregel Dure Geneesmiddelen: BDG) is maintained by the Dutch Health Care Authority (NZa) and is based on Article 57 of the Health Care Market Regulation Act (WMG).

and in new combinations with other treatments). To counter the rapid introduction and reimbursement of these new medicines, policymakers ensured that the BDG was introduced with the prerequisite to maintain the option to reconsider earlier reimbursement decisions. Whereas in the past the regulation of expensive medicines was based on the (modeled) outcomes of trial research and fitted within a 'yes' or 'no' reimbursement regime, the BDG shows a new and broader view toward the assessment of appropriate medicine use. It is based on ongoing data retrieval from clinical practice demonstrating effectiveness in daily practice. The conditional listing is used by policymakers to collect 'missing' data to decide on a pharmaceutical's effectiveness in practice and on further reimbursement. Data must be collected for three years on a medicine's cost-effectiveness and effectiveness in clinical practice (College Tarieven Gezondheidszorg 2002; Nederlandse Zorgautoriteit 2006; Nederlandse Zorgautoriteit 2008).

Like the GH Database, PHAROS is built upon an existing registry -a regional cancer registry that is part of the Dutch Cancer Registry- in combination with follow-up data retrieved from medical records. Oncolytics thus have a history of registration in medical practice and will continue to be registered. Since 1989, the Dutch Cancer Registry has been collecting data on cancer patients in order to map the national occurrence of cancer (see http://www.ikcnet.nl). The regional cancer registry contains medical data on patient, disease and treatment (tumour identification, diagnostics, and treatment), and administrative data concerning other characteristics (name, date, address, etc.) of all cancer-diagnosed patients from the cooperating hospitals in the region.

> PHAROS will look at the influence of newly introduced diagnostic- and therapeutic developments on the care delivery process and its outcomes. (. . .)
>
> PHAROS serves for scientific sound reporting on the amount of influence newly introduced so-called expensive medicines have on costs and especially benefits. This way, the data in PHAROS can also be used for cost-effectiveness analysis, as meant by the High-Cost Medicines Policy Regulation. (Uyl & Huijgens 2009, Description PHAROS project translated by MN)

The data stored in PHAROS enables the detection of: trends in diagnostics, treatments, treatment results, and survival for patients with haematological malignancies. PHAROS also enables the analysis of the effective use in daily practice of two high-cost medicines: Ibritumomab tiuxetan and Alemtuzumab.

> *Respondent 3: Most important is that the medical professionals are provided with a tool [the PHAROS database] that can enhance the quality of care. And suppose this database shows that on average only three courses of treatment with medicine X are provided . . . that is rather remarkable since the label states that eight*

> *courses should be given. These are the kind of munitions which medical professionals can use to discuss appropriate treatment. Thus, a database can enhance the quality of care and simultaneously allows for monitoring whether treatment according to guidelines occurs. If there is no guideline adherence, the medical professionals should discuss whether the provided treatment is inappropriate or guideline adjustments are required. (Employee Pharmaceutical Manufacturer, 2008).*

With the PHAROS databases, physicians took on the obligation to achieve results that matched with the results of a clinical trial. As shown in clinical trials, appropriate drug use can only be achieved in clinical practice if the same or similar guidelines are followed and similar patient groups are selected. Yet in the particular context of Ibritumomab tiuxetan and Alemtuzumab used in tertiary cancer care (PHAROS) -and most other cancer treatments on the BDG list- medical practice is already highly regulated and preregistration research is highly protocolized. Therefore, the difference between the regulations in trial settings and clinical practice is relatively small.

> *Respondent 4: In some cases the situation in clinical practice is controlled to such an extend, that, for example with regard to the hematological diseases, you can almost say it matches a randomized clinical trial. The patients are so tightly monitored that the border between clinical practice and an experimental setting just isn't that rigid anymore. (Policymaker CVZ, 2008).*

The protocols used for Ibritumomab tiuxetan and Alemtuzumab in clinical trials are also used in daily practice after their market authorization and thus continue to dominate the use of oncolytics in clinical practice after their registration. However, the effectiveness in daily practice differs from the trial settings due to, for example, more variation in the patient groups and, more importantly, ongoing insights in pharmacotherapy. It is such differences, alongside the continuation of data collection, that are the object of continuous reflection.

PHAROS combines clinicians, researchers, and so on from various disciplines in order to reflect upon, shape or adjust the conventions and regulations in clinical practice, with the aid of objects such as information systems combining clinical and administrative data, protocols, and methodologies. The PHAROS data and conventions are discussed at least twice a year by the various actors in the PHAROS collective.

> *Respondent 5: The steering committee on the data registration of expensive oncological medicines meets once every six to eight weeks. Professor Z takes her two PhD-students with her and together we take a look at the data generation and*

> *registration . . . The committee also includes representatives from the Health Care Insurance Board [CVZ]. (Medical professional, 2008)*

These discussions not only lead to innovative treatments but also give shape to an innovative form of regulating clinical practice. To assure quality of treatment as well as maintain both up-to-date and effective treatments, the PHAROS collective depends upon an arrangement of conventions (data collection, data analysis, and discussion) which must be considered when prescribing or adjusting appropriate doses of Ibritumomab tiuxetan and Alemtuzumab, possibly in combination with other treatments. What is considered up-to-date, effective and assured quality of treatment has become the subject of formal regulations and reflections.

Externalization of regulatory work in clinical practices

It may not be a coincidence that both databases we explored are used to control already highly regulated medicines. Prescribing these expensive medicines is often preserved for specialized medical centers. Highly protocolized health care practices, such as GH treatment and tertiary cancer care, enable the collection of standardized data. In both cases, the data registries predated the government's prerequisite of data collection for financial compensation. In fact, the development of both databases is closely connected to the development of guidelines and protocols. The GH guideline has been developed at the request of the Dutch Minister of Health in order to ensure the GH treatment was provided appropriately, meaning, according to the conditional reimbursement regulation. This official national GH treatment guideline mainly determined what data are collected in the GH Database (1998-2001). Therefore, while the definition of the different patient categories for GH treatment (Table 1) points to a situation which is both protocolized and easily quantifiable, it actually is the result of much foregoing work; the bureaucratic innovation preceding the development of data collection technologies (Bowker 2005). Similarly, the tertiary cancer care involves much preregistration research, which requires highly protocolized practices. Therefore, it may not be coincidental that most of the medicines listed in the BDG are used in cancer treatments (seventeen of the thirty by October 2008). In this way, government regulation is based on the regulatory work of the clinic which is assessable through guidelines, protocols, and data collection. Both cases depict a history of regulatory work, the registration of clinical data, and prior bureaucratic innovations such as guideline development within clinical (research) practice. Data registration merely has facilitated the externalization of the regulatory work already inherent and constitutive to clinical practice (Keating & Cambrosio 2004; Cambrosio et al. 2006; Keating & Cambrosio 2009).

Collective internal regulation and external supervision

It appears that regulatory authority is delegated to a network of physicians, who achieve control by self-regulation and uphold quality assurance. Would the presence of internal regulation and the externalization of the regulatory work within clinical practice, allowing for policymakers to supervise appropriate pharmacotherapy and its reimbursement, then mean that the gap between policy and practice has been bridged? In this section, we explore whether and how databases changed the relation between clinical and policy practices, using the GH and PHAROS cases as an example. In particular, we focus on how databases construct 'evidence' or 'objective data' potentially leading to new forms of regulating medicines. We follow the dynamic process of the constant adjustment of conventions on appropriate medicine use within clinical practice, and its relation to the construction of evidence informed reimbursement regulations.

Adoptions in GH guidelines and reimbursement decisions

The GH case shows how the collective shaping of clinical practice regulation was formed around the uncertainty of unknown side effects of GH treatment. Dutch paediatric endocrinologists meet four times a year in the Advisory Group on Growth Hormone (AGH). On the request of the AGH, the LRG analyses the GH database data. The LRG, for example, compares all patients with partial GHD and reports on the clinical results of their treatment. These data are then fed back into the guideline-development process. Draft revisions of the guideline are discussed with all paediatric endocrinologists in the Netherlands at their annual meetings. The purpose of these discussions is to reach shared agreements on best practice. If these agreements are reached, all paediatric endocrinologists receive an update or a supplement to the guideline. The following two quotations depict how the diagnostic criteria of GHD, and its categorization, have become the subject of clinical practice's reflexive assessment.

> *Respondent 6: There's also much debate on . . . Let's put it this way, there's a lot of discussion whether you should treat all people who meet the criteria. That is what is heavily debated.*
>
> *Interviewer: Where do these debates then take place?*
>
> *Respondent 6: Ehm, mostly on conferences and within the literature. The question is if someone who meets the standard criteria . . . , who, according to the tests, of which I believe the ITT is de most important test, is eligible for growth hormone treatment, should also be given the growth hormone. (Medical professional, 2004)*

The GH database allowed for internal consensus on how to proceed objectively, as part of the continual and endogenous development of regulation within (clinical) practice.

> *Respondent 7: The indications have shifted. For example, if we think this is a neurosecretory dysfunction we used to have a problem with how to act upon this, what norms we should use and so on. Well, at a certain point in time the Advisory panel Growth Hormone has documented this; this is the way we define neurosecretory dysfunction in The Netherlands. When in doubt a growth hormone profile should be made. In the past these growth hormone profiles in turn would be point of discussion; "What are the normal values? Is there a difference between laboratory results?" Well, these normal values have been documented and the laboratories have been aligned. In this sense, the GH database has offered a clear threshold. (Medical professional, 2004)*

In 2005, the LRG presented more detailed data about patients who use GH (see Table 4.2). In the report to CVZ, the professionals concluded that 2 percent of the patients treated with GH should not have received the drug according to the guideline. The policymakers disagreed. According to them, 13 percent of the patients did not meet the formal indication criteria for GH treatment and thus for reimbursement. Whereas the policymakers compared the decisions to treat patients with the predefined decision framework -the published and authorized guidelines- the professionals referred to the most recent guidelines. Over the years, professional norms and more specifically the guidelines shifted as scientific work progressed. The database and its infrastructure allowed for the continual adaptation, updating, and modification of the side effects and diagnostic categories. Accordingly, the technical description of the patient categories and the likelihood of diagnosis GHD changed. Subsequent to a new indication, the professionals adjusted their clinical guidelines whereupon the first authorized GH guideline became outdated, as the LRG explained. This continual and reflexive assessment of the uncertainty around the formation of GH regulation is endogenous to and essential for the dynamics in the GH network. Yet, CVZ insisted that 13 percent of the decisions to treat GH were inconsistent with existing regulations. Despite requests for more explanation and additional investigation and several meetings, policymakers and professionals did not come to an agreement. Regardless of the formal national regulations the professionals seemed to feel it was unthinkable to go against their professional norms. CVZ took the opposite stance and seemed to find it unthinkable to go against national regulations, especially as the professionals shifted their norms without informing policymakers and patient representatives.

Table 4.2: Distribution of decisions according to CVZ authorized and updated professional guideline

Diagnosis	Categories	Distribution of patients according to CVZ authorized guideline	Distribution of patients according to updated professional guideline
Certain GH deficiency	Categories 1-4	84%	96%
Uncertain GH deficiency	Category 5	2%	2%
Certainly no GH deficiency	Categories 6 and 7	13%	2%

GH: growth hormone
Source: (de Bont, Stoevelaar & Bal 2007)

CVZ had no problem understanding the explanation given. The problem was, as a CVZ employee explained in an interview, ‘‘how to rule when the rules change.’’

With the introduction of the GH database, meant to supervise and regulate clinical practice, the relation between CVZ and the professionals became less defined by the interpretation of the regulations. In fact, the relation became more defined by standards and the knowledge of professionals as embedded in the database and translated to updated guidelines. Not only did regulations change guidelines, the guidelines also changed the regulations. With that, new adoption problems between policy and practice emerged. In the GH case, the collective production of evidence ultimately, rather than bridging the divide between clinical and policy practice, rearticulated the relationship between the two in terms of differing time frames or, more specifically, in a dichotomy between dynamic and static regulations.

The process of PHAROS data registration and policy decisions

In the PHAROS case, policymakers had learned from the GH case and changed coordination practices accordingly. In order to cope with the constantly changing regulations in clinical practice, CVZ decided not to steer by the outcome of regulation as with GH but by its process. Therefore, the configuration of the evidence informing appropriate medicine use and reimbursement in practice should be a derivative of the data collected and registered in a database in the three-year research period by the collectives of researchers, medical professionals, and pharmaceutical industry. By focusing on the regulatory process in clinical practice, CVZ acknowledged the dynamic nature of clinical research and practice.

> *Respondent 4: When pharmaceutical industry and medical profession apply for additional reimbursement we do not ask to just provide [cost-effectiveness] data, we only say: 'explain how it should be . . . provide an indication of the medicine's efficiency'. And, when they explain how they will collect data on and research the (cost-) effectiveness of the medicine in clinical practice, then, in essence we are done for t=o [Start of the research period MN]. And then, in essence the product can be admitted to the policy regulation. Only after three years we look at the provided evidence in order to give us the feeling that it can be uphold [whether the medicine's additional reimbursement should be continued]. (Policymaker CVZ, 2008)*

In the PHAROS case, CVZ did not define a prior decision framework or threshold but focused on how to use data collection as a reflexive instrument for clinical practice. Moreover, whereas within the GH database, the medical professionals solely decided what data were lodged in the registry, in PHAROS, other stakeholders such as the pharmaceutical partners, The Netherlands Organization for Health Research and Development[5] and CVZ were able to co-decide what data should be collected.

> *Respondent 8: That is why we decided in yesterday's meeting by telephone [with the pharmaceutical manufacturers and professor Y of the comprehensive cancer center] to write a letter to The Netherlands Organisation for Health Research and Development in which we state not to agree upon the proposed research construction. We want to maintain the population based registry. We will include some detailed data because the Health Care Insurance Board [CVZ] is also interested in over- and under dosages. The pharmaceutical industry has asked this question which is based on their experience in earlier dossiers. The clinicians preferred not to include these data, however after a separate phone call with the Dutch Cooperative Group on Hemato-Oncology they have agreed upon this. (Professor in health technology assessment, 2008)*

CVZ decides what evidence is required to determine the effectiveness in daily practice, what type of test provides acceptable evidence and how it will be judged and by whom. These data are used to steer clinical practice. In turn, the data available for collection in clinical practice determines the kind of decisions the policymakers can make.

However, despite the 'common language' offered by PHAROS, and its focus on the process of data collection, it did not reduce the distance between policy and practice. In the end, CVZ is expected to account for the continuation of reimbursement of an expensive medicine when the process of data collection is or

[5] The Netherlands Organisation for Health Research and Development (ZonMW) manages the subsidies for the process of evidence building (databases) required by the BDG.

should be finished (BDG allows for a three-year period of data collection). It was expected that more dynamic regulation would follow dynamic clinical practice, yet would allow for the control of cost-effectiveness in medicine use too. CVZ, however, has to freeze this dynamic process at a particular moment in time to make choices based on the process of data collection and the evidence provided thus far. Whereas clinical practice regards evidence as 'in process,' policymakers must treat the information as an available outcome, at least at the moment a decision has to be made. This pressure for transparency and accountability for the additional and conditional funding of expensive medicines comes not only from the political context (democratic legitimacy) but more importantly also from the pharmaceutical industry which lobbies government to steer on outcomes and prior defined decision frameworks and thresholds.

> *Respondent 9: And how will we distinguish later on . . . the situations of which we believe the applicants have a good report on the process of data collection, that allow for regulating (cost-) effective use in clinical practice, but lack outcomes and therefore are given the benefit of the doubt. Of course we need to try to maintain that group of medicines as small as possible. So, the group 'yes' [inclusion in the regulation MN] should be as big as possible as well as the club of 'no'- decisions. The grey area in between should be as small as possible. (Policymaker CVZ, 2008)*

At that point, the focus of CVZ changes from process to outcomes. The outcomes are modelled, by means of health economic methodologies, into the best prediction of long-term effects and cost-effectiveness, and so on. At this point precisely, policy and clinical practice rearticulate their relation in the form of the static-dynamic dichotomy. The regulatory environment of policy requires ending the process of data analysis as the focus is on fixed categories to account for and decide upon appropriate medicine use and reimbursement. In contrast, the regulatory environment of clinical practice requires further data analysis as its focus lays in gaining new insights (e.g., in patient categories or dosages) and address uncertainties in appropriate medicine use.

Discussion

In this chapter, we sought to analyze how the use of databases has transformed the regulation of clinical practices through case studies of the Dutch GH and PHAROS databases. The Dutch government requires physicians to collect clinical data into a database as a condition for the reimbursement of certain, expensive drugs. The government supported the development of drug databases to gain oversight in prescription and reimbursement practices. The ideal of appropriate drug use, however, is reached not so much through direct steering based on the outcomes of the databases, but indirectly by stimulating data collection and the

continuous reflection upon the data by researchers and clinicians. These internal regulations provide a framework for establishing the 'appropriate medicine use' on which to base decisions on pharmaceutical reimbursement by health policy regulators. Without the demand for data collection through the conditional reimbursement regulations, this process of clinical practice regulation would have remained implicit and more importantly have less connection to the realm of health policy. Moreover, since health policy regulators codetermine what data should be collected, they are able to steer what information the medical professionals use to inform their practice. The databases are in this way coproduced by the collectives of clinicians, researchers, and policymakers who set regulations in clinical practice about what is considered appropriate medicine use.

Does, the presence of internal regulation and the externalization of the regulatory work within clinical practice mean that the gap between policy and practice has been bridged? Not so. Rather, the existence of regulatory objectivity in clinical practice added further complexity to the relation between policy and practice. Rather than bridging the policy-clinical practice divide through the collection of data or through the delegation of regulated authority to clinical practice, the continual process of reflection of appropriate pharmacotherapy led to new frictions. Regulations within clinical practice are formed in response to the constant adaptation, updating and modification surrounding the uncertainties of pharmaceutical treatment. The collectively determined conventions only temporarily provide closure on the uncertainties related to the effective use of expensive pharmaceuticals in daily clinical practice (Cambrosio et al. 2009). The 'closed' uncertainties are continually challenged because of the clinicians' reflexive use of data in the databases in combination with their experience in daily practice. Clinical work has become integral to regulatory bodies such as CVZ, and regulatory bodies have become integral to the dynamics of clinical practice (cf. Cambrosio et al. 2006; Hogle 2009). Yet, the ultimate goal of the current policy regime thus far remains a stable and closed list with reimbursable drugs. Whereas regulations in clinical practice are continually being reshaped, governmental practices -because of the need for accountability- still require some static moments of 'proven appropriate medicine use.' In fact, the requirement of databases in the new conditional reimbursement regulation has stimulated the dynamic and ongoing process of data collection and interpretation in clinical practice. However, the actual policy decisions to be made in the end still require the closing down of this process in a single 'yes' or 'no' decision about reimbursement. Moreover, the reimbursement regulation is monitored as if rules did not change, despite decision-makers' intention to allow for a dynamic regulation.

