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CHALLENGES IN THE ASSESSMENT OF MEDICAL DEVICES: THE MEDTECHTA PROJECT

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ABSTRACT

Assessing medical devices (MDs) raises challenges which require us to reflect on whether current methods are adequate. Major features of devices are: (i) device–operator interaction can generate learning curve effects; (ii) incremental nature of innovation needs to be addressed by careful identification of the alternatives for comparative and incremental cost-effectiveness analysis; and (iii) broader organizational impact in terms of training and infrastructure, coupled with dynamic pricing, requires a more flexible approach to costing.

The objective of the MedtecHTA project was to investigate improvements in HTA methods to allow for more comprehensive evaluation of MDs. It consisted of several work packages concerning (i) the available evidence on the currently adopted approaches for regulation and HTA of medical devices; (ii) the geographical variation in access to MDs; (iii) the development of methodological frameworks for conducting comparative effectiveness research and economic evaluation of MDs; and (iv) the organizational impact of MDs.

This introductory paper summarizes the main results of the project and draws out the main overarching themes. This supplement represents a comprehensive report of all the main findings of the MedtecHTA project, and it is intended to be the main source for researchers and policy makers wanting information on the project. © 2017 The Authors. *Health Economics* published by John Wiley & Sons, Ltd.

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1. BACKGROUND TO THE MEDTECHTA PROJECT

Health technology assessment (HTA) has become increasingly important in health care decision making in Europe. Although in principle HTA can be applied to all health technologies, its major use in a decision-making context has been in the pricing and reimbursement of pharmaceuticals. However, there are over 200,000 medical devices on the European market (Fraser *et al.*, 2011). These represent a very heterogeneous family of technologies that needs to be better classified for the purpose of HTA. 'Medical device', according to the EU Directive (2007) 2007/47/EC amending Council Directive 93/42/EEC, is defined as 'any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination.… to be used for human beings for the purpose of diagnosis, prevention, treatment, monitoring or alleviation of disease'.

While some devices require very simplified assessment, others need to be assessed through a full evaluation of safety, efficacy, effectiveness and economic impact. A thorough HTA would require consideration of final outcomes in terms of life expectancy and health-related quality of life, going far beyond the assessment that devices currently undergo to obtain a CE (European Conformity) mark, to enable them to be

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marketed in the European Union. This is particularly true for implantable devices used in cardiology (Boriani *et al.*, 2009; Boriani *et al.*, 2010; Tarricone & Drummond, 2011), which represent the main focus of the MedtecHTA project.

The current EU legal framework already requires all devices, especially class III devices, to have safety and performance testing for the decision on the CE mark. Essentially, manufacturers must accomplish a conformity assessment and undergo an inspection and certification procedure by one of the Notified Bodies within the EU. In addition, there is stringent post-marketing surveillance, requiring manufacturers of devices to implement a post market clinical follow-up plan and a medical device vigilance system to monitor their products once they are on the market (Cohen & Billingsley, 2011). Conversely, in the United States, a much greater importance is given to pre-market approval (PMA), requiring clinical testing to inform the market about safety and effectiveness. Nevertheless, a much lighter ex-post conformity assessment is in place. It must be noted, however, that the EU Directives for the regulation of medical devices have been the object of relevant amendments in recent years and, although the final document is not available yet, the orientation is for more stringent clinical evidential requirements in the pre-market phase (European Commission, DG Growth, 2016).

Nevertheless, medical devices have traditionally been less regulated than pharmaceuticals, and the amount of evidence collected for licensing medical devices is generally lower (Fattore *et al.*, 2011; Schreyögg *et al.*, 2009; Taylor & Iglesias, 2009). The EU directive in 2007 made some significant changes in this respect by recognizing that it is necessary to enhance the provisions on clinical evaluation, including clarification that clinical data are generally required for all devices (2007/47/EC). Consequently, medical devices placed on the EU market or put into service after 21 March 2010 must be in conformity with these new requirements. However, in contrast to the requirements for pharmaceuticals, because of peculiarity of medical devices, the studies can be small clinical trials or even non randomized clinical investigations, and long-term efficacy data are not generally required in the premarketing phase, although a post market clinical follow-up is required, thus reducing the knowledge base for subsequent HTA activities.

A full HTA, such as that applied to pharmaceuticals in many EU member states, would require a thorough examination of the clinical and cost-effectiveness of devices. However, medical devices differ from other health technologies in a number of respects: (i) they often change rapidly; (ii) clinical outcomes often depend on the training, competence and experience of the end-user (Ramsay *et al.*, 2001); (iii) pricing is typically more dynamic than that of pharmaceuticals; and (iv) costs often comprise both procurement costs (including the associated infrastructure) and running costs (including maintenance and consumables).