As our research on the evolution of databases as regulating instruments provides a glimpse of the period 2004-2009, it will be interesting to see how data collection for regulatory purposes develops in the future, especially in the field of innovative medicines. Professional networks developing around the regulatory medicinal- or population-based databases will gain in importance, similar to the increasing importance of benefit-package management. This form of coordination is about to define key areas of medical governance (ACP meeting, Health Care Insurance Board, September 11, 2009). The cases we studied have made some steps toward this. Compared to the collectives using the GH database, PHAROS shows an increasing focus on the process of data collection and reflection. This widening of the governmental focus has led to a more dynamic regulatory environment in both policy and clinical practices. Regulating pharmaceutical care via databases is a promising approach for stimulating appropriate medicine use and reimbursement. Especially when the focus is maintained on the continual process of collective production of evidence, combining data provided by the databases and reflections on the data collection, regulatory tools such as guidelines or models of action will be produced, stimulating appropriate medicine use and reimbursement in clinical practice. However, legitimating policy decisions currently stands in the way of such dynamic practices as they imply fixing 'appropriate medicine use' at a particular moment. Whereas initially policymakers believed databases promised insight in clinical practice and subsequently control, the PHAROS case provides a glimpse of the renewed promise of databases and regulation of 'appropriate medicine use.' In the PHAROS case, CVZ tried to shift focus from health outcomes toward a process of evidence building and the constant and dynamic adjustment of pharmaceutical care regulations. This dynamic process of continual data collection and reflexivity by medical professionals and researchers fulfilled the health regulators' goal of stimulating appropriate medicine use and reimbursement in clinical practice during the three-year period of data collection. However, the current Dutch legislation does not (yet) allow for such a shift, since it is based on an 'in' or 'out' logic of benefit package management.

We should be aware that not all medical practices can be regulated through this new form of governance –coverage with evidence development through data collection in clinical practice. Especially in clinical practice settings where data are less likely to be registered as part of clinical work, one should be hesitant about governing (pharmaceutical) care through data collections. For example, conditional reimbursement of statins (cholesterol-lowering medication) has already been shown to be rather problematic, and most likely this will also hold true for medical aids (Niezen et al. 2007; Zuiderent-Jerak & Van der Grinten 2008). An implication for clinical practice is that eligibility for additional funding, based on the prerequisite of data collection, depends on the degree of regulatory work already existing in

clinical practice. Both of the databases we analyzed existed prior to the policy requirements to collect data. Rather than developing new databases, the policymakers built on this existing infrastructure. They stimulated and subsidized the development of the databases to inform regulations. In the event conditional reimbursement and its prerequisite of data collection increase in importance as a policy tool and the requirements concerning the effectiveness in clinical practice increase, we expect the less protocolized clinical practices will find eligibility for funding more difficult. In this event, other types of governing care might have a better fit.

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Chapter Five

(De)constructing legitimate decision-making in health care

Based on: Maartje G.H. Niezen & Samantha A. Adams. (De)constructing legitimate decision-making in health care. Submitted to *Journal of Health Politics, Policy and Law*.

Introduction

Legitimate decision-making is an issue on many policy agendas. Especially when public goods such as health care are at stake, justifying and accounting for policymakers' decisions is crucial. Legitimate decision-making entails that the public considers the decision-making framework, process and outcomes to be just or socially robust. The limited resources for health care in general – and medicines, more specifically – have led to an increased awareness for legitimate and/or fair priority setting processes related to medical technologies, including pharmaceuticals (Hoedemaekers & Dekkers 2003; Daniels 2000; Lehoux 2006; Cookson & Dolan 2000). Governments and regulatory agencies must decide how to divide and allot scarce resources and, for example, define a minimum benefit package that is paid for collectively. Issues related to legitimate decision-making are normative and the choices that are made can easily be contested. The legitimacy of decision-making is highly important since decision makers need to maintain the credibility and authority that enables them to continue making difficult rationing decisions.

Health technology assessment (HTA) is the main response in dealing with the problem of health technology and the prioritization and allocation of the public good 'health care' (Lehoux 2006; Drummond et al. 2008; Noorani et al. 2007). HTA entails the promise of an evidence based approach to decision-making. Prioritization decisions, in this logic, are based on objective scientific research on the safety, clinical and cost-effectiveness of medicines. These evidence based criteria are expected to secure the decisions' legitimacy. Subsequently, within the Netherlands, much like in most other Western countries, it is believed that services should only be reimbursed – and preferably used – if scientific evidence is strong (Briggs and Gray 2000; Drummond, Jonsson & Rutten 1997; Stolk, Brouwer & Busschbach 2002; Van Oostenbruggen et al. 2005; Niezen et al. 2009). The benefit package advice provided by the Dutch Health Care Insurance Board (CVZ) to the Ministry of Health focuses on the clinical effectiveness and cost-effectiveness of medicines based on scientific research such as randomized clinical trials (College voor zorgverzekeringen 2007; Raad voor de Volksgezondheid en Zorg 2007a). Similarly, the work of the National Institute for Clinical Excellence (NICE) in appraising the cost-effectiveness of (mainly expensive) new medical technologies in the UK is based on explicit and national rationing (Drummond et al. 2008; National Institute for Clinical Excellence 2004). While the US has lagged behind HTA developments compared to European countries, President Obama's proposed reforms now also emphasize a greater attention to e.g. comparative effectiveness research and renewed attention to just

organisation of health care provision (Bridges et al. 2010). European experiences are therefore increasingly relevant to US health policymakers.
However, not all HTA activities and decisions are received uncontested by the public and other relevant stakeholders (Syrett 2003). The technocratic solution offered by HTA is argued to be insufficient to warrant legitimate decision-making (Lehoux 2006; Syrett 2003). For example, decision-makers must often deal with incomplete and / or inconclusive scientific evidence, potentially diminishing the rationality of their decisions (Ashmore, Mulkay & Pinch 1989; Sendi & Al 2003). As science becomes more important for political decision-making, its authority is increasingly questioned (Bijker, Bal & Hendriks 2009). Alternatively, the impact of HTA on decision- and policy-making and active dissemination of HTA findings is called into question (Battista et al. 1994; Battista et al. 1999). For example, a lack of long-term planning and decision-makers' vested interests limits the use of HTA (Hivon et al. 2005). Moreover, to account for the reasonableness of prioritization decisions, the processes of these deliberations and evaluations of scarce health care resources should be transparent (Daniels & Sabin 2008).

In response to these criticisms, many health regulatory agencies emphasize that an evidence based approach is the way forward, and the decision-making process itself should be more transparent. How evidence is incorporated into actual decisions should be more apparent to those not involved in this process. Therefore, to govern the process of priority setting a set of 'meta-rules' should be created (formalization) (Holm et al. 1998).This increase in demands for transparency can be observed in all aspects of health care over the last few years (Bijker, Bal & Hendriks 2009).

Despite a clear decision-framework (scientization), and a transparent decision-making process (formalization), policy-makers still experience problems in the execution of reimbursement decisions. The execution of health regulations in daily practice appears to deviate substantially from the intended policy and its underlying principles (Niezen et al. 2007). "The evidence that NICE guidance has made a difference either to the quality of care or to variations in practice is mixed" (Sheldon et al. 2004, p.6). The definition of formulary lists (medicines eligible for funding) presumes that appropriate medicine use and reimbursement not only can be defined, but subsequently can be implemented in health care provision. Like NICE and other national agencies, CVZ uses multiple structures, procedures and responsiveness to stakeholders in order to construct its legitimacy in health care decision-making. Nonetheless, these formal forms of legitimacy do not appear to be sufficient for stakeholders and public to adhere to decisions. These problems may be due to the incompleteness of the decision framework, because health

regulators always require more evidence, or because regulation lags behind the dynamic clinical practice (Niezen, Bal & De Bont forthcoming). The deviation between policy and practice, and the debate of reimbursement decisions, points at potential legitimacy problems requiring further research. Is legitimacy achieved when evidence in the form of (economic) modelling and decision procedures are applied appropriately, or is the legitimacy of decisions otherwise constructed? And if so, in what way?

Currently, the activity of 'making legitimate choices' in health care is related to concepts such as public accountability (informing about one's conduct), transparency (full and open information) and the public interests involved (e.g. the principles of quality, accessibility and efficiency of health care) (Daniels 2000; Daniels & Sabin 2008; Bal, Bijker & Hendriks 2004; Jasanoff 2009; Suchman 1995). Many national governments are searching for a 'grand solution' to the problem of legitimate decision-making and its related normative questions, such as: when is decision-making regarding the prioritization of medicines considered legitimate, or even, how it can be made legitimate? Yet, legitimacy of decision-making needs work. The public's trust in the carefulness and accuracy of the deliberation concerning prioritization is not given, but depends on different building blocks.

In this article, we analyze how legitimate choices are made during Dutch decision-making on the reimbursement of medicines. Making use of the Sociology of situated judgement in combination with a Science and Technology Studies (STS) approach, and following the footsteps of Moreira (2005), we explore how health decision-makers in the Netherlands (try to) construct legitimacy for decisions in complex situations, such as choices on how to divide scarce resources (Thevenot 2002; Moreira 2005). The objective of this exploration is not to provide for a 'grand solution' to the problem of legitimate decision-making, but to provide insight in both the dynamics of argumentation used, and the organizational and material arrangements used, to support or complement a given line of argumentation. Exploring three case studies, we examine what it means for decision-makers to deal with the claims for legitimate decision-making, and how the different stakeholders involved regard 'justifications' (Thévenot 2007) for argumentations and evaluations differently. The three case studies are: the conditional reimbursement of a) outpatient and b) inpatient medicines and c) the possible addition of a decision criterion to the decision framework respectively. Below, we first describe our research methodology; we provide a short description of the three case studies, as well as the empirical data and theoretical lens we use. In section 'Dutch benefit package management infrastructure' we outline the context of Dutch benefit package management infrastructure and the way legitimacy currently is

constructed. In section 'The legitimacy of prioritization decisions and knowledge claims' we focus on what forms of knowledge are considered and produced in the prioritization decision-making process and how these underpin legitimacy of prioritization decisions. We identify the different repertoires present in the decision-making process, and how each repertoire differs in attributing worth to a medical technology and its reimbursement decision. In the section 'Interaction between the different repertoires in the reimbursement decision-making process' we examine more closely the interplay between the different knowledges or repertoires (as defined in section 'The legitimacy of prioritization decisions and knowledge claims') and the way this interplay is incorporated in the decision-making process. Finally, we discuss how current benefit package management infrastructure is performative in shaping the legitimacy of prioritization decisions.

Method

In order to analyze legitimacy problems within health care decision-making, we draw upon the following three case studies: a) the conditional reimbursement of medicines in the outpatient setting, b) the conditional reimbursement of medicines in the inpatient setting, and c) the possible addition of a new rationing criterion to the decision-framework for benefit package management; 'budget impact'. These case studies provide insight in how the Dutch benefit package management system aims to produce legitimacy for its decisions. They involve the exploration of policy measures and tools aimed to govern appropriate drug reimbursement and use (conditional reimbursement) and the exploration of the construction of evidence used in decision-making (budget impact). The first case study examines the conditional reimbursement of outpatient medicines (Schedule 2 of Health Insurance Regulation[1]). This policy tool makes the reimbursement of particular medicines conditional to specific criteria or rules. For example, the use of medicines is restricted to specific categories of patients (e.g. based on indications) and/or place in treatment lines (e.g. step-up treatment). By conditionally reimbursing specified drugs, the Health Care Insurance Board expected to stimulate the appropriate use in practice supported by evidence based policy (College voor zorgverzekeringen 2005). The second case study has a starting point in 2006, when the conditional reimbursement regulation was extended from outpatient medicines to inpatient medicines through the High-Cost Medicines Regulation. Importantly, the High-Cost Medicines Regulation includes the prerequisite of evidence development on the effectiveness and cost-effectiveness of listed medicines in clinical practice (Raad voor de Volksgezondheid en Zorg 2007a; College voor zorgverzekeringen 2006; Nederlandse Zorgautoriteit 2006).

[1] The Health Insurance Regulation regulates the execution of the Dutch Health Insurance Act (ZVW).

The evidence development based on data collection in databases was intended to inform and govern decision-making on the reimbursement of inpatient medicines, as well as to promote rational prescribing. The last case study does not focus on how a policy tool might contribute to the legitimacy of the decision-making infrastructure, but on the possible completion of the decision framework. The current Dutch decision framework explicitly entails the criteria of effectiveness, cost-effectiveness, and severity of illness. The role of budget impact remains less obvious despite the official request for budget impact estimates to inform the decision-makers in the decision-making process (Niezen et al. 2009; Cohen, Stolk & Niezen 2008). Exploring the possible addition of budget impact as a rationing criterion to the decision-making process or framework allowed for insight in the type of evidence used in decision-making and gaining legitimacy of the decision-making process. We do not explore how each case study contributes to legitimate decision-making individually, but rather focus on how they, taken together, provide insight in the activity of making legitimate decisions.

Data from field research on the three cases orient the analysis, and are offered as evidence throughout this paper. The data consist of various sorts of 'texts' and observations collected from several sources; in-depth interviews with the key participants (N=80), documents such as pharmacoeconomic reports, and reports on meetings and public statements put out by CVZ, Ministry of Health and other relevant stakeholders. In each case similar stakeholders were interviewed, and similar texts retrieved. The interviews, observation reports, documents and minutes were hand-coded independently in two rounds. In the first round we used in vivo coding (creating codes using words from the empirical data, without paraphrasing) to determine a saturation point (no new information) and generate an inductive code list (paraphrasing and categorizing) related to the different aspects and / or perceptions of the concepts 'legitimacy' and 'legitimate decision-making'. In the second round we coded deductively, using theoretical perspectives on legitimacy and legitimate decision-making to further order and analyze our data using insights from Thevenot (2002) and Moreira (2005) – see further in section 'The legitimacy of prioritization decisions and knowledge claims'. We developed a framework of different forms of judgement and coded the various repertoires found in the evaluation of medicines in the three cases studied. We use this framework to structure the analysis of empirical data below.

Dutch benefit package management infrastructure

In this section, we provide a description of the current benefit package management infrastructure for health care allocation in the Netherlands. The Dutch drug reimbursement system is based on a political decision-making model. The

Ministry of Health formally requests advice from the Dutch Health Care Insurance Board (CVZ) on benefit package decisions. As an independent agency of the Ministry of Health that must function in a political setting, CVZ tries to remain incorruptible, reliable and sensitive. The main focus of CVZ in providing legitimate decisions is to strive for transparency in the criteria and values that have been judged as an appropriate base for evaluating a medicine. In line with the international trend, CVZ mainly bases their assessments on the criteria of efficiency, effectiveness and severity of illness and focuses on an evidence based procedure, and puts much effort in rationalising the decision-making procedure. In its assessments, it aims to have a societal perspective in mind, which in the Dutch case represents strong principles of justice and solidarity. Since the Dutch government represents the citizens of the Netherlands, and CVZ takes into account a societal perspective in health care prioritization procedures, it is expected that the resulting choices and policies have value for the Dutch citizens.

The Health Care Insurance Board decision-making process has evolved from a consensus model on appropriate reimbursement to a technological assessment of medical technologies and more recently, to a two-phased organisation of the decision-making process. In the first phase a technological assessment is conducted by the Medicinal Products Reimbursement Committee (CFH). This Committee consists of external experts, such as hospital pharmacists, mathematicians and oncologists. They systematically assess the therapeutic value of medicines (based on health outcomes research and when relevant experience, feasibility and user-friendliness) for as long as scientific evidence is available of new medicines in comparison to standard treatment, or care as usual. Moreover, the CFH estimates the costs related to admission (budget impact) prior to admission in the benefit package on behalf of CVZ. A CFH-meeting on a particular medicine focuses on several elements that together result in a 'rational consideration' of the eligibility of this medicine for reimbursement (College voor zorgverzekeringen 2000b). The assessment phase is followed by an appraisal of the medical technology (societal exam) by the Advisory Committee Benefit Package (ACP). The ACP consists of external experts with experience and knowledge on the fields of social security, care and insurance from a scientific-, practice- and patient- perspective. The ACP appraises the value of medical technologies from a societal perspective, e.g. taking into account the collective solidarity principle and the possibility for equal access to a particular medicine. According to CVZ, the evidence found in the two phases is subsequently presented as objectively as possible, after which the Ministry makes a final decision on the admission of a drug in the benefit package (College voor zorgverzekeringen 2007). The resulting definition of the benefit package presumes that appropriate medicine

use and reimbursement can be defined *and*, subsequently, be implemented in health care provision.

The legitimacy of prioritization decisions and knowledge claims

In this section we focus upon the formal regulatory intervention of prioritization decision-making and explore how legitimacy of prioritization decisions is constructed. There are different approaches in exploring legitimacy of health care allocation decisions. According to the sociology of organizations approach, as described by Suchman, legitimacy involves "a generalized perception or assumption that the actions of an entity are desirable, proper, or appropriate within some socially constructed system of norms, values, beliefs and definitions" (Suchman 1995 p.574). Legitimacy then is connected to the authority of an organization. Another approach is the deliberative democracy perspective, of which the accountability for reasonableness framework by Daniels is most known (Daniels 2000; Daniels & Sabin 2008). The health economic perspective on legitimacy in decision-making is one of the main approaches in current practice of health care allocation. Legitimacy can be achieved when complexity is reduced and the argumentation for choices is narrowed down to a set of standardized criteria and principles. All three approaches assume that legitimate decision-making, reached either through attribution of authority, proper organisation of the decision-making process and / or well functioning economic modelling in decision-making, results in implementation and execution of such reimbursement policies and decisions in clinical practice.

We believe that the exploration of the act of constructing legitimacy for decisions might benefit from an alternative approach. Recently, Moreira (2005) explored the diversity in clinical guidelines, drawing on a combination of the Sociology of situated judgement and the Social Science and Technology approach, to understand the relationship between knowledge practices and political processes in setting rationing standards. In line with Moreira's article we further explore how the evaluation of medicines is constructed in order to reach legitimate decisions (Thevenot 2002; Thévenot 2007; Moreira 2005). In contrast to the Sociology of organizations perspective or deliberative democracy approach, the analysis from the Sociology of situated judgement approach takes into account how each context might require or involve different repertoires (see further, below), subsequently resulting in different lines of action. The construction of legitimacy is no longer related to the social acceptance of an organization or the amount of scientization and formalization of the decision-making process, but is more case-specific and relates to the different repertoires of evaluation of medical technologies that link knowledge claims and conceptions of justices and fairness (Moreira 2005; Moreira

2011). In contrast to the other approaches to legitimacy in health care decision-making, the 'knowledge' and values used in the decision-making are not separate domains. There are, however, different forms of knowledge. This diversity of knowledge is linked to different forms of (collective) judgement on the value of public goods. It is these collective judgements, or repertoires of evaluation, that we are interested in; not only at a macro or meso-level, but also at the micro level. Such an analysis is highly relevant, since the perceived legitimacy of the policy tools, by different stakeholders, increasingly seems to be connected to the actual implementation of the policy in daily practice.

The French sociologist Laurent Thevenot considers legitimacy to be situational at all times. Whether the actions of regulators are considered legitimate is enclosed in the interplay between the regulators and their environment (Thevenot 2002). Thevenot approaches the different 'repertoires of evaluation' and diverse criteria within evaluations and regulations justifying these repertoires, from a political philosophy point of view. The evaluation of medicines can, in its striving for 'objectivity,' not be seen separately from politics and morality. In fact, the activity of making legitimate decisions can be seen as situational in different social styles and institutions (Boltanski & Thevenot 2006; Thevenot 2002). Thevenot focuses on how actors draw upon common modes of judgement to orient their involvement in disputes. These are not merely 'rationalisations'. Rather, they are "recurrent forms of judgement deployed by social actors in considering the worth of an object, person, etc. as means of harmonizing their actions with others" (Moreira 2005, p.1977). Each repertoire has its own characteristics and dynamics providing actors with symbols, stories, world views, material and organizational arrangements from which they can select different elements to shape their action and solve problems. Moreover, each repertoire is in principle accessible to everybody to draw from, in order to shape one's evaluation of a health technology (Te Kulve 2006). The repertoires used, and the actions attributed to these repertoires, are connected to the ordering of the objects – in this case, the prioritization of medicines. Thus, in order to be able to compare one public good with another, value is attached to each particular public good. The prioritization process of medicines involves the evaluation of their worth as a public good. This evaluation involves multiple criteria and various types of expertise.

Since the evaluation of medicines can, in its quest for 'objectivity', not be seen separately from politics and morality, we find it worthwhile to explore what types of repertoires are used to evaluate a medical technology and how these repertoires are incorporated in the current drug reimbursement decision-making process. In this section, we make use of the conception of the 'different orders of worth', or 'repertoires of evaluation,' as defined by Boltanski and Thevenot, and follow the

footsteps of Moreira, in identifying the set of repertoires used within the Dutch reimbursement decision-making process (Thevenot 2002; Boltanski & Thevenot 2006; Moreira 2005). In the coded material, four primary repertoire themes are evident: 1) the repertoire of science, 2) the repertoire of clinical practice, 3) the repertoire of equity and 4) the repertoire of process. By discussing each repertoire individually, we show how each repertoire entails different forms of knowledge, which, in turn, attribute value to a particular reimbursement decision. We then show how these repertoires can interact within one setting and how this interaction is important in establishing which (combination of) repertoires can produce legitimacy at a certain point in the decision-making process. Each repertoire resembles the conceptions of justice or legitimacy connected to the knowledge claims to which different groups within the deliberative process adhere (Moreira 2011). The labelling and identification of the various repertoires is based upon the categorization used by the interviewees when talking about health care decision-making. Subsequently, we explore what forms of knowledge are considered and produced in the decision-making process and gain insight in the work needed to legitimize decisions.

The repertoire of science; robustness of evidence

The 'repertoire of science' is focused on the technological assessment of a medical technology, and its users are concerned with the technical robustness of the evidence presented to base the prioritization decision on (Moreira 2005). Questions asked in the 'science repertoire' to judge the value of a medical technology are: What is the technical robustness of the evidence presented regarding its health (economic) performance? What quantity of reliable studies and / or number of patients is involved? What criticism could health researchers and specialists have on the provided evidence? The efficiency of a medical technology, more specifically the costs per QALY, is often the main outcome under discussion.

The Medicinal Products Reimbursement Committee (CFH) is one particular location in which the science repertoire dominates. A CFH meeting on a particular medicine focuses on several elements that together result in a 'rational consideration' of the eligibility of this medicine for reimbursement. The results of these meetings are reported in both a phamaco-therapeutic report and a CFH-report, in which the committee's findings and conclusion regarding the assessment of the medicine is described. The CFH assesses a medicine in comparison with other available medicines or (non-pharmaceutical) treatments preferably through the assessment of randomized double blind and comparative research (College voor zorgverzekeringen 2000b). According to a former secretary of the CFH, a medicine is found eligible for reimbursement when it has added value compared to

the standard treatment, preferably established in two or more independent researches.

> *No, you have to have more on offer. You need to offer more effectiveness or fewer side effects for the patient. That's what we think is really an improvement. And, if you can show that, preferably through two independent research studies, then I am always of the opinion that you must be well-grounded if you want to prevent such a drug from being put on the market. That also doesn't happen. Because then the social pressure is large, the pressure from physicians, acting on behalf of patients, to get reimbursement is enormous (Secretary CFH, 2008)*

When evidence is lacking (despite experience in daily practice), the CFH claims it cannot conduct a proper assessment, and therefore cannot provide advice for inclusion or exclusion in the benefit package. The assessment thus leans heavily on the availability and quality of scientific evidence. The reimbursement decision procedure seen from a scientific repertoire leans on a hierarchy of evidence in which the randomized clinical trial (RCT) delivers the highest value of evidence. Outcomes of certain types of research receive more weight than other outcomes produced by less-valued research (Raad voor de Volksgezondheid en Zorg 2007b). A part of the hierarchy of evidence becomes visible in the recent re-assessment of etanercept, a drug used in autoimmune diseases. The re-assessment focuses on the possible extension of etanercept's reimbursement conditions to include treatment of therapy-resistant uveitis. The CFH reports to have conducted a literature review of the most recent files in Medline, Embase and Cochrane, and using appropriate search terms. This literature review, the CFH reports "... resulted *merely* in two clinical studies on treatment with etanercept for therapy-resistant uveitis and *no* randomized, double-blind and placebo-controlled study" [italics added] (College voor zorgverzekeringen 2011). The CFH therefore concludes, based on available information, there is insufficient evidence for a rational therapy of therapy-resistant uveitis with etanercept. In this hierarchy of evidence a meta-analysis of multiple RCTs is regarded as the highest form of evidence and the uncontrolled studies and expert opinions represent the lowest form of evidence. This does not imply that expert opinions on e.g. effectiveness in daily practice are not included in the CFH assessment, however these have less weight.

The repertoire of science characteristically leans heavily on systematic and objective evaluation of outcomes research information. The internal structure of its logic makes use of the hierarchy of evidence, of which the RCT is valued highest. This structure allows for assessing the quality of evidence presented on a particular health technology and assumes that this evidence is unproblematically derived from experiments. Infrastructural requirements for making legitimate prioritization

decisions then are a complete and non-contradictory set of rational and evidence based decision rules.

The repertoire of clinical practice; evidence from daily practice

The repertoire of clinical practice refers to a medical-professional 'model' that acknowledges a pharmaceutical treatment as appropriate as soon as medical professionals find the evidence for efficacy and effectiveness to be sufficient, and the treatment is better than or different from the standard treatment (Trappenburg 2005). The evidence under discussion includes scientific publications in acknowledged medical journals combined with experience in particular treatments in trials and in daily practice. In comparison to the scientific repertoire, evidence is not only based on scientific research (preferably RCTs) or claims by health economists, but evidence originating from clinical practice itself is as important. Whenever the treatment is used in medical practice, it should be eligible for reimbursement. Members of this repertoire are concerned whether the value of a medical technology is based upon the possibility to change the health care practice for the better. 'For the better' then, does not necessarily mean the best health outcomes in terms of effectiveness. Clinical expertise may point at other outcomes of delivered care, such as better quality of life, or better support in an illness (Mol 2008). Since each patient is unique, the treatment should be based on the appropriateness of the treatment for a particular patient, and not the appropriateness within a national framework. Clinical knowledge thus plays an important role in the clinical practice repertoire.

In order to evaluate the worth of a drug reimbursement decision, the participants using the clinical practice repertoire rely on consensus building within the medical professional associations and the individual health care delivery institutions. In this consensus building, medical professionals appraise the value of reported research and combine this with their experience in daily practice. A logical place to find this type of repertoire is within clinical practice.

> *We have evening-courses in which we discuss recent studies and amplify the current guideline for a particular treatment. After these meetings, everyone returns to practice, is given additional training, and is up-to-date in current treatments… thus we are practicing evidence based medicine as desired by the Minister of Health. And then we are hindered by a health insurer representative, claiming that we go on ahead of reimbursement regulations. Yet, we truly believe this treatment is in the patient's best interest (Medical professional 1, 2004).*

Although the medical professional associations play a marginal formal role in the two-phased decision-making process - they can only react to CVZ's (preliminary)

decisions by invitation - the clinical practice repertoire can be found in the decision-making process. Whereas the CFH is supposed to do the technological assessment including the assessment of the clinical value of a medicine based on scientific research outcomes, the Advisory Committee Benefit Package (ACP) is asked to take a societal perspective in the evaluation of a medicine. Yet, in the discussion on acetylcysteine, for example, the ACP departs from the preliminary advice provided by CFH to exclude the medicine from the benefit package.

> *ACP-member 1: "Do you know anything else about those who use it? How many people are there? And, what categories of people use acteylcysteine and why? Can we connect the objections by the NVALT and NCFS with specific patient groups? …The NVALT thinks that there's an indication in the area of pulmonary fibrosis and the NCFS in the area of intestinal obstruction".*
>
> After short discussion, the chair of the ACP concludes that the ACP will, in the interest of being careful, take the position of requesting that the CVZ try again via the patient association to collect evidence regarding the reasons for use or to eradicate doubts that something has been missed.
>
> *Chair ACP: "If we want to give a careful advice, then we need to clarify these points. That is, we can follow the exclusion advice, but under the condition that CVZ returns to this issue of the specific patient group" (Observational notes ACP meeting 2008)*[2]*.*

The knowledge to make a carefully deliberated decision on the exclusion of acetylcysteine from the benefit package requires knowledge on the use of the medicine in daily practice for a specific patient group. Because the relevant professional association has lodged objection to complete exclusion of the medicine from the benefit package, the ACP is of the opinion that their knowledge should be included in the decision-making process, prior to final decision-making. Subsequently, this might lead to an appropriate advice on the reimbursement status of acetylcysteine and its execution in clinical practice. This example shows that within the clinical repertoire, experiential knowledge from medical professionals about the worth of a medical technology for specific patients is valued.

A segment, characteristic of the clinical practice repertoire, is the consensus building model in which scientific research is combined with experiential knowledge. Whereas the dominating view in the repertoire of science relates to impersonal experimental knowledge, building on the value of a prioritization

[2] Respondents represented in the observations of the ACP-meetings are referred to as ACP-members, and with no reference to their function(s) outside the ACP.

decision for entire patient groups, the repertoire of clinical practice leans more on professional and experiential knowledge building on the value of a prioritization decision for each unique patient. In other words, the internal structure of logic within this repertoire builds on evidence derived from both experiment and experience and assumes that evidence is perishable.

The repertoire of equity; solidarity and other societal considerations

In the repertoire of equity, the relevance of evidence for the admission of a medicine in the benefit package is discussed from an equity perspective. Users of this repertoire wonder whether the prioritization decision reflects the minimal provision of health care in order to be able to participate as a citizen in Dutch society. In other words, this repertoire reflects the moral worth of (individual) patients as citizens. The repertoire of equity is highly visible within the ACP. The evidence used includes data on the necessity and severity of illness of pharmaceutical treatments. Also, the expertise of the different members plays an important role in the discussions. The experts vary from a patient representative and a former Minister of Justice, to professors in Health Technology Assessment and in Health Care Ethics. The goal of the discussions is to reach consensus on the societal aspects related to a pharmaceutical treatment, which should be part of the Minister of Health's deliberation about possible admission in the benefit package.

Within Dutch society, solidarity is a principle that has been highly valued since the establishment of health insurance after WWII. The Advisory Committee Benefit Package appraises a medicine on its worth for society, implicitly taking into account the collective solidarity principle. They explicitly discuss the possibility for equal access to a particular medicine. The tension between collective regulation based on rational decision-making frameworks and evidence based standards on the one hand, and individual patient situations on the other hand, is often discussed by the ACP.

> *ACP-member 1: I have a moral dilemma… I miss the entire empathy with people who are ill! I am wondering whether I, as a representative for the patients' perspective, even should participate in this type of commission in which the method of QALY's and severity of illness are central and shifts [in perspective] are difficult.*
>
> *ACP-member 2: I am quite happy, even as a surgeon, with this entire rational and quantitative approach. That does not exclude also taking a good look at the individual level.*
>
> *ACP-member 3: I think you fall short on yourself as a patient representative.*

> *ACP-member 1: Well, I wonder to what extend does empathy with people and society fit with the discussed framework of severity of illness?*
>
> *ACP-member 2: What kind of decision-making do you want then? Decision-making based on media attention? Hopefully not!*
>
> *ACP-member 4: This is exactly the problem. We have to do the PR that we, as ACP, are specifically here to also take into account the individual cases in the decision-making process. We are here to make sure that the money is allocated to those people who need it the most.*
>
> *Chair ACP: We are here to get a feel for such questions and experiential knowledge. We cannot do that without facts about interventions. The economic models are needed to put into perspective the degree to which the numbers play a definite role in the decision. Patient representation in the ACP is thus very important! (Observational notes ACP meeting 2008)*

In the discussion on biosimilars[3], again the balance between the interests of individual patients and the collective interests is at stake.

> *ACP-member 4: the problem with the file on biosimilars is that we struggle with two ethical directives. One, what is the best thing to do for the patient? And two, how can the costs of the system be contained, also for the future? When the individual patient's interest is put at risk, there should be strong arguments to go ahead with replacing previous medication with biosimilars. So far, I have not heard such arguments, and I am of the opinion that an existing patient is damaged when he or she is prescribed a biosimilar (Minutes ACP-meeting 2011).*

The moral dilemma, the ACP faces, is how the individual patient is represented in the abstract reports on medicines. The committee realizes that chopping up the appraisal, according to different criteria and related documents, is an aid supporting the ACP in formulating advice on how to allocate available money to the people who need it the most. The committee must therefore take up the task to make a socially just appraisal and cannot miss the facts and figures on the interventions or diseases. However, in dealing with the abstract reports on cost-effectiveness and necessity (severity of illness) the ACP remains to put the individual ill human central in its appraisal of the worth of a medicine (Minutes ACP-meeting, 2008, 2011).

Because the ACP is relatively new (it was erected in 2008) the societal repertoire is not only found in the locus of ACP meetings, but also in other situations, such as

[3] Biosimilars are new (sometimes slightly adapted) versions of existing biopharmaceuticals made by a different pharmaceutical manufacturer following patent and exclusivity expiry on the innovator biopharmaceutical.

when patient representative organizations use this repertoire to plea for access to specific medicines, and more specifically, at the Ministry of Health. The Ministry of Health in the end has the ability to deviate from the advice provided by CVZ based on political and societal considerations, although this does not often happen. One of the best-known cases was the Ministry of Health's decision not to include sildenafil (Viagra®) in the benefit package. Through an official notification on the decision on sildenafil, the Ministry of Health states:

> Among the medicines that will not be included is the new medicine for erectile dysfunction (Viagra). Given that the value of this medicine is largely a result of the increased ease of use, and that this medicine is not more effective than the medicine that is already included in the package, the Minister is of the opinion that the high costs that accompany inclusion of Viagra is not justified. (Monthly use of 4 tablets by 75,000 persons would result in costs of 60 million Dutch guilders per year.) By excluding Viagra, the Minister will create room to include medicines that, in the interest of public health, absolutely must be included in the package (for example, new breakthrough medicines intended for severe diseases) (http://www.minvws.nl, April 12, 2000).

This decision departs substantially from CVZ's advice to admit sildenafil under conditions for a specific patient group, based on scientific evidence for the cost-effectiveness of this treatment (Stolk, Brouwer & Busschbach 2002).

The repertoire of equity is a rather dynamic and evolving repertoire. The (discussion on the) conceptualization of equity and the fundamental values on which human dignity depends is drawn upon by the repertoire of equity users. A characteristic segment is the negotiations about how to define solidarity, for example regarding life style diseases. These negotiations are less formal and less systematic. The hierarchy of logic within the equity repertoire highly values social sciences such as ethics. Evidence derived from social studies or personal experience, however, is not received unproblematically, but debated on its value for the conceptualization of equity in each case.

The repertoire of process; transparency and participation

In the repertoire of process, members are concerned with the procedure through which prioritization decisions are reached. Users of the repertoire of process reflect upon the appropriateness of the amount of transparency and the participation of stakeholders within the decision-making process and the final reimbursement status of a medicine. Does the outcome of the entire deliberation process match with the evidence and methods used in this process? It is therefore important, within this repertoire, to map the different objectives at stake. This process can take place self-reflexively by the health regulators, but is also part of the discussion on the drug reimbursement status by other stakeholders such as representatives of

the pharmaceutical industry, medical specialist organisations and other stakeholders.