It has been claimed that these special characteristics of devices raise additional challenges which require the HTA community to reflect on whether the current methods are adequate (Drummond *et al.*, 2009). Three major features of devices deserve special attention: (i) the device–operator interaction can generate learning curve effects and thus risk biases in estimating the size of the benefits; (ii) the incremental nature of innovation (e.g. longer battery life, improvement of the software systems, miniaturization) needs to be addressed by careful identification of the alternatives for comparative and incremental cost-effectiveness analysis (Fattore *et al.*, 2011; Sorenson *et al.*, 2011; Tarricone & Drummond, 2011; Taylor & Iglesias, 2009); and (iii) the broader organizational impact in terms of training and infrastructure, coupled with dynamic pricing, requires a more flexible approach to costing. Whether these differences between medical devices and pharmaceuticals require a different framework for HTA needs to be investigated.

2. THE MEDTECHTA PROJECT

The objective of MedtecHTA project was to investigate improvements in HTA methods to allow for more comprehensive economic evaluation of medical devices. The project consisted of seven work packages (WPs), organized in three parts (see Table I).

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Table I. Overview of project work plan

Parts of the overall project	Work packages included
I: Cross-country analysis of HTA practices and utilization of medical devices	WP 1 Cross-country analysis of HTA WP 2 Geographic variation in access to medical devices
II: Methodological issues in HTA of medical devices	WP 3 Comparative effectiveness of medical devices WP 4 Economic evaluation of medical devices: overview of different approaches WP 5 Uncertainty and value of information for medical devices WP 6 Organizational impact of medical devices
III: Conclusions, synthesis and recommendations	WP 7 Recommendations on HTA methods for medical devices

2.1. CROSS-COUNTRY ANALYSIS OF REGULATION AND HTA OF MEDICAL DEVICES

Part 1 of the project was essentially preparatory and included the necessary groundwork for the subsequent research activities. WP 1 considered the available evidence on the currently adopted approaches for the HTA of medical devices and on international regulatory guidance on the licensing of medical devices. Tarricone *et al.* (2014) reviewed regulatory practices in the EU, US and five other countries and concluded that a number of actions are required to make the clinical evidence gathered through the regulatory process more relevant to HTA. These include the development of international standards on the types of clinical evidence required for the market approval of medical devices and agreement on the balance of clinical data collection pre- and post-launch. The latter is important because of the possibility that, owing to the learning curve and the organizational impact of devices, data from pre-launch clinical trials may not be ideal for assessing effectiveness and cost-effectiveness.

Ciani *et al.* (2015) reported the results of a cross-country analysis of HTA guidelines and available HTA reports on medical devices in assigned countries using a standardized template for comparison. In order to analyse the state of the art in the application of guidelines reviewed, a sample of HTA reports was selected from the University of York Centre for Reviews of Dissemination HTA database and systematically reviewed at three levels: (i) assessment of the nature of evidence included in the reports; (ii) HTA methods applied by reports considering medical devices; and (iii) assessment of approaches and methods used to address uncertainty. They found that although 75% of the agencies surveyed had adopted HTA-specific approaches for medical devices, these were largely organizational or procedural in nature. Only one agency had adopted methodological guidelines specific to medical devices.

In the second paper in this supplement, Ciani *et al.* (2017) focus on the second phase of their research, in which they analysed a sample of HTA reports in the field of cardiovascular disease in order to assess whether there are any key differences in how methods are applied. They found that there were several differences, in the types of clinical studies forming the basis for the HTAs, how the health problem and use of the technology were considered, the description and technical characteristics of the technology and the consideration of the organizational aspects of the use of the technology. Most of these differences arose because of the relative 'complexities' in the use of devices, in terms of the number of interacting components. These include the number and difficulty of the actions required by those delivering or receiving the intervention, the number of groups and organizational levels targeted by the intervention, the number and variability of the outcomes and the degree of flexibility or tailoring of the intervention.

2.2. GEOGRAPHICAL VARIATION IN THE USE OF MEDICAL DEVICES IN THE EU

Work Package 2 considered the geographical variation in the use of medical devices in EU countries by estimating the rate of adoption of selected medical technologies in the field of electrophysiology. This subspecialty of cardiology widely uses implantable medical devices whose efficacy has been demonstrated by a number of randomized clinical trials. In one respect these devices resemble pharmaceuticals as they have a curative and/or

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a secondary prevention function and might be tested in clinical trials similar to those conducted on drugs. On the other hand, they differ from pharmaceuticals because they are subjected to incremental changes (e.g. dimensions and software), learning curve effects because of device–operator interactions and price dynamics which mean that trial designs similar to pharmaceuticals are not always suitable for medical devices. These overall characteristics make the area of electrophysiology an interesting case to study.