> *Many professional organizations fail to realize how the policy of admission and reimbursement of medicines works. It is much more of a closed procedure between the manufacturer and the commission for pharmaceutical aids (technological assessment). It all happens out of sight of the public at large, but also of doctors (Pharmaceutical manufacturer, 2004).*

Only the pharmaceutical industry is able to participate in the decision-making procedure, since they request the admission of a medicine to the benefit package. The participation of the pharmaceutical industry, however, is limited to the procedural aspects of the decision-making process and not the (medical) content of the CFH advice in the assessment phase, or the societal considerations in the appraisal phase. Other stakeholders are rarely involved, and therefore have limited insight in the decision-making procedure, and even less influence on the outcomes of the decision-making process. The repertoire of process is most often used when actors believe the outcome of the prioritization process insufficiently reflects all available knowledge on the appropriateness of a medicine for admission in the benefit package.

During the development of a manual for outcomes research for expensive inpatient medicines, the repertoire of process also played an important role. A team of experts was asked by CVZ to write a manual for the outcomes research, to be conducted in a timeframe of three years, to demonstrate the cost-effectiveness of the medicine in clinical practice. The discussion focused on the methodological choices for the required data registration, in order to be eligible for the conditional reimbursement measure. The working party defined ‘outcomes research’ and what data was needed. Subsequently, this was discussed in an invitational conference with attending stakeholders, amongst which representatives from the pharmaceutical industry, patient organizations, medical professional associations, health insurers and health researchers. Several experts of the working party presented the different elements in the manual, for example the clinical data and patient characteristics, the costs, the patient reported outcomes or modelling versus empirical studies.

After the presentation of the different elements, the attendees of the conference were allowed to respond to the presentations. Most of the questions asked related to the procedural and methodological aspects of the manual. “Why does the manual focus on quality adjusted life years for which a panel from society is needed and not on the descriptive ‘quality of life’- questionnaires?” “Are registries suitable for comparing treatments considering the enormous bias in registries?” “Is

the argumentation of a drug's efficiency more important than its outcome?" "I understand that besides the term of three years of research, there is also some uncertainty about how the research should be conducted?" (Observational notes invitational conference, 2007). These questions all reflect concerns whether the process of outcome research –what stakeholders are involved and what type of data is collected– appropriately affects the final decisions on the admission in the reimbursement regulation. Whereas the working committee focused on an appropriate procedure for outcomes research, the pharmaceutical industry argued that the manual was incomplete. They argued that a final decision framework, upon which decisions are based, was lacking.

> There needs to be an assessment framework in order to interpret the results of research. If the decision-making process is eventually based on a cost-effect ratio, then the question is how to deal with this. [It] is still unclear how the results of the efficacy research will add to long-term decision-making. We are of the opinion that this central question must be answered first, before any scientific meaning can be added (Letter from a representative organization of the pharmaceutical industry to the working committee, 2007).

The industry uses the repertoire of process by referring to the idea that legitimacy of decisions is only possible when the outcomes research on the medicines are similarly interpreted and subsequently assessed.

Another location where the repertoire of process can be found is in the ACP. Although its members most often make use of the repertoire of equity, they sometimes also reflect upon the question whether the outcome of the deliberation process so far is an appropriate reflection of the evidence and methods used to reach that particular preliminary decision. Below a discussion on the task of the ACP is depicted between its members.

> *ACP-member 2: NICE has a certain distantiation from the population. Use the formula approach and then also indicate what that means for individual cases.*
>
> *Chair ACP: How do we present the considerations? How do we communicate that to the outside world? These are relevant questions for the ACP.*
>
> *ACP-member 5 indicates that he would like to have the data and information regarding the technological assessment of certain medicines. "Then we can make an appraisal. Now, we can't".*
>
> *ACP-member 2: The CFH is responsible for the assessment, but we can still look at it and see if we agree.*

> *Chair ACP: Bottom line, we need to see the background information, so we can see if all available evidence has been included.*

The ACP members conclude that how they present their considerations (transparency) is of highest value for appropriate decision-making. Therefore, they also need to (re)consider evidence from the earlier assessment phase in the decision-making process.

Although the repertoire of process is one of the less dominating repertoires, it often surfaces whenever a decision is debated on the representativeness of its outcome with the evidence and methods used in the process. Both, in the ACP discussion and in the development of the manual for outcomes research of inpatient expensive medicine, this repertoire has indirect influence on the final reimbursement decision. It might lead to a renewed assessment based on the addition of previously unconsidered evidence, or the involvement of new participants providing knowledge upon which the decision can be refined. Thus, the repertoire of process discusses the value of prioritization decisions based on the amount of transparency of the priority setting process as well as the way it has taken into account the interests of all relevant groups.

Interaction between the different repertoires in the reimbursement decision-making process

In the previous section we established that, throughout the decision-making process, different forms of knowledge dominate in the different repertoires for determining the value of prioritization decisions. Although the decision-making process of CVZ clearly depicts the presence of the different repertoires within the decisions process, even within one phase or committee, the interaction between the repertoires seems limited. Current decisions and recommendations by CVZ reflect a rather formal approach to the entire decision-making process. In fact, CVZ distances itself from attributing values to the different evidence presented in the two phases and aims to present the different rationalities regarding a particular medical technology as objectively as possible.

> *What we must assess in the assessment phase, as benefit package managers, is the burden of illness, costs, effectiveness, etc. We'll also organize the societal debate in the appraisal. Then, we try to explain to the Ministry of Health, what the different social issues are. These are thus other rationalities we want to add to our advice. But, it is still the case that we don't make the decisions – that's up to the politicians. Since, politicians, at a certain point, have to attribute a certain amount of weight to the various arguments. We don't (Director CVZ, 2008).*

This approach to decision-making results in what Moreira would call a public dialogue model in which legitimacy is gained by integrating the different values and perspectives on appropriate reimbursement in the decision-making process, yet still implies that science and society can be seen as separated domains (Moreira 2005). Such an approach to legitimacy problems in decision-making continues to preserve the tension between science and values, and does not permit an interaction between the different phases in the decision-making process or even between the different repertoires. Then how do the different repertoires interact? And, how are these different repertoires (the different judgements on how knowledge entails morally sanctioned actions) balanced in prioritization decisions? These questions prove relevant, since even CVZ itself struggles with the different forms of knowledge, and subsequently different evaluations of medical technologies, and possible new ways of governing appropriate medicine use and reimbursement in practice.

Since CVZ offers advice, including transparent arguments for choices made or values attributed to specific types of knowledge, one can expect that the interaction between the different repertoires can also be seen in the current decision-making process. An example of such interaction between different repertoires is a discussion on the 'quit smoking program'. In 2008 CVZ published its report, *Supporting stop smoking: insured care?*, in which it claimed that many preventive interventions already were reimbursed, and the nicotine replacing medicines, bupropion and varenicline were excluded from reimbursed pharmaceutical care. However, in 2009 the discussion on 'stop smoking programs' and reimbursement continued and focused on whether an integral program including medicines should be admitted in the benefit package.

> *ACP-member 4: I read the report by replacing 'smoking' with 'obesity'. Since this report is likely to be followed by similar reports I think it is of importance to take a good look at the arguments used here.*
>
> *ACP-member 2: What is so different from 2008? There are more general remarks, yet there is no known RCT of an integral treatment compared to mono-treatment.*
>
> *ACP-member 5: In 2008 we concluded that stop smoking treatments did not belong to necessarily reimbursed care. The treatment costs can fall under one's own account since the costs of treatment are somewhat similar to the costs of smoking itself. Moreover, the effect of reimbursing or not reimbursing in relation to the participation in the stop smoking program is unclear. And the current research is questionable.*
>
> *CVZ-employee: The material, the evidence, is the same as in 2008. However, now we have a different focus. The material that supports the combination, the integral*

treatment, will follow since it is currently still in research. However, the preliminary results affirm the cost-effectiveness of combination therapy.

ACP-member 5: For me, the escape clause is that smoking harms others and that could be a reason to define the treatment as not one's own responsibility. Can you provide numbers for the harm done to the environment?

ACP-member 2: In general I believe there is need for more evidence. In one year I would like to re-evaluate (Observational notes ACP-meeting 2009).

The discussion above reflects how different repertoires interact within one committee (appraisal phase). Yet, the interaction between the different repertoires does not take place across the borders of the phased decision-making process. Since the ACP-members are uncertain about the provided scientific evidence regarding the stop smoking program, engaging a discussion with the scientific repertoire (e.g. in the form of CFH-members using this repertoire) could be worthwhile in exploring the certainty of the knowledge used within each repertoire and co-determining the weight which should be provided to each repertoire and subsequently possibly producing new knowledge. However, since the scientific repertoire reflects the scientific assessment of a medical technology and the equity repertoire the societal appraisal, they are perceived as separate domains that should not interact. Such interface does not, and should not, take place. The precedent effect of admission bears witness of a process repertoire, while the discussion on (the lack of) evidence of effectiveness reflects a scientific repertoire. The normally dominating equity repertoire is used when the ACP members wonder what arguments can be provided to indeed admit the stop smoking program in the benefit package. Since, amongst others, admitting this program might restrain the admittance of other more necessary care, the ACP adviced not to admit the program in the benefit package (equity repertoire). In the final report to the Ministry of Health, again the ACP's different arguments from different repertoires are presented separately. Without a thorough interaction between the different repertoires, available in the different phases of the decision-making process, the Board of CVZ decided to advice the Ministry of Health to admit the program to the benefit package since the potential preventive effect was provided more weight than the ACP's argumentations. In other words, the different knowledge types remain different attributes of a medical technology which should be discussed separately. Subsequently, the knowledge base for the reimbursement decisions is not generated by a collective co-production of (new) knowledge, but merely generated by a display of the separate repertoires and related knowledge in the decision-making process. Based on these different forms of knowledge presented, a decision is made. However, an interaction between the different repertoires might have led to another hierarchy of evidence. Both, the certainty of the knowledge

reflected, and the situation in which the reimbursement decision should be executed, could have been part of the discussion. This example shows that the challenge of the different repertoires to interact, is not merely to present the different types of knowledge that shape the attributed value to a prioritization decision. The challenge lies in combining these different repertoires, attributing weight to each repertoire, and perhaps even co-producing new knowledge.

This challenge is problematized, however, by the current arrangement of the decision-making process. Although current decision infrastructure acknowledges the presence and value of the different repertoires, combining these repertoires and attributing weight to them is more difficult.

> *In the new health care system, the CVZ has the important task of managing the insurance packages. Yes, this gives us the task of being responsible. Thus, we have a lot on our plate, we also have to think about the whole issue of breadth in the package; how heavily does the severity of a condition weigh? How do you weigh the availability of alternatives? Where do we set the limit for efficiency – is there even such a limit? ... There's not a delineated decision-tree. I don't think there is a formula that comprises all of these issues because the… you also have societal interests that also play a role of course. … The severity of the illness, the availability of alternatives, but also the costs for the individual patient… (Director CVZ, 2008).*

In other words, CVZ struggles with the formal norms laid upon them to provide transparent and evidence based decisions (primarily making use of the scientific repertoire) and the judgements related to the different forms of knowledge embedded in the decision-making process (such as the clinical or equity repertoire). More specifically, in practice, CVZ is asked for an advice and thus required to formulate, based on its findings, a 'judgement' on the most appropriate prioritization decision. The following quote shows how the director of CVZ acknowledges that value-free advice is difficult to provide, for example, when asked when budget impact, an implicit rationing criterion (see Niezen et al. 2009), will likely play a role in the decision to admit a medicine to the benefit package:

> *Interviewer: And thus, budget impact only plays a role for CVZ as one of the criteria that VWS asks about? <Yes.> And that's it for the CVZ?'*
>
> *Director CVZ: Yes, in principle, we have an informing function, but not really a valuing function. However, that could change, because as soon as you begin working with opportunity costs, it's almost impossible to be value neutral. What you are going to select as reference points, or alternatives, interventions that we could exclude – that can hardly be value neutral.*

Decision-making in practice thus offers more leeway in incorporating well-founded choices and/or values in reimbursement advices than the formal procedure suggests.

> *Interviewer: Is it important that CVZ's advice is always value neutral?*
>
> *Director CVZ: No, and we're not afraid to make certain choices and give transparent arguments to support them. But then we are far removed from the traditional pattern of expectation from the Ministry of Health, which sees the CVZ as medical advisor, and is primarily interested in cost-effect analysis of the therapeutic value of a medicine.*
>
> *Interviewer: Is the CVZ free to formulate the advice as they want?*
>
> *Director CVZ: We do have some freedom. Moreover, the debate with VWS takes place at two different levels: on the one hand, it is about the theoretical division of roles and then it's difficult for us; on the other hand it's about the cases in practice and then VWS is very happy with all of the information that we give them. It turns out okay (Director CVZ, 2008).*

While CVZ is expected to assess a medicine on the most up to date evidence from science and clinical practice, CVZ's director also acknowledges the situational character of prioritization decisions. The request by the Ministry of Health for an advice, and the delegated freedom in how to fill in this advice, provides room for a more situational approach.

In order to be able to attribute weight to each repertoire and co-produce new knowledge, the context in which the reimbursement decision should be made and executed, must be part of the decision-making process. The situational approach allows for the incorporation of other types of knowledge, and specifically the interaction between these knowledge types in the decision-making processes. By making use of different knowledge bases, a prioritization decision can be grounded in its context. Context can influence which (combinations of) repertoires may produce legitimacy at a certain point in the decision-making process. Examples of the importance of context are reflected by the ACP's consideration of the decreasing economy (this section) or in the discussion on specific patient categories in the area of pulmonary fibrosis (section Dutch benefit package management infrastructure). The decreasing economy is no issue in the discussions by the CFH, yet of importance for the ACP to make use of the equity repertoire in supporting argumentations for inclusion in, or exclusion of, the benefit package. An analysis of legitimacy and the act of making legitimate decisions therefore cannot take place without an analysis of the context. Hereby, a more

situational approach is arguably more able to cope with the complex reality, which is difficult to grasp in solely (economic) modelling or a fixed process.

One of the important contexts that should be taken into account in the decision-making process is the connection between health regulation and execution. The repertoire best representing the knowledge from a policy execution's perspective is the repertoire of clinical practice. This repertoire has been acknowledged as containing relevant knowledge for decision-making since it is reflected in both the CFH and ACP meetings. It is also important because it shows the contingency of certain processes on the contexts in which they take place. The repertoire of clinical practice deviates from the repertoire of science and current ideas on legitimate decision-making as it is less rationalistic and more contingent (Bal 1998). Exactly this more contingent characteristic of the repertoire of clinical practice allows for the addition of knowledge on whether the policy decision likely will be implemented in practice. In an earlier paper, Niezen, Bal & De Bont (forthcoming) have shown how regulation of medical technologies is constitutive of the practice in which the medical technology is used. Regulation produces information that, in turn, entails a transformation of the medical technology informed about. This can lead to new forms of governing appropriate medicine use and reimbursement that are in line with latest scientific research and are feasible and executed in clinical practice as well (Niezen, Bal & De Bont forthcoming). The contingency of the repertoire of clinical practice allows for the deliberate and conscious formation of prioritization decisions that are situation dependent and not the production of abstract decisions that embody the ideal of (context-free) objectivity.

Importantly, the interaction between the different repertoires in the decision-making process should not involve the elimination of the phased assessment and appraisal of medical technologies. As (Bal 1998) argues, heterogeneity of repertoires within one phase or forum does not contribute to optimal decision-making. In fact, the different repertoires should be separated from one another organizationally. This separation, allows for channelling potential conflicts and for the opportunity to refer uncertainties to other repertoires. In addition to Bal, Moreira argues that these repertoires should interact whenever uncertainties or disagreements between repertoires arise, subsequently leading to the generation of new knowledge (Moreira 2011). This implies on the one hand that the different and separate committees within CVZ should assess and appraise a medical technology's worth. On the other hand, when uncertainties arise within these committees on the knowledge presented, for example the technological possibilities or societal willingness to pay for a medical technology, conscious acknowledgement and addressing of different knowledge types and the context within which prioritizations decisions should be made and implemented is necessary. To facilitate such

acknowledgement and addressing of different knowledge types and relevant context, some sort of forum for interaction is required. This forum allows for the interaction of the different repertoires in such way that it may lead to new knowledge on the value of a prioritization decision. However, the current vertical organisation, the two-phased and linear decision-making process, insufficiently allows for such interaction.

Co-production of knowledge and legitimacy in decision-making

The purpose of this paper has been to analyze how legitimacy for decisions in health care allocation is constructed. The current benefit package management system in the Netherlands is organized in a rather rational-logical process – a linear two phased decision-making process – presuming that appropriate medicine use and reimbursement not only can be defined, but subsequently can be implemented in health care provision. However, problems in the implementation of (non-) reimbursed medicines and medicine regulations in clinical practice point at a tension between the different perspectives on appropriate medicine use and reimbursement and subsequently the legitimacy of prioritization decisions. In section 'The legitimacy of prioritization decisions and knowledge claims' we demonstrated that the activity of decision-making is based on the use of different repertoires. Each evaluation of and subsequent decision on of a medical technology's worth, can be regarded from different perspectives, and entails different types of knowledge and related conceptions of the moral economy. Acknowledging this diversity of forms of knowledge in the construction of legitimacy of decisions, might be a fundamental step in understanding the lack of impact of some of these prioritization decisions.

By examining CVZ's decision-making process on the admission of medicines to the benefit package, making use of the combination of the Sociology of situated judgement and Social Science and Technology approach, we demonstrated that legitimacy in practice is closely related to the interaction between the repertoires and the context influencing what (combination of) repertoires can produce legitimacy at a certain point in the decision-making process. The importance of context is already established by Lehoux & Blume (2000) when analyzing the HTA of the cochlear implant. Lehoux & Blume (2000) argue that HTA should be informed by a broader set of perspectives, taking into account the wider (social) context in which technologies, such as medicines, are used. The interaction between the different repertoires allows for the inclusion of these different perspectives and the social context of a medical technology. By analyzing the presence of different repertoires in the decision-making process, the relationship

between the different forms of knowledge and attributing worth to a medical technology in making prioritization decisions becomes more contextualized.

Although the current prioritization decision-making process does take into account other forms of knowledge and related values – that is, other repertoires – these different repertoires have limited possibilities to interact. The current decision-making process has been developed to focus on the governmental (macro) level of decision-making, with limited consideration of the regional or community (meso) level, or the physician-patient (micro) level. The context of a medical technology (the location in which it is used and by whom, as well as the organizational and material arrangements in place), is lacking. Subsequently, the current organization of the decision-making process provides more theoretical value for legitimacy than practical utility since it lacks context.

This rather formal approach to the decision-making process, results in a public dialogue model in which legitimacy is gained by integrating the different values and perspectives on appropriate reimbursement in the decision-making process, yet still implies that science and society can be seen as separated domains (Moreira 2011). In addition, Moreira claims, a co-production of knowledge model departs from the view that science and society are intimately linked, and allows for a pragmatic balance between rules and cases. Moreover, such an approach acknowledges that regulation is an integral component of medical technology innovations and practices; regulation and practice are not separate domains.

In practice, this means that the formal decision-making process can be interrupted by ad hoc public discussions of controversies regarding a medical technology. In these discussions membership is open, the general public (representing lay knowledge), together with experts and e.g. patient representatives, discuss the uncertainties regarding a medical technology on an equal base. The focus within these discussions is on the relationship between the technical and the political within the knowledge claims. Exactly this interaction between different repertoires allows for contextualisation. Also, it allows for the debate of evidence or knowledge from different perspectives as well as existing uncertainties on this evidence and knowledge. Such debate, subsequently, leads to generation of new knowledge which in turn can make related decisions more socially robust (Moreira 2011).

The exploration of uncertainty should be the core of health care priority setting systems and supplies increased social robustness (Moreira, May & Bond 2009; Bijker, Bal & Hendriks 2009). Especially, to gain legitimacy for decisions regarding medicines with much uncertainty, the co-production of knowledge can be a solution to derive at socially robust decisions. The current framework is limited in this

respect as it is based on the assumption that legitimacy can be gained and maintained by putting (knowledge of) clinical practice at a distance. These repertoires should not be added to the decision-framework as a separate criterion or a decision phase in order to complete or close this framework, but rather should find a place in the decision-making process in relevant situations. Health regulators, for example, could check what repertoires are relevant in the decision-making process in order to integrate social, political, and ethical aspects of health technology in the evaluation of its worth.

Despite the fact that this research is based in the Netherlands, it can be of value to other countries with regard to organizing reimbursement decision procedures and prioritization of medical technologies. Depending on the different political and institutional systems, other strategies for decision-making procedures and policy measures will be used. However, similar repertoires are likely to be found important to integrate in the decision-making procedures (see e.g. Moreira 2005 on NICE). In this paper, we have predominantly focused on CVZ, the benefit package manager, since it is responsible for constructing the decision-making process and decision-framework. Yet, the relation between CVZ as benefit package manager and advisor to the Ministry of Health is worthwhile to examine further. The relationships between advisory agencies such as CVZ, NICE, FDA and a final decision-maker such as the Ministry of Health, NHS and Medicare / Medicaid respectively, might influence the potential of re-designing the prioritization decision infrastructure. There is space between the considerations in the assessment of a medicine and the ultimate political considerations regarding the final prioritization decisions. Note also that although we speak of “final” decisions, these merely define the preliminary end station of medicine’s reimbursement status until new evidence or uncertainties rise, requiring renewed analysis of the medicine’s value once more.

In conclusion, we argue for a decision-making process in which different repertoires can interact when uncertainties arise, since the current benefit package management infrastructure insufficiently addresses how to promote the design of innovations that are likely to be more valuable than others (Lehoux 2006). Whether the products of HTA, the recommendations of appropriate drug reimbursement and use, are disseminated depends on the network of providers, consumers, manufacturers and the habits, routines, established practices, expertise, rules and laws that regulate the relations and interactions (Lehoux 2006; Edquist & Johnson 1997). Yet, HTA as a means of implementing knowledge-based change within health care systems falls short since the linear, rationalistic process underlying the benefit package management fails to take into account its environment; to sufficiently seek dialogue with or consult the network, and to integrate related routines and regulation. Our analysis of the (interaction) between the different

repertoires provides insight in the infrastructure, its environment and regulatory mechanisms that may contribute to the implementation of reimbursement decisions. Yet, such an approach in the prioritization decision-making process requires the development of an alternative decision-making model. In this model the focus lies on providing a forum for different repertoires, and the potential discussion and co-production of knowledge between these repertoires, when necessary, even outside the borders of the formal organization of the decision-making process. It is the process and the activity of decision-making that warrants the legitimacy of prioritization decisions and not the robustness of evidence or the formal procedure followed alone.

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Discussion and Conclusion

The research in this thesis has started with the question how current infrastructures govern appropriate medicine use and reimbursement and construct legitimacy for prioritization decisions. In my study, I was guided by a science and technology studies (STS) perspective. In particular, the notion of 'infrastructure' allowed for gaining insight in the practice of medicine evaluation. It is the infrastructural work in defining units to measure, putting into place a set of agreements embodied in practice that allows for priority setting, and defining appropriate use and reimbursement of medicines. I have studied the knowledge practices in prioritization decision-making processes, in order to gain insight in the different aspects of the work needed to legitimize decisions. In particular, I was interested in what kind of (new) forms of knowledge, objectivities and social relations are produced by the new approaches of the Dutch national government and the Health Care Insurance Board (CVZ) –an independent agency within arm's length of the national government- in governing appropriate medicine use and reimbursement. In this thesis, the different solutions to legitimize prioritization decisions enacted by Dutch decision-makers are explored. The questions addressed in this study were:

- What work is conducted to legitimize decision-making regarding appropriate drug use and reimbursement?
- How does the decision-making infrastructure, such as the conditional reimbursement regulations and databases, govern appropriate drug use and reimbursement in (clinical) practice?
- What (new) forms of social relations, objectivity and knowledge does the benefit package management infrastructure produce, and how might this lead to new governing mechanisms of appropriate drug use and reimbursement?

In the period 2003-2009, I conducted three case studies of drug reimbursement regulation and related policy tools: a) the conditional reimbursement of outpatient medicines, b) the conditional reimbursement of inpatient medicines and c) the exploration of the possible addition of a new explicit rationing criterion to the decision-framework for benefit package management –'budget impact'. These case studies depict a continual quest for legitimate decision-making. Below, I will shortly present the findings of the previous five chapters in relation to the research questions, as articulated above.

Research findings

How current infrastructure legitimizes prioritization decisions

Dutch priority setting infrastructure presumes that its evidence based character, as well as a transparent and consistent decision procedure, result in legitimate decisions. Much effort has gone into the scientization and formalization of the decision-making process. Legitimizing decision-making, in these accounts, entails improving the transparent use of evidence to inform decision-making processes. However, despite the expansions of this infrastructure, the problem of legitimacy remains.

Chapter one has set the stage for this thesis and indicated that for decision-makers to deal with the problem of medicines, appropriate use and reimbursement should be stimulated by making prioritization choices. The chapter depicted how Dutch government tried to cope with the exponential growth of health care costs relating to pharmacotherapy. The 'regulation expensive medicines' was introduced to aid hospitals in their financial distress. It listed several high costs medicines pressing on the hospital budget which were to be co-financed for 75% by the Dutch health insurers. Although this regulation provided (temporarily) relieve, it also had perverse effects. Pharmaceutical manufacturers now aimed at reaching the prognostic threshold of consuming at least 0,5% of the total pharmaceutical expenses of hospitals, to be incorporated on the regulation. Moreover, medical professionals argued that this co-financing would not solve the problem of high cost medicines and subsequently postcode prescribing. The solution should not be sought in improving technical efficiency –the more effective provision of care–, as has been the case in the 1980s and 1990s. But, the solution can be found in stimulating the productive efficiency –the maximization of health outcome for a given cost, or the minimization of cost for a given outcome. Productive efficiency leads to a better quality of health care provision, as well as sustainability of health care costs. In other words, the solution for governing appropriate medicine use and reimbursement lies in the use of scientific and clinical evidence in decision-making.

In chapter two, I observed that the legitimacy of the conditional reimbursement tool was contested. The legitimacy of the instrument was sought in the evidence based decision-making, and subsequently controlling and sanctioning. CVZ relied on constructing evidence based boundaries in defining appropriate medicine use and reimbursement and subsequently expected these boundaries to be found legitimate by health insurers, medical professionals, pharmaceutical industry and patient organizations. Yet, health insurers and pharmaceutical industry disputed

the legitimacy of the policy tool, referring to the lack of transparency of the decision-making process and the lack of consistency in the use of decision criteria.

Not only was the legitimacy of prioritization decisions sought in evidence based decision making, the decision framework was also made more precise by adding new criteria. Chapter three therefore focused on completing the decision framework, by exploring the possibility of making the budget impact criterion explicit by providing for a rationale. Budget impact's implicit use and influence on decision-making has already been established in previous research (Van Luijn 1999; Trueman, Drummond & Hutton 2001; Stolk, Brouwer & Busschbach 2002). The elaboration of the framework allowed for increased transparency, since the criteria upon which the decisions are based are made explicit. Four rationales were identified for considering the budget impact of new drugs when a reimbursement decision needs to be made: opportunity costs, loss aversion, decision uncertainty and equal opportunity. Whereas decision uncertainty seemed a plausible and pragmatic explanation for the implicit use of budget impact in the decision-making process (see also Koopmanschap, Stolk & Koolman 2010) it is especially the last rationale that might offer some ethical foundation from a societal perspective. The equal opportunity rationale reflects that people may strive for resource allocation fairness by some form of procedural justice that ensures availability of treatment for all.

Despite the expansions of the decision-making infrastructure, the problem of legitimacy remained. For example, the 'equal opportunity rationale' for budget impact calls into question whether it is fair to allocate resources on the basis of a utilitarian principle alone. Implications for the decision framework will then go beyond the need to facilitate application of cost-effectiveness, and require rethinking of the basis for resource allocation decisions. If legitimate decision-making consists of the use of explicit criteria and a completed decision framework, this has important consequences for the efficiency and complexity of the decision-making process and might even decrease the legitimacy of priority setting decision-making.

How current policy tools and regulations govern appropriate medicine use and reimbursement in practice

The current decision-making infrastructure assumes that by constructing evidence based boundaries to the reimbursement of a drug, the practice of prescribing by medical professionals and reimbursing by health insurers will be inclined to follow. My analyses in chapter two and four demonstrate how the current decision-making infrastructure indeed enables governing appropriate drug use and reimbursement.

Yet, not in the way health decision-makers had expected it would. Decision-makers expected strict control and real time monitoring to stop inappropriate medicine use. The conditional reimbursement regulations however provided new governing mechanisms in current decision-making infrastructure, i.e. a changed relationship between policy and practice and new forms of self-regulation of clinical practices.

Chapter two gave a detailed example of the difference between the expected and developed practices. In this chapter, the outcomes of my analysis of conditional reimbursement as a policy tool for stimulating the appropriate prescription and reimbursement of outpatient medicines are described. Although in general the conditional reimbursement instrument was regarded by all stakeholders as promising, its execution in daily practice was lower than expected. In practice, the established evidence-based boundaries of appropriate medicine use, by specifying conditions for reimbursement, were crossed more often than anticipated. Analysis of expected versus observed volumes points at substantial unauthorized drug use in a number of cases. In contrast, medical professionals felt the regulation restricted the provision of appropriate care, which is supported by our findings that adherence to professional clinical guidelines is higher than to restrictions related to conditional reimbursement.

Similarly, the production of evidence did not contribute to informing both policy and clinical practice as was expected. Chapter four explored and compared how two databases, the Growth Hormone Database and the PHAROS registry, were intended to be employed to control the use of growth hormone, Ibritumomab tiuxetan and Alemtuzumab. In my study, I analyzed how the two databases, that were part of the infrastructural work in defining units to measure, supported the production, maintenance and regulation of both policy and clinical practice. I showed that the databases did not dissolve the separation between policy and practice. The differences in the dynamics of policy- and clinical practices complicated the relationship. Policy rules and internal regulations in clinical practices differed in how quickly they could change. While the employment of databases in clinical practices resulted in a constant adjustment of the protocols, policy-makers required the databases to provide for static moments of ‘proven appropriate medicine use’, in order to account for and define a fixed and closed formulary.

The conditional reimbursement regulations, however, also depicted a changed relationship between policy and practice and new forms of self-regulation of clinical practices. For example, chapter two demonstrated how the effect of the policy measure was connected to the informal work conducted during the decision-making process. This informal work influenced clinical practice’s medicine

prescription and the execution of the conditional reimbursement regulation. It consisted of shaping the reimbursement conditions based on, amongst others, the knowledge of policy executing stakeholders, such as medical professionals. Rather than monitoring, it is the extension and involvement of the actors, their objectives and their mutual relationships that seemed to affect the clinical practice of medicine prescriptions. This informal work changed the relationship between policy and practice.

Likewise, the use of databases entailed a new governing mechanism (chapter four). Appropriate medicine use was not reached through direct steering on the outcomes of the databases. Instead, appropriate medicine use was reached indirectly, by stimulating data collection and the continuous reflection upon the data by researchers and clinicians. In fact, the prerequisite of data collection and storage shaped both the work of decision-makers and medical professionals. The norms and knowledge of medical professionals guided reimbursement decisions. Vice versa, health policy regulators codetermined what data needed to be collected. Subsequently, they were able to steer what information the medical professionals used to inform their practice. In both policy measures the new governing mechanisms have shifted focus towards collective forms of expertise, combining people (clinicians, researchers, administrators, patients, etc.) and objects (entities, instruments, tools, techniques, etc) and thus creating new types of (regulatory) objectivity.

How the production of (new) forms of social relations, objectivity and knowledge, and new governing mechanisms of appropriate drug use and reimbursement, can contribute to legitimate decision-making

Deconstructing the infrastructure of benefit package management has also allowed me to observe how the infrastructural work enabled the production of (new) forms of knowledge and objectivity to emerge. A decision-making infrastructure is an evolving structure, i.e. it embodies processes of discussion, negotiation and compilation that facilitate the emergence of new governing mechanisms. These new governing mechanisms have the potential to substantially contribute to legitimizing decisions as they focus on the process, the activity of decision-making.

Chapter two, for example, demonstrated that the effect of conditional reimbursement was tied into the way prescribing conditions were developed, and how this informal work changed the relationship between policy and clinical practices. According to both policy-makers and medical professionals, the networks in which medical professionals, decision-makers and health insurers collaborated in establishing ‘appropriate drug use and reimbursement’, were regarded the most

successful knowledge infrastructures. For example, the medical professionals and health insurers regarded conditions for reimbursement as appropriate, when timely adjustments of the conditions were made possible. These timely adjustments were possible through the involvement of central assessment committees, incorporating both medical professionals and health insurer representatives. The committee kept the connection between policy and practice tight.

The development of databases as a prerequisite for the reimbursement of expensive medicines, explored in chapter four, is another example of a new form of governing appropriate medicine use and reimbursement that contributed to legitimizing the decision-making on appropriate medicine use. The databases enabled the production of a new form of objectivity. The databases allowed for regulatory objectivity to emerge endogenously from clinical and research activities. To be able to produce evidence for appropriate medicine use the collectives set regulations in clinical practice; regulatory work became inherent and constitutive to clinical practice. Once the databases were turned into policy instruments, these internal regulations provided a framework for defining 'appropriate medicine use'. In addition, the databases stimulated reflexivity as part of the continual development of clinical practice's regulation. The collectively determined conventions only temporarily provided closure on the uncertainties related to the effective use of expensive pharmaceuticals in daily clinical practice. The constant adjustment of regulations now defined the relationship between policy and clinical practice. In fact, the dynamic process of continual data collection and reflexivity by medical professionals and researchers fulfilled the health regulators' goal of stimulating appropriate medicine use and reimbursement in clinical practice during the three year period of data collection and contributed to legitimizing prioritization decision-making.

Making use of the sociology of situated judgement in combination with science and technology studies, chapter five demonstrated that legitimizing decision-making has much to do with incorporating relevant repertoires. The evaluation of medicines can, in its' pursuit of 'objectivity', not be seen separate from politics and morality. I identified four different repertoires used to evaluate a medicine in prioritization decision-making processes. These repertoires are labelled as the science, clinical practice, equity, and process repertoire. The different repertoires included different perspectives on what legitimate decision-making and decisions constitute of. These repertoires combined knowledge claims and conceptions of justice and fairness. Moreover, each repertoire had its own characteristics and dynamics, providing actors with symbols, stories, world views, material and organizational arrangements from which they could select different elements to shape and legitimize prioritization decision-making. Also, each repertoire entailed different

forms of knowledge, such as health economic, experiential, ethical, or methodological knowledge. The different forms of knowledge, in turn, attributed value to a medicine in terms of cost-effectiveness, effectiveness in daily practice, equal access and transparency of the decision-making process. For example, the repertoire of science lend heavily on systematic and objective evaluation of outcomes research information. Only an infrastructure with a complete and non-contradictory set of rational and evidence based decision rules, preferably including cost-effectiveness information based on randomized clinical trials, could legitimize decision-making. In contrast, the repertoire of equity was a dynamic and evolving repertoire. Knowledge was generated through continuous negotiations on how to define solidarity, for example, regarding life style diseases. These negotiations were less formal and less systematic. The acknowledgement of the diversity of forms of knowledge in the construction of medicine decisions, I argued, therefore might be a fundamental step in understanding the lack of impact of some of these decisions.

The challenge for decision-makers to legitimize their decision-making, however, did not lie in merely presenting the different types of knowledge that shaped the attributed value to a prioritization decision. The challenge lied especially in combining these different repertoires, attributing weight to each repertoire and even co-producing new knowledge. In chapter five, I argued that the interaction between the different repertoires can lead to another hierarchy of evidence, since the certainty of the knowledge reflected as well as the situation in which the reimbursement decision should be executed is part of the discussion. Such a form of decision-making produces information that, in turn, entails a transformation of the medicine informed about. This leads to a different form of governing appropriate medicine use and reimbursement, and likely also leads to legitimizing decision-making. For example, uncertainty related to a medicine is not transformed into a certainty, yet becomes acknowledged. In turn, difficult decisions are acknowledged and not shoved away. Thus, legitimizing decision-making also depends on the co-production of knowledge on appropriate medicine use and reimbursement in the decision-making process.

General discussion

The aim of this thesis has been to enrich our understanding of decision-making in a context of scarce resources. Specifically, this thesis focused on the limits and possibilities of the current decision-making process on expensive drug regulations. Based on the findings described above, three main findings can be distilled. First, the benefit package management infrastructure struggles with the construction of two separate domains; policy and practice. The current infrastructure enacts an

artificial separation that shuts out knowledge from (clinical) practice in policy; it excludes morality and politics from decision-making. Second, legitimacy of decision-making is not something one can simply construct, but entails much work. Therefore, the legitimacy of prioritization decisions should be redefined towards the activity of legitimizing decision-making. Last, such a redefinition entails that reimbursement decisions are not regarded as the end of the decision-making process, yet as merely one, albeit important, point in the process of governing appropriate medicine use and reimbursement.

First, the use of evidence in decision-making, and transparent decision-making procedures, have contributed to the perceived authority of health decision-makers, and therefore the acceptance and validity of their argumentation. The assessment of pharmaceutical care is increasingly being standardized, as if it is a model of reality which can be completed by adding criteria, disregarding the need for a situational approach when appropriate. This 'instrumental rationality' guiding the evidence based policy approach insufficiently takes into account that policy-makers have to make difficult decisions while dealing with moral and factual ambiguity (Sanderson 2006). In other words, the authority of science and its exclusive claim on knowledge about reality is at best only partly a solution to legitimize prioritization decisions.

In addition, this thesis has showed that current infrastructure of benefit package management pays little attention to the management of diverging rationalities about (the value of) medicines. Yet, working towards legitimacy in decision-making is about constructing socially robust decisions. Dutch benefit package management infrastructure's central political objectives are good and affordable care for all citizens. What is believed to be the public good 'health care' appears to be valued differently by different stakeholders.

Although these problems with the infrastructure of benefit package management were acknowledged, the solutions were sought in more scientization and formalization. One of the solutions sought was, for example, optimizing the benefit package management system. Making an implicit rationing criterion explicit –see chapter three on budget impact– increased the decision-making process' transparency. To legitimize decision-making through the use of scientific evidence and increasing transparency alone, within the current infrastructure, required further formalization of the reimbursement decision-making processes. It is questionable whether the continuous quest for transparency actually contributes to the efficiency and robustness of decision-making (cf. Bijker, Bal & Hendriks 2009).

Second, chapters four and five demonstrated how another perspective on the legitimacy of decision-making contributed to governing appropriate medicine use and reimbursement. Legitimizing decision-making was related to the acceptance and validity of the activity of decision-making. This approach acknowledged the importance of the way knowledge and knowledge infrastructures are shaped. It showed how a decision-making infrastructure is an evolving structure. An infrastructure embodies processes of discussion, negotiation and compilation that can facilitate the emergence of new governing mechanisms. These new governing mechanisms have the potential to substantially contribute to legitimize decision-making.

In chapter four, I demonstrated how the activity of legitimizing decision-making was not only found on a governmental level, e.g. within CVZ, but was also embodied in the different policy tools (cf. Bejerot & Hasselbladh 2011). These policy tools became a coordination regime, facilitating the interaction between the different stakeholders, especially policy, scientific and clinical practice, and objects, such as databases, evaluation techniques, etc. This interaction allowed for the emergence of new forms of objectivity and regulation. Regulatory objectivity, in essence, was shaped in the interaction between the policy practice of decision-making and clinical (research) work. It was based on findings in clinical work and transformed, through the use of databases, in information usable for scientific research as well as policy practice. In this process, appropriate medicine use was shaped.

Acknowledging the diversity of repertoires in evaluating a medicine also contributed to the activity of legitimizing prioritization decision-making. The different repertoires led to different actions and decisions regarding appropriate drug use and reimbursement. In the incorporation of the different repertoires in decision-making, it was elementary to realize that the different repertoires entailed different appraisals of the value of a medical technology. The question “what medical technologies should be collectively paid for?” has multiple answers, since the domains of ethics, economics and quality are ranked and valued differently. These differently attributed values might even conflict or at least compete with one another for precedence. The acknowledgement of the diversity in different repertoires did not reduce the complexity of governing appropriate medicine use and reimbursement. Instead, it allowed for a more complete evaluation of a medicine, making use of relevant repertoires, when uncertainties regarding the value of a medicine arise.

The different forms of knowledge and knowledge infrastructures affect the process of legitimizing decision-making. The different notions of knowledge (infrastructures) supporting and informing health care prioritization decision-making were illustrated

in both the interaction between policy, science and clinical practice (chapter four), and the analysis of the different repertoires used to appraise a medicine (chapter five). Understanding of the role of (socially robust) rationalities in decision-making, and continual reflection on the knowledge embedded in governing mechanisms, therefore is crucial. Reimbursement decisions were regarded as legitimate, when the underlying principles were perceived as just, fair, and transparent, and did not conflict with or neglected the existing repertoires. Moreover, the underlying principles were traceable in daily practice of appropriate medicine use and reimbursement too. They were woven into the interactions between medical professionals and health care reimbursement decision-makers and resulting governing mechanisms. Governing appropriate medicine use and reimbursement thus requires room for different repertoires and the potential discussion and co-production of knowledge between these repertoires, when necessary even outside the borders of the formal organization of the decision-making process (cf. Moreira 2011).

Last, legitimizing decision-making entails that reimbursement decisions are merely one point in the process of governing appropriate medicine use and reimbursement. The inclusion, or exclusion, of a medicine in a pharmaceutical formulary, should be regarded as the start of the stimulation of appropriate medicine use and reimbursement. Shaping the appropriate use and reimbursement of pharmaceuticals requires a continual reflection on the effects of a medicine in daily practice, as well as the value attributed to the medicine. This study emphasized the need for new governing mechanisms of appropriate medicine use. Studied examples of new governing mechanisms, were based on the notion of 'regulatory objectivity' and the acknowledgement of the different repertoires in attributing value to a medicine. This does not mean that, for example, the explored databases should stand model for constructing legitimacy of decisions, since this would require e.g. far-reaching standardization of care. Instead the governing mechanisms embodying interaction between policy and clinical practice, as depicted in the exploration of the conditional reimbursement regulations, however, should stand model for the activity of legitimizing prioritization decision-making. For example, whenever uncertainty arises about the value of a medicine, relevant repertoires –that combine people and objects–, such as the clinical practice repertoire, should find room in the decision-making process. Not as a separate phase, yet interacting with the other repertoires in the decision-making process, and in the further development of defining appropriate medicine use and reimbursement.

Implications for the evaluation of medicines

Dutch government has responded on the quest for legitimacy with the collection of more scientific evidence and more transparency requirements. Completing the decision framework, however, as I argued, is not likely to increase its legitimacy. In spite of the above mentioned challenges, this quest for legitimacy is fed by a basic optimism about the role of scientific knowledge that remains embedded in western liberal democratic political systems (Sanderson 2006). The solution of complex social problems is believed to require "better evidence of 'what works' in terms of policy intervention, and more 'rational' policy-making processes in which such evidence can play a stronger role in policy decisions" (Sanderson 2006, p.124). There are at least two implications worth mentioning of this rational policy process model which can be distilled from this thesis.

First, within this rational model, the focus is on improving the 'instrumental' use of research and evaluation (Sanderson 2006). Thus, the policy constructed at a distance of its execution not only provides legitimacy, but is expected to be executed in practice as well. However, currently, more and more health regulators feel the need to improve the dynamic nature of health regulation, of which conditional reimbursement regulations are good examples. At present, the way the benefit package management infrastructure is designed, does not allow for such transformation in steering appropriate drug use and reimbursement. The formulation of a benefit package with a positive list of medicines to be reimbursed requires 'yes' or 'no' decisions. The conditional reimbursement regulations already show a more dynamic nature of steering appropriate medicine use and reimbursement. However, in the end, they require a similar 'yes' or 'no' decision. The steering mechanism based on regulatory objectivity, as shown in chapter four, indicates how appropriate medicine use and reimbursement can be stimulated and even somewhat controlled on a continual basis of reflection. A next step in further embracing these new forms of steering health care, I believe is worthwhile to experiment with, lies in making adjustments in the political system. For example, the ownership and thus financial responsibility of the databases, as discussed in chapter four, are heavily debated. The Ministry of Health's financial support to stimulate the development of these databases is crucial. It allows for generating data that stimulates reflection about appropriate medicine use in clinical practice. Moreover, it stimulates clinical practice and policy to co-produce knowledge on appropriate medicine use and reimbursement. Although these new governing mechanisms and adjustments of the political system sound as drastic changes, they are mostly a continuation of the process of incremental changes in the health system and governing the collective funding of public goods.

Secondly, the rational process of decision-making consists of different phases in determining the policy problem, the appropriate measures and subsequently their implementation and sometimes also their evaluation. Moreover, this rational model of policy-making sees the different phases in decision-making as sequential and unequivocally separate (Bal 2006). This can be illustrated by the division of the drug reimbursement decision-making process in a technical assessment, followed by a societal appraisal phase. The inclusion of an appraisal committee, reflecting upon any societal considerations to trump or deviate from the preliminary decision in the technology assessment phase, bears witness of gained insight in the action of legitimate and effective decision-making. However, currently this appraisal committee is seen as a final hurdle in the process of formulating an advice to the Ministry of Health about the admission of a medical technology. Yet, in this final phase, it appears that much debate concerns the validity or even existence of evidence in the assessment phase (based on observations of ACP meetings). If the societal appraisal, or even other relevant repertoires, would be better integrated or valued in the decision-making process, its efficiency might be improved, as well as its legitimacy and effectiveness.

A more dynamic and reflective regulation of drug reimbursement, might even be a logical continuation of already existing processes. In this dynamic and reflective regulation, the various repertoires gain importance, and infrastructures for stimulating appropriate medicine use and reimbursement are (further) constructed. The PHAROS database is exemplary for a new form of governing medicines based on the notion of regulatory objectivity. Making use of a knowledge infrastructure that requires continual reflection on the relevant knowledge for the decision-making process is the essential element. The evidence used exists, on the one hand, of objects, such as databases or RCT's and outcomes research. On the other hand, it consists of the interpretation and reflection, by medical professionals or other relevant repertoire owners, on this evidence. The type of data to be collected is discussed between policy and clinical practice. This discussion takes place, both in the process towards the data collection, and during the data collection period itself. The discussion and negotiation allows for the emergence of a new steering mode, contributing to the objectification and regulation of appropriate medicine use and reimbursement. Note, this does not take away the importance of a proper technology assessment and the need for a prioritization decision framework. On the contrary, both scientization and formalization have enormously contributed to constructing legitimacy in prioritization decision-making. However, further optimizing current decision-making infrastructure, I have demonstrated, should not be sought in the robustness of evidence or the formal procedure. Further optimizing prioritization decision-making should be sought in the process and the activity of decision-making. Whereas in 1998 Holm argued for the second phase of

priority setting activities, entailing the realization that simple solutions for priority setting are flawed and focusing on the priority setting process itself and its transparency, I argue for a third phase of priority setting activities (Holm et al. 1998). In this third phase, prerequisites for a good evaluation of medicines are the incorporation of relevant repertoires, especially that of clinical practice, when uncertainty about a medicine's appropriate use and reimbursement in practice arises, and (the stimulation of) the interaction between the different repertoires allowing for the co-production of new knowledge on appropriate medicine use and reimbursement.

More general, this thesis demonstrates how social sciences can provide insight in the use of knowledge in decision-making infrastructures. Social scientific research and evaluation of decision-making in complex situations, develops knowledge about how and why policy measures do, or do not, 'work'. It addresses questions such as: Is it possible to define a decision framework for the prioritization and allocation of scarce resources in such way it strikes the right balance between the legitimacy and effectiveness of the policy decisions? Or, do the continuous legitimizing problems of policy-makers require another perspective on the creation and use of scientific evidence, objectivity and transparency? These questions entail the exploration of the prerequisites for legitimate and effective policy measures. Policy experiments can provide input for social scientific research, such as the exploration of the databases in the conditional reimbursement regulation. This type of research, as conducted in this thesis, does not focus on the management or organization of public service agencies, but focuses on the activity of making policy measures effective and legitimate. Similar research has proven fruitful in exploring the construction and use of prescription data, by pharmacists and GPs, as performance indicators in The Netherlands. In their study on performance measurement by local pharmaceutical consultation groups, De Bont & Grit (2012) opened up the black box of the performance indicator, by focusing on the active role of the measurements in governing rational drug use. Subsequently, they "were able to describe the advantages of a simple and general measurement to performance management in comparison to a more extensive set of performance indicators". Exactly this understanding of the role of scientific evidence and other (socially robust) knowledges in decision-making, and the way the influence of these knowledges is prioritized, is highly relevant in current organization and management of the health care arena.

Research reflections

The combination of research material gained through both qualitative and quantitative methods has not only proved to be fruitful, yet included much and

complex work as well. It is exactly this aspect of my research I would like to reflect upon in the final pages of my thesis. Especially, since believing in the incompatibility of the quantitative and qualitative research paradigms and associated methods, is still much alive in the science practices informing health policy. The approach taken in this thesis is a qualitative one. The rigour of my analysis and findings is not based on systematically testing and empirically justifying a hypothesis. The quality of my research is safeguarded by strategies such as triangulation and member checking. However, throughout my research period, I was able to observe and actively participate in the two research cultures. The question how to collect and analyze data on the Dutch drug reimbursement decision-making process, to gain insight in legitimate and effective decision-making, has resulted in interesting debates and research struggles. These struggles were not only fed by the different methodological approaches, but most often by the different perspectives on how, and in what way, social sciences should inform health policy decision-making. Like Lehoux (2006), who claims that in her research on 'The problem of Health Technology' she worked on border zones of various research domains (industrial design, public health, epistemology, sociology of science and technology, etc.), I have been looking for insights resulting from combining the border zones of health economics and STS. Working with and observing my colleagues from the disciplines of health economics and STS has taught me that holding on to, for example, the principle of 'multiple realities'; "the contradictory, but equally valid accounts of the same phenomenon", is worthwhile but entails challenges in working together too (Johnson & Onwuegbuzie 2004, p.16).

It is not the associated methods with the research paradigms that caused debates in the teams I worked with, but much more the underlying principles on the position of science in (re)constructing reality to inform the public at large, fellow researchers, policy etc. From a quantitative research paradigm, in specific the health economics it is up to the decision-makers to decide upon the research's value to the policy. Once research is conducted and its results and underlying principles presented, the work of the researchers is finished. From a qualitative research paradigm, in specific in STS, it is exactly the interaction between the researcher and policy-makers which attracts a lot of attention. Therefore, I claim it is not the incompatibility between the qualitative and quantitative research paradigm the discussion should focus on, but on the discussion how the combined efforts will likely contribute to informing health policy.

For future mixed method research projects, I would advice to acknowledge these fundamental differences early in the research process and make them part of joint discussion. It is wise to try to establish a basic set of agreed principles, and

subsequently methodological strategies to allow for a better mix of combined research methods and paradigms. Integrating data and findings from both qualitative and quantitative research in one study has proven rather difficult. Discussing methodological strategies might aid in improving such integration. However, the underlying discussion on the principles and focus on the purpose and concept of science should not be forgotten. Nevertheless, in practice, mixed method research remains difficult; O'Cathain et al. (2008) show how many "researchers mainly ignore the mixed methods design and only describe the separate components of a study" (O'Cathain, Murphy & Nicholl 2008, p.92). Though the promise of mixed methods research, an opportunity for synthesis of research traditions and insights a mono approach would not achieve, is worthwhile to pursuit for, especially in complex research arenas such as health care.

Final conclusion

In this thesis, I have analyzed several solutions searched for by Dutch health policy-makers to complete the decision framework, as well as analyzed new approaches taken in drug reimbursement decision-making processes. In particular, I explored the –knowledge– practices in prioritization decision-making processes, to gain insight in the different aspects of the work needed to legitimize prioritization decisions. This exploration has led to three main findings. First, the benefit package management infrastructure struggles with the construction of two separate domains; policy and practice. The current infrastructure enacts an artificial separation that shuts out knowledge from (clinical) practice in policy; it excludes morality and politics from decision-making. Second, legitimacy of decision-making is not something one can simply construct, yet legitimizing prioritization decision-making entails much work. Therefore, the legitimacy of prioritization decisions should be redefined towards the activity of legitimizing the decision-making. Last, such a redefinition entails that reimbursement decisions are not regarded as the end of the decision-making process, yet as merely one point in the process of governing appropriate medicine use and reimbursement. These findings demonstrated that the search for improving prioritization decision-making should make room for the insights of the social scientific discipline in the understanding of legitimizing decision-making. Further social scientific research on the infrastructure of benefit package management can contribute to insights in how current benefit package infrastructure can be organized in a way the interaction between the different repertoires becomes part of the evaluation of medicines. The incorporation of, amongst others, lay knowledge in the debate on the value of a medicine, I demonstrated, legitimizes the prioritization decision to be made. Therefore, an exploration of the possibility of a 'co-production of knowledge'-model in Dutch benefit package management system, could be a next step in legitimizing the drug

reimbursement decision-making processes. A 'co-production of knowledge'-model, for example, allows for the ad hoc inclusion of public debate on controversial health technology decisions (Moreira 2011).

To end, this thesis demonstrated that working towards legitimacy entails a different approach to governing appropriate medicine use and reimbursement. In this approach, the drug reimbursement process is not the end, but merely the beginning of legitimating prioritization decisions. This requires an infrastructure of benefit package management that is (re)designed to stimulate a continual interaction between policy, science and (clinical) practice, to reflect upon appropriate medicine use. Acknowledging the diversity of forms of knowledge in legitimizing prioritization decision-making, is a fundamental step in establishing new governing mechanisms for appropriate medicine use and reimbursement. In the end, it is the process and the activity of decision-making that warrants the legitimacy of prioritization decisions and not the robustness of evidence or formal procedure followed alone.

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Summary in English

The research in this thesis starts with the question how current infrastructure of benefit package management governs appropriate medicine use and reimbursement, and constructs legitimacy for prioritization decisions. In this thesis, the Dutch drug reimbursement decision-making and related policy instruments are studied. The sharp rise of both the costs of (innovative) medicines and the ageing population put pressure on the entire health system. Consequently, there is a need for priority-setting. Governments try to ensure that the scarce resources available to health care are put to optimal use. The priorities for the allocation of scarce resources, such as medicines, are set via principles, values and/or defining practices. Given what is at stake for patients affected by reimbursement decisions, governmental regulators are also expected to establish legitimacy of their decision-making. Legitimacy of decision-making entails that the public considers the decision-making -framework, -process and -outcomes, to be just or socially robust. Currently, governmental decision-makers shape the legitimacy of decision-making via the scientization and formalization of the decision-making process. Accordingly, the decision-making infrastructure is expanded. Despite these expansions, the problem of legitimacy remains; e.g. the evidence based boundaries to the reimbursement of a drug are disputed by medical professionals and health insurers, and do not incline (clinical) practice to follow. Therefore, this thesis demonstrates, another perspective on the legitimacy of decision-making is needed in order to contribute to governing appropriate medicine use and reimbursement. A decision-making infrastructure is an evolving structure; i.e. it embodies processes of discussion, negotiation and compilation that facilitate the emergence of new governing mechanisms. These new governing mechanisms have the potential to substantially contribute to legitimizing decisions as they focus on the process, the activity of decision-making.

In chapters one, two and three, current medicine regulations and decision framework are explored and evaluated, in order to understand how scientization and formalization stimulate appropriate medicine use and reimbursement. This evaluation demonstrates that the execution of health regulations in daily practice deviates substantially from the intended policy and its underlying principles. Current infrastructure of benefit package management pays little attention to the management of diverging rationalities about (the value of) medicines. Therefore, it does not come as a surprise that health regulators still experience difficulties explaining the basis for their drug reimbursement decisions. The expansions of the decision-making infrastructure do not seem to have solved the problem of legitimacy. At least, not in the sense of socially robust prioritization decisions. In chapters four and five, this thesis focuses on the (knowledge) practices and the Dutch benefit package management infrastructure, making use of a social scientific perspective. The analyses in these chapters show that policy and clinical practice

are working towards legitimacy in decision-making. Yet, not in the way decision-makers had expected, through strict control and monitoring. But, by shifting focus towards the process of decision-making; by stimulating the interaction between policy, science and practice as well as acknowledging the different rationalities in prioritization decision-making.

Chapter one depicts how Dutch government has tried to cope with the exponential growth of health care costs relating to inpatient pharmacotherapy in the late 1990's. Dutch government aimed to solve the cost problem in the inpatient pharmaceutical care sector, through regulating the (additional) financing of expensive inpatient medicines and transferring responsibility of access to care to health insurers and hospitals. Yet (clinical) practice depicts this policy as inadequate and potentially leading to legitimacy problems regarding the equal distribution of care. Thus, despite the efforts of health regulators, the expensive medicines regulation did not have the desired effects. Next, this chapter points at the call by both policy makers and medical professionals for the development of more evidence based policy and evidence based mechanisms in order to gain legitimacy for decision-making. Making evidence based prioritization choices is thought to stimulate appropriate medicine use and reimbursement in practice.

In **chapter two** the evaluation of the conditional reimbursement of outpatient medicines as a policy tool, shows that evidence based decision-making does not automatically lead to appropriate medicine use and reimbursement in clinical practice. The Health Care Insurance Board, an independent agency within arm's length of Dutch government, responsible for the benefit package management, focuses on defining and stimulating appropriate medicine use and reimbursement. In order to promote effective and efficient use of certain pharmaceuticals, the reimbursement of a medicine is made conditional to specific criteria or rules (e.g. specific patient groups and health providers). Mostly, conditions apply to those drugs that are considered expensive and/or have a risk of inappropriate use. Conditions are defined to limit off-label drug use and promote drug use for indications where effectiveness has been established. This evidence based character of the conditions should warrant the policy tool's legitimacy. Additionally, the Health Care Insurance Board expects that the scientization of the decision-making inclines the practice of prescribing (medical professionals) and reimbursing (health insurers) to follow. However, health insurers and pharmaceutical industry contest the legitimacy of the conditional reimbursement policy tool. They refer to the lack of transparency of the decision process and the lack of consistency in the use of decision criteria. In practice, it appears, the evidence based conditions for appropriate medicine use and reimbursement are crossed more often than anticipated. Instead, the cases that include knowledge from policy executing

stakeholders, such as medical professionals, to formulate the reimbursement conditions, are regarded as examples of legitimate decision-making. These cases also prove rather influential on clinical practice's medicine prescription. This chapter therefore shows that the amount of effect of the policy measure is not attributed to its evidence based character, yet to the way the conditions for reimbursement are developed and executed. The latter involves a changed relation between policy and practice.

Not only was the legitimacy of prioritization decisions sought in evidence based decision making, the decision framework was also made more precise by adding new criteria. **Chapter three** therefore focused on completing the decision framework, by exploring the possibility of making the budget impact criterion explicit by providing for a rationale. Whereas the current Dutch decision framework explicitly entails the criteria of effectiveness, cost-effectiveness, and severity of illness, the role of budget impact remains less obvious. Explicating budget impact as a rationing criterion, assumes that this explication contributes to the transparency of the decision process and therefore the accountability of the decision-makers. This chapter identifies four rationales for considering budget impact in reimbursement decision-making: opportunity costs, loss aversion, decision uncertainty and equal opportunity. Especially equal opportunity might offer some ethical foundation. Equal opportunity reflects that people may strive for resource allocation fairness by some form of procedural justice that ensures availability of treatment for all. Yet, this particular rationale for budget impact calls into question if it is fair to allocate resources on the basis of a utilitarian principle alone –the ethical foundation for the cost-effectiveness criterion. Implications for the decision framework will then go beyond the need to facilitate application of cost-effectiveness, and require rethinking of the basis for resource allocation decisions. Provided that legitimate decision-making consists of the use of explicit criteria and a complete decision framework, the acknowledgement of budget impact as an explicit rationing criterion has important consequences for the efficiency and complexity of the decision process. It might even decrease the legitimacy of priority setting decision-making. Thus, despite the expansions of the decision-making infrastructure, the problem of legitimacy remains.

Chapter four demonstrates how the activity of legitimate decision-making is found on a governmental level, and simultaneously is embodied in its policy tools, such as the databases. The exploration of the Growth Hormone database and PHAROS registry shows whether and how the efforts to accumulate and organize clinical data and the increasing use of databases in clinical, research and policy practices have transformed the regulation of clinical practices. We demonstrate how databases have become a coordination regime. The databases facilitate both, the

interaction between policy and clinical practice, and the interaction between collective forms of expertise. The latter entails the combining of people (clinicians, researchers, administrators, patients, etc.) and objects (entities, instruments, tools, techniques, etc). These interactions allow for the emergence of new forms of objectivity and regulation, such as regulatory objectivity. Subsequently, the relationship between clinical and policy practice is reconfigured. Although the databases do not allow for real time monitoring as expected by the health regulators, the dynamic process of continual data collection and reflexivity by medical professionals and researchers does fulfil the health regulators' goal of stimulating appropriate medicine use and reimbursement in clinical practice. By adapting new governing mechanisms, such as databases, in current decision-making infrastructure, it becomes possible to stimulate appropriate medicine use and reimbursement in clinical practice and concurrently facilitate working towards legitimate decision-making.

Chapter five combines and explores the three case studies within this thesis: a) the conditional reimbursement of medicines in the outpatient setting, b) the conditional reimbursement of medicines in the inpatient setting, and c) the possible addition of a new rationing criterion to the decision-framework for benefit package management; 'budget impact'. The cases are explored and analysed with respect to the dynamics of legitimate decision-making from a situational approach to regulatory behaviour. The sociology of situated judgement provides insight in the process and the different ways actors legitimate their action of decision–making, and has contributed to the definition of a framework of different 'repertoires of justification'. Each repertoire has its own characteristics and dynamics, providing actors with symbols, stories, world views, material and organizational arrangements from which they can select different elements to justify their action. The conception of the repertoires is used to identify four different repertoires of evaluation in Dutch drug reimbursement decision processes: the science, clinical practice, equity, and process repertoire. Each repertoire entails different forms of knowledge (such as tacit, clinical, methodological, health economic knowledge) which in turn attribute value to a pharmaceutical (decision). Based on the identification of these repertoires, this chapter demonstrates that legitimacy in practice is closely related to the interaction between the repertoires and the context influencing what (combination of) repertoires can produce legitimacy at a certain point in the decision process. Therefore, the (lack of) impact of some prioritization decisions can be understood by the (insufficient) incorporation and interaction of the different repertoires in the decision process. Finally, we argue for a decision process that sufficiently takes into account its environment when uncertainties arise; seeking dialogue with or consultation of the network, integrate related routines and regulation.

In the **discussion and conclusion** this thesis reflects upon the question how current benefit package management infrastructure governs appropriate medicine use and reimbursement and constructs legitimacy for prioritization decisions. The evaluation and exploration of the different policy tools have led to three main findings. First, the benefit package management infrastructure struggles with the construction of two separate domains; policy and practice. The current infrastructure enacts an artificial separation that shuts out knowledge from (clinical) practice in policy; it excludes morality and politics from decision-making. The use of evidence in decision-making, and transparent decision-making procedures, have contributed to the perceived authority of health decision-makers, and therefore the acceptance and validity of their argumentation. Yet, little attention is paid to the management of diverging rationalities about (the value of) medicines. Second, legitimacy of decision-making is not something one can simply construct, but entails much work. Legitimizing decision-making is related to the acceptance and validity of the activity of decision-making. Last, such a redefinition entails that reimbursement decisions are not regarded as the end of the decision-making process, yet as merely one, albeit important, point in the process of governing appropriate medicine use and reimbursement. The inclusion, or exclusion, of a medicine in a formulary by the Ministry of Health is the beginning of the stimulation of appropriate medicine use and reimbursement.

To end, this thesis demonstrates that working towards legitimacy entails a different approach to governing appropriate medicine use and reimbursement. In this approach, the drug reimbursement process is not the end, but merely the beginning of legitimating prioritization decisions. This requires an infrastructure of benefit package management that is (re)designed to stimulate a continual interaction between policy, science and (clinical) practice, to reflect upon appropriate medicine use. Acknowledging the diversity of forms of knowledge in legitimizing prioritization decision-making, is a fundamental step in establishing new governing mechanisms for appropriate medicine use and reimbursement. In the end, it is the process and the activity of decision-making that warrants the legitimacy of prioritization decisions and not the robustness of evidence or formal procedure followed alone.

Nederlandse samenvatting

Het onderzoek in dit proefschrift start met de vraag hoe de huidige infrastructuur van pakketbeheer het gepast gebruik en vergoeden van geneesmiddelen stuurt, en legitimiteit van prioriteringsbeslissingen construeert. Dit proefschrift bestudeert de besluitvorming van geneesmiddelenvergoedingen en gerelateerde beleidsinstrumenten. Zowel de sterke stijging in de kosten van (innovatieve) geneesmiddelen en de vergrijzende populatie drukken op het gehele gezondheidszorgstelsel. Hierdoor is er een noodzaak tot prioritering. Overheden proberen te waarborgen dat de schaarse middelen die beschikbaar zijn binnen de gezondheidzorg ook optimaal worden ingezet. De prioritering van de allocatie van deze schaarse middelen, zoals geneesmiddelen, wordt vastgesteld aan de hand van principes, waarden en/of het definiëren van praktijken. Aangezien er voor die patiënten die geraakt worden door de vergoedingenbeslissingen heel wat op het spel staat, moeten beleidsmakers zich ook verantwoorden voor de legitimiteit van de genomen beslissingen. Legitimiteit van besluitvorming houdt in dat de beslissingscriteria, het proces en de uitkomsten van de besluitvorming door het publiek gezien worden als rechtvaardig of sociaal robuust. Op dit moment wordt de legitimiteit van besluitvorming vormgegeven door de verwetenschappelijking en formalisering van het besluitvormingsproces. Zodoende wordt de besluitvormingsinfrastructuur volgens deze structuur uitgebreid. Ondanks deze uitbreidingen, blijft het legitimiteitprobleem bestaan; bv. de evidence based condities voor geneesmiddelenvergoedingen worden door medische professionals en zorgverzekeraars betwist en dragen niet bij aan het volgen van de regelgeving in de (klinische) praktijk. Daarom laat dit proefschrift zien dat een ander perspectief op legitimiteit van besluitvorming nodig is om bij te dragen aan het sturen van het gepast gebruik en vergoeden van geneesmiddelen. Een besluitvormingsinfrastructuur is een evoluerende structuur; i.e. het belichaamt processen van discussie, onderhandeling en compilatie die de opkomst van nieuwe sturingsmechanismen vergemakkelijken. Deze nieuwe sturingsmechanismen hebben de potentie substantieel bij te dragen aan het legitimeren van beslissingen, omdat deze focussen op het proces, de activiteit besluitvorming.

In de hoofdstukken een, twee en drie, zijn hedendaagse geneesmiddelenregulering en beoordelingskader onderzocht en geëvalueerd, met als doel inzicht te krijgen in hoe verwetenschappelijking en formalisering van besluitvorming bijdragen aan de stimulering van gepast gebruik en vergoeden van geneesmiddelen. De evaluatie laat zien dat de uitvoering van gezondheidsregulering in de dagelijkse praktijk substantieel blijkt af te wijken van het beoogde beleid en haar onderliggende principes. De huidige infrastructuur van pakketbeheer schenkt weinig aandacht aan het beheer van de uiteenlopende rationaliteit ten aanzien van (de waarde van) geneesmiddelen. Daarom is het

weinig verrassend dat beleidsmakers nog altijd moeilijkheden ervaren in het uitleggen van de grondslagen van de geneesmiddelenvergoedingen besluiten. De uitbreidingen van de besluitvormingsinfrastructuur hebben niet voldoende bijgedragen aan het oplossen van het legitimiteitprobleem. Althans, geen legitimiteit in de zin van sociaal robuuste prioriteringsbesluitvorming. Vervolgens focust dit proefschrift, in de hoofdstukken vier en vijf, specifiek op de (kennis) praktijk en (de ontwikkeling van) de infrastructuur van het Nederlands pakketbeheer, gebruik makend van een sociaalwetenschappelijk perspectief. De analyses laten zien dat beleid en klinische praktijk werken naar legitimiteit in besluitvorming. Echter, niet op de wijze zoals verwacht door de beleidsmakers, strikte controle en monitoren. Maar, door de focus te verleggen naar het proces van besluitvorming; door de interactie tussen beleid, wetenschap en praktijk te stimuleren, en de verschillende rationaliteiten in de prioriteringsbesluitvorming te erkennen.

Hoofdstuk één laat zien hoe de Nederlandse overheid heeft geprobeerd om te gaan met de exponentiële groei in gezondheidszorgkosten gerelateerd aan de ziekenhuisgeneesmiddelen eind jaren negentig vorige eeuw. De Nederlandse overheid beoogde het kostenprobleem op te lossen in de farmaceutische ziekenhuiszorg sector door middel van de regulering van (additionele) financiering van dure ziekenhuisgeneesmiddelen en het overhevelen van de verantwoordelijkheid van de toegang tot zorg naar de zorgverzekeraars en ziekenhuizen. Echter, de (klinische) praktijk beschrijft dit beleid als inadequaat en mogelijk leidend tot legitimiteitproblemen ten aanzien van de gelijkwaardige verdeling van zorg. Ondanks de inspanningen van de beleidsmakers had de dure geneesmiddelen regulering niet het gewenste effect. Vervolgens, duidt dit hoofdstuk de roep van zowel beleidsmakers and medische professionals om de ontwikkeling van meer evidence based beleid en evidence based mechanismen om de legitimiteit van besluitvorming te vergroten. Door evidence based prioriteringsbeslissingen te maken zou het gepast gebruik en vergoeden van geneesmiddelen in de praktijk worden gestimuleerd.

In **hoofdstuk twee** laat de evaluatie van het conditioneel vergoeden van extramurale geneesmiddelen als beleidsinstrument zien dat evidence based besluitvorming niet automatisch leidt tot gepast gebruik en vergoeden van geneesmiddelen in de (klinische) praktijk. Het College voor zorgverzekeringen, een onafhankelijke overheidsorganisatie verantwoordelijk voor het pakketbeheer in Nederland, focust op het definiëren en stimuleren van gepast gebruik en vergoeden van geneesmiddelen. Om het effectieve en efficiënt gebruik van bepaalde geneesmiddelen te promoten, zijn aan de vergoeding van deze medicijnen voorwaarden verbonden (bv. specifieke patiëntengroepen en

zorgverleners). Veelal zijn voorwaarden verbonden aan de vergoeding van die geneesmiddelen die gezien worden als duur en/of een risico op oneigenlijk gebruik hebben. De voorwaarden worden gesteld om zo het off-label medicijngebruik te beperken en het gebruik voor indicaties waarvan de effectiviteit is vastgesteld te promoten. Het evidence based karakter van de condities zou de legitimiteit van het beleidsinstrument moeten waarborgen. Daarbij verwacht het College voor zorgverzekeringen dat, door de verwetenschappelijking van de besluitvorming, voorschrijvers en zorgverzekeraars het beleid zullen volgen. Echter, zorgverzekeraars en farmaceutische industrie betwisten de legitimiteit van de conditionele geneesmiddelenvergoeding. Zij refereren hierbij naar het gebrek aan transparantie van het besluitvormingsproces en het gebrek in consistentie in het gebruik van de beoordelingscriteria. In de praktijk, zo blijkt, worden de evidence based condities voor gepast gebruik en vergoeden van geneesmiddelen vaker overschreden dan verwacht. De cases waarbij kennis vanuit beleidsuitvoerders (zoals medische professionals) wordt gebruikt in het formuleren van de vergoedingsvoorwaarden, worden vaker gezien als voorbeelden van legitieme besluitvorming. Deze cases blijken bovendien ook meer invloed te hebben op de voorschrijfpraktijk. Dit hoofdstuk laat dientengevolge zien dat de mate van effect van een beleidsmaatregel niet is verbonden aan het evidence based karakter van, maar aan de wijze waarop vergoedingsvoorwaarden zijn ontwikkeld en uitgevoerd. Het laatste houdt in dat de relatie tussen beleid en praktijk verandert.

Niet alleen werd de legitimiteit van prioriteringsbeslissingen gezocht in evidence based besluitvorming, het beoordelingskader werd ook verfijnd door nieuwe criteria toe te voegen. **Hoofdstuk drie** focust daarom op het complementeren van het beoordelingskader. Het exploreert de mogelijkheid om van budget impact een expliciet criterium te maken door deze van een onderbouwing te voorzien. Het huidige beoordelingskader omvat de criteria effectiviteit, kosteneffectiviteit en ziektelast. De rol van budget impact in dit kader is minder duidelijk. Met het expliciteren van budget impact als beoordelingscriterium wordt verondersteld dat explicitering bijdraagt aan de transparantie van het besluitvormingsproces en daarmee de verantwoording van de beleidsmakers. Dit hoofdstuk identificeert vier grondgedachten voor de inachtneming van budget impact in vergoedingen besluitvorming: opportuniteitskosten, het vermijden van verlies, onzekerheid in besluitvorming en gelijke gelegenheid. Vooral de grondgedachte van gelijke gelegenheid kan een ethische grondslag bieden voor het opnemen van budget impact als beoordelingscriterium in de besluitvorming. Gelijke gelegenheid houdt in dat mensen streven naar een rechtvaardige allocatie van middelen op basis van een procedurele rechtmatigheid dat een beschikbaarheid van behandeling voor allen waarborgt. Echter, deze specifieke grondgedachte voor budget impact betwijfelt ook of het rechtvaardig is om middelen te verdelen op basis van een

utilistisch principe alleen (de ethische grondslag voor het kosteneffectiviteitcriterium). Indien de legitimiteit van besluitvorming bestaat uit het gebruik van expliciete beoordelingscriteria en een compleet beoordelingskader, heeft de inclusie van budget impact als expliciet criterium belangrijke consequenties voor de efficiëntie en complexiteit van het besluitvormingsproces. De inclusie zou zelfs de legitimiteit van prioriteringsbesluitvorming mogelijk doen afnemen. Dus, ondanks de uitbreiding van de besluitvormingsinfrastructuur, blijft het legitimiteitprobleem bestaan.

Hoofdstuk vier laat zien hoe de activiteit van legitieme besluitvorming zichtbaar is bij de overheid, en tevens is ingebed in beleidsinstrumenten als geneesmiddelen databases in de praktijk. De exploratie van de Groeihormoon database en PHAROS register demonstreert, of en hoe de inspanningen om klinische data te verzamelen en organiseren, én het toegenomen gebruik van databases in klinische-, onderzoek- en beleidspraktijken, de regulering van klinische praktijken heeft getransformeerd. We demonstreren hoe databases een coördinatie regime zijn geworden. De databases faciliteren zowel de interactie tussen beleid en klinische praktijk, als de interactie tussen collectieve vormen van expertise. Het laatste houdt in het combineren van mensen (clinici, onderzoekers, beheerders, patiënten, etc.) en objecten (entiteiten, instrumenten, hulpmiddelen technieken, etc.). Deze interacties maken het mogelijk dat nieuwe vormen van objectiviteit en regulering, zoals gereguleerde objectiviteit, ontstaan. Daardoor verandert de relatie tussen beleid en klinische praktijk. Hoewel de databases dus niet het onvertraagde en continue monitoren mogelijk maakte, zoals verwacht door de beleidsmakers, heeft het dynamische proces van continue dataverzameling en reflectie, door medische professionals en onderzoekers, wel het doel van de beleidsmakers bereikt. Namelijk, het stimuleren van gepast gebruik en vergoeden van geneesmiddelen in de klinische praktijk. Door nieuwe vormen van sturingsmechanismen aan te nemen in de huidige besluitvormingsinfrastructuur, zoals databases, wordt het mogelijk het gepast gebruik en vergoeden van geneesmiddelen in de (klinische) praktijk te stimuleren, en tegelijkertijd het werken naar legitieme besluitvorming te bevorderen.

Hoofdstuk vijf combineert en exploreert de drie case studies van dit proefschrift: a) de conditionele vergoeding van extramurale geneesmiddelen, b) de conditionele vergoeding van intramurale geneesmiddelen, en c) the mogelijke toevoeging van budget impact als criterium in het beoordelingskader van het pakketbeheer. De cases zijn verkend en geanalyseerd wat betreft de dynamiek van legitieme besluitvorming vanuit een situationele benadering van regulerend gedrag. De sociologie van gesitueerde beoordeling geeft inzicht in het dynamische proces en de verschillende wijzen waarop actoren hun acties of besluitvorming legitimeren op

basis van de definiëring van een kader van verschillende “repertoires van rechtvaardiging”. Elk repertoire heeft zijn eigen karakteristieken en dynamiek, en voorziet actoren van symbolen, verhalen, wereldbeelden en materiële en organisatorische arrangementen, waaruit zij verschillende elementen kunnen selecteren waarmee hun acties worden gerechtvaardigd. De conceptie van repertoires is gebruikt om vier verschillende “repertoires van evaluatie” in de Nederlandse geneesmiddelenvergoedingen besluitvorming te identificeren: de repertoires van wetenschap, klinische praktijk, billijkheid, en proces. Elk repertoire omhelst verschillende vormen van kennis (bv impliciete, klinische, methodologische, gezondheidseconomische kennis), die achtereenvolgens waarde toekennen aan geneesmiddelen (beslissingen). Op basis van de identificatie van deze repertoires, laat dit hoofdstuk zien dat legitimiteit in de praktijk nauw verwant is aan de interactie tussen de verschillende repertoires, en aan de invloed van context op (de combinatie van) repertoires die legitimiteit produceren op een bepaald moment in het besluitvormingsproces. Het (gebrek aan) effect van sommige prioriteringsbeslissingen kan hierdoor begrepen worden als de (ontoereikende) incorporatie en interactie van de verschillende repertoires in het besluitvormingsproces. Ten slotte, pleit dit hoofdstuk voor een besluitvormingsproces dat voldoende rekenschap geeft van zijn omgeving zodra onzekerheden zich aandienen; het zoeken naar de dialoog met of consultatie van het netwerk, en het integreren van gerelateerde routines en regulering.

De **discussie en conclusie** van dit proefschrift reflecteert op de vraag hoe de huidige infrastructuur van het pakketbeheer het gepast gebruik en vergoeden van geneesmiddelen stimuleert, en legitimiteit voor prioriteringsbeslissingen construeert. De evaluatie en exploratie van de verschillende beleidsinstrumenten heeft geleid tot drie hoofdbevindingen. Ten eerste, de huidige infrastructuur worstelt met de constructie van twee aparte domeinen: beleid en praktijk. De huidige infrastructuur verordent een artificiële scheiding, die de kennis vanuit de (klinische) praktijk buitensluit van beleid; het laat moraliteit en politiek in de besluitvorming niet toe. Het gebruik van bewijs in besluitvorming en transparante procedures hebben bijgedragen aan de vermeende autoriteit van gezondheidsbeleidsmakers, en daarmee de acceptatie en validiteit van hun argumentatie. Echter, er wordt weinig aandacht besteed aan de verschillende rationaliteiten ten aanzien van (de waarde van) geneesmiddelen. Ten tweede kan legitimiteit van besluitvorming niet simpel worden geconstrueerd, maar bestaat dit uit veel werk. Het legitimeren van besluitvorming is gerelateerd aan de acceptatie en validiteit van de activiteit ‘besluitvorming’. Ten laatste, een dusdanige herdefiniëring houdt in dat vergoedingsbesluiten niet gezien moeten worden als het einde van het besluitvormingsproces, maar als slechts een enkel doch belangrijk punt in het proces van sturen van gepast gebruik en vergoeden van

geneesmiddelen. De opname, of verwijdering, van een geneesmiddel in het basispakket of in een regeling door het Ministerie van VWS staat daarmee aan het begin van de stimulering van het gepast gebruiken en vergoeden van geneesmiddelen.

Tot besluit, het werken naar legitimiteit van besluitvorming vereist een andere benadering van het sturen van het gepast gebruik en vergoeden van geneesmiddelen, zo laat dit proefschrift zien. In deze benadering staat het proces van geneesmiddelenvergoedingen niet aan het einde, maar aan het begin van het legitimeren van prioriteringsbeslissingen. De infrastructuur van het Nederlandse pakketbeheer zal dan zo moeten worden (her)ontworpen, dat deze de continue interactie tussen beleid, wetenschap en praktijk stimuleert en daarmee ook reflectie op het gepast gebruik van geneesmiddelen. Het (h)erkennen van de verscheidenheid aan kennisvormen die prioriteringsbeslissingen legitimeren, is een fundamentele stap in het vestigen van nieuwe sturingsmechanismen voor het gepast gebruik en vergoeden van geneesmiddelen. Uiteindelijk is het het proces en de activiteit van besluitvorming dat de legitimiteit van prioriteringsbeslissingen waarborgt, en niet de robuustheid van bewijs of de formele procedure alleen.

Dankwoord

Op deze plek wil ik iedereen bedanken, die in de afgelopen jaren samen met mij ‘het promotiepad’ heeft bewandeld. Sommigen hebben zij aan zij met mij gewandeld. Anderen trokken juist even de kar of gaven mij een duw de goede kant op. Dan zijn er ook nog wandelaars, die er zich niet eens bewust van zijn dat ik hen dank schuldig ben.

Allereerst mijn (co)promotoren Roland Bal, Elly Stolk en Antoinette de Bont. Waar ik eerst met eenieder apart ben gaan rondstruinen, zijn we geëindigd in een gezamenlijke verkenning van het weelderige woud van geneesmiddelenbesluitvorming. Jullie visie en inzichten waren inspirerend en maakten dat ik dit woud vanuit vele invalshoeken heb mogen verkennen. Dat dit soms botsingen van ideeën met zich meebracht, heeft er toe geleid dat ik een uitdagend maar ook mooi pad heb bewandeld; hoewel misschien niet volgens de kortste route. Roland, zeker in de laatste twee jaren van mijn promotietraject is jouw begeleiding op het STS-pad van grote waarde geweest. Door mee te zoeken naar passende analytische begrippen om de grote hoeveelheid empirisch materiaal te ordenen en door mij aan te sporen tot (meer) conceptueel denken, is mijn expeditie vele malen mooier geworden. Elly, jouw vertrouwen in mij als sociaalwetenschappelijk onderzoeker binnen de gezondheidseconomische wereld was zo groot, dat je het lef had mij drie maanden voor mijn zwangerschapsverlof aan te nemen op het ‘Third Man-project’. Dat vertrouwen zal in de loop der tijd af en toe wel deuken hebben opgelopen, toch hoop ik dat je nu met trots kunt zeggen: “dat is mijn promovenda”. Antoinette, jij weet als geen ander wanneer richting te geven, zij aan zij te wandelen, of juist op gepaste afstand toe te kijken hoe iemand zijn eigen weg zoekt en vindt. Die gave maakt van jou een unieke en prettige begeleider op het promotiepad. Ik ben dan ook zeer dankbaar dat ik jou heb mogen ontmoeten.

Eén reden die deze wandeling langer maakte, is het werken in multidisciplinaire onderzoeksteams. Herman Stoevelaar, Arthur Eyck, Louis Niessen, Antoinette de Bont, Elly Stolk, Jan van Busschbach en Joshua Cohen, ik heb veel plezier gehad tijdens onze samenwerking. Herman, dankzij jou heb ik mijn eerste stappen gezet in de onderzoekswereld: ze smaakten naar meer! Arthur, jij nam me letterlijk en figuurlijk mee op excursie door de wondere wereld van de gezondheidszorg. Onze inspirerende gesprekken rondom interviews of bij jou thuis zullen mij zeker bij blijven. Joshua, het bezoek aan Boston was onvergetelijk; omdat jij het mogelijk maakte een gedeelte van de summer course bij Norman Daniëls aan Harvard School of Public Health te volgen. Maar minstens zo dankbaar ben ik je vanwege ons bezoek aan mijn eerste NBA-wedstrijd ooit!

Mijn respondenten bedank ik voor de interessante en informatieve gesprekken en de tijd die ze daarvoor hebben genomen. Speciaal wil ik de medewerkers van het College voor zorgverzekeringen en het Ministerie van VWS bedanken. Sommigen heb ik meermaals gesproken en steeds was ik welkom. Ook Carin Uyl en Adri Steenhoek wil ik bedanken, omdat zij altijd bereid waren mijn vragen te bespreken over het onderzoek naar dure geneesmiddelen. ZonMW en MagMW bedank ik voor het financieren van de verschillende projecten, waardoor een langdurig verblijf in het woud van de geneesmiddelenbesluitvorming mogelijk was.

In mijn tijd bij het iBMG, waarvan de laatste jaren bij de sectie Health Care Governance, heb ik vele mensen mogen ontmoeten die eenzelfde pad aan het bewandelen waren, bewandeld hebben, hier juist mee stopten, of op andere wijze betrokken waren bij mijn promotietraject. Graag wil ik daarom mijn (ex)collega's bij het iBMG hartelijk danken voor de gezellige en inspirerende lunches, discussies en congresbezoeken. Vooral ook dank aan alle kamergenoten die ik in de loop der jaren heb versleten: Addy, Femke, Floor, Hester, Jolanda, Joyce, Lonneke, Maarten, Marit, Marjan en Zarah. Jolanda, voor jou een speciaal woord van dank, omdat jij bereidt bent om het laatste uur van mijn tocht letterlijk aan mijn zijde te staan als paranimf. Maar vooral ook, omdat jouw bemoedigende woorden mij op cruciale momenten overeind hebben gehouden. Onze gesprekken over het combineren en balanceren van werk en gezin, met alle mooie en minder aangename aspecten daarvan, maakte het promotiepad ook op persoonlijk vlak zeer waardevol. Hester, jouw humor en sarcasme zijn verfrissend en maakten het werken bij iBMG tot een plezierige tijd. Sonja, je bent een mooi en warm mens. Ik heb genoten van onze samenwerking bij het vak Health Care Governance. Met veel vertrouwen heb ik het coördinatorschap aan jou overgedragen. Samantha, zonder jouw kritische opmerkingen en stijlverbeteringen was ik nu nog aan het schrijven geweest. Ik dank je voor jouw steun, maar vooral ook voor je vertrouwen in mij: dat ik het echt zelf kon, Thanks!

Inmiddels werk ik met veel plezier bij Tranzo, een inspirerende werkomgeving, waar ik met hernieuwde energie mijn proefschrift heb kunnen en willen afschrijven. Hoewel ik Tranzo vaak omschrijf als een duiventil waar iedereen te pas en te onpas in- en uitvliegt, is het ook een warm nest. Leonieke, onze koffiemomenten koester ik en ik hoop dan ook dat ze zullen blijven tot het einde van jóuw promotietraject. Henk, wat was ik de eerste keer verbaasd dat jij persoonlijk alle 'Tranzuelen' kwam uitnodigen voor de lunch en nog meer toen dat de volgende dag weer gebeurde. Het staat symbool voor de warmte van het Tranzo-nest. Jolanda, wat is het heerlijk dat jij mij de gelegenheid biedt om mijn geleerde kennis nu in de praktijk te brengen en daarmee uit te breiden.

Dan zijn er nog de mensen die, zonder dat ze het weten, heel belangrijk zijn geworden voor het bereiken van het einde van deze wandeling. Lieve Charlotte, Merla en Maike, jullie zijn er altijd voor mij, ook als ik weer eens tijden niets van me heb laten horen. Onze etentjes, gesprekken en vakanties zijn soms therapeutisch, maar vooral gezellig. Charlotte, samen met jou op en buiten het basketbalveld, maakt van het leven een feest. En ondanks dat je geen idee had wat het inhield om mijn paranimf te zijn, heb je volmondig ja gezegd. Die onvoorwaardelijke steun betekent veel voor mij. Merla, elke keer dat we weer een etentje plannen, kijk ik daar enorm naar uit. Niets is prettiger dan samen met jou over onze kinderen, familie, werk, wensen en dromen te praten. Maike, al vanaf het Hertog Jan delen we onze levenspaden, de ene keer lopen ze wat dichter bij elkaar dan de andere, maar ik weet dat jij er altijd bent en hoop dat jij mij blijft vinden.

Dan het finale stuk van het promotiepad. Hier komen de mensen aan bod aan wie ik misschien wel de meeste dank verschuldigd ben. Lieve pa Ben en mam, soms zullen jullie je afvragen waar jullie drie promoverende dochters aan te danken hebben (in goede en slechte zin). Ik denk, pap, omdat jij laat zien dat leren niet iets is van school alleen, maar als je aan het leven en je werk hecht, een continu proces van verrijking is. En mam, ik herken mij in jouw doorzettingsvermogen en interesse in het welzijn van anderen. Eén ding staat buiten kijf, zonder jullie steun zou dit pad voor mij en mijn gezin niet te bewandelen geweest zijn! Renske en Jonne, lieve zussen, dank voor jullie oprechte interesse in mijn proefschrift, het kritisch bekijken van de (op één na) laatste versie en de fijne gesprekken buiten het promoveren om. Mijn schoonouders, Jan en Kitty, bedankt voor jullie steun en het vele oppassen. Ook Jacqueline, Dirk, Robert en Ramon, bedankt voor jullie gezonde (des)interesse in mijn proefschrift.
Lieve Maurice, samen met jou het levenspad bewandelen is mooi. De afgelopen jaren zijn uitdagend geweest met vele mooie hoogtepunten. Jouw humor, warmte en vertrouwen, maakte dat mijn promotiepad goed begaanbaar bleef. Samen wil ik over een tijdje wel weer een nieuw avontuur aangaan, maar voor nu mogen we even rustig doorwandelen en genieten van wat we samen hebben bereikt. Mirte, Silke en Pim, tijdens mijn promotietraject hebben jullie me altijd weer op het rechte pad gekregen, daar waar het in de wereld echt om draait. Dat ik jullie mag begeleiden en mag toekijken hoe jullie je ontwikkelen en steeds meer je eigen weg kiezen, is een voorrecht waar ik nog lang van hoop te genieten.

Maartje Niezen
April 2012

About the author

Maartje Niezen - van der Zwet was born in 1979 in Leiden, the Netherlands. She is a 1998 graduate from Scholengemeenschap Were Di in Valkenswaard. She studied Arts and Social Sciences, with a major in Technological Culture at Maastricht University from 1998 to 2003. She graduated in 2003, and in the same year started working as a social scientific researcher at the Institute of Health Policy and Management at the Erasmus University in Rotterdam. She developed a particular interest in decision processes in the prioritization of health care, and the employment of knowledge infrastructures in these processes. She coordinated and taught the master course 'Health care governance', and has been involved in several other courses on qualitative research methodologies. She was a guest lecturer in the course 'Health Technology Assessment' in the master 'Innovation Sciences' at the Technical University Eindhoven. Since 2011, Maartje Niezen - van der Zwet has worked at Tranzo, the scientific centre for care and welfare at Tilburg University. She researches triage of infants in the youth health care.
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