Results obtained in this field also have a higher degree of transferability to other class III medical devices. Through the analysis of national/local guidelines and data from registries and administrative databases, rates of utilization were mapped to provide evidence of different degrees of access within member states, and whether this adoption is in line with the existing evidence on clinical and cost effectiveness. Valzania *et al.* (2015) reported a systematic review of the literature on implant rates for cardiac implantable electrical devices (CIEDs) in Europe. They found that there had been a recent rise in implant rates, with large geographic differences. For example, the ratio between the regions with the highest and lowest implant rates within the same country ranged from 1.3 to 3.4 for cardiac pacemakers, whereas the ratio between the countries with the highest and lowest implant rates ranged from 2.3 to 87.5. The determinants of these differences (namely epidemiological, cultural and socio-economic factors) were only partly explored, and differences in study methodology could be one reason for the reported differences.

Therefore, in a subsequent phase of the research, reported in the third paper in this supplement, Torbica *et al.* (2017) undertook a new study of implant rates, the first to use the national hospital discharge datasets available in 5 EU countries. They provide evidence on differences in use of medical devices within and between member states, investigate the determinants of differences in access to CIEDs and assess the potential and limitations of administrative databases for the analysis of utilization rates of medical devices in electrophysiology.

It is the first international paper to explore simultaneously differences both between countries and within the regions of those countries. Results show that higher levels of tertiary education among the labor force and % of aged population are positively associated with implant rates of CIED. Regional per capita GDP and number of implanting centers appear to have no significant effect. Institutional factors, captured by fixed country effect, are shown to be important for the diffusion of CIED.

However, even after controlling for clinical, epidemiological and (crude) economic indicators, significant variation in implant rates still exists. They argue that there should be closer examination of the role of organizational factors and clinical preferences in the adoption of devices. These issues are explored further in WP6 of the MedtecHTA project (discussed below).

2.3. METHODS FOR ASSESSING THE COMPARATIVE EFFECTIVENESS OF MEDICAL DEVICES

The core part of the project (Part II) sought to develop an improved methodological framework for conducting HTA of medical devices by acknowledging the complexities which arise from their integration into clinical practice. The research conducted in WP3 began by considering the approaches and methodologies used for comparative effectiveness research by conducting a systematic review of the methodological literature. It was found that, although most of the good research practices in the evaluation of all health technologies apply to medical devices, the interventions involving the use of medical devices should be considered as complex interventions, owing to the importance of user and context independence. Therefore, specific randomized controlled trial designs need to be considered, dealing with surgeons' and patients' preferences, incremental product development and user dependence. In addition, high quality disease- or device-based registries are needed to assess safety and long-term effectiveness (Schnell-Inderst *et al.*, 2016).

This preliminary research activity provided the basis for the development of improved methods for evaluating comparative effectiveness of medical devices including recommendations for analytic methods and data collection. The research was an important input to the development of guidelines for the evaluation of Therapeutic Medical Devices under the auspices of the EUnetHTA Joint Action 2 (EUnetHTA, 2015).

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The framework and new methodological approaches were then tested on medical devices at different stages of development and diffusion within the health care system. First, the use of a method of evidence synthesis that allows for the meta-analysis of RCT and observational data, using bias adjustment based on a formal elicitation exercise involving experts, was explored in the case of total hip replacement. This is reported in the fourth paper in this supplement (Schnell-Inderst *et al.*, 2017).

2.4. METHODS FOR THE ECONOMIC EVALUATION OF MEDICAL DEVICES

Work Package 4 focused on exploring different methods for economic evaluation of medical devices currently adopted in EU countries in order to make suggestions about the development of new methods and offer guidance on future directions in the use of economic evaluation for medical devices. The first part of the research considered how differences in culture and values in EU countries lead to differences in the methodology and use of economic evaluation for policy decisions such as coverage and reimbursement without distinguishing between health technologies (e.g. pharmaceuticals and medical devices). For example, in northern Europe, economic evaluation is widely used in decisions about the reimbursement of new health technologies and cost-utility analysis (with the quality-adjusted life-year as the primary measure of benefit) is the predominant approach. In UK, the National Institute for Health and Care Excellence (2011) has differentiated between health technologies and has developed the Medical Technologies Evaluation Programme to specifically assess medical devices and diagnostics. In contrast, in central and southern Europe, there is more resistance to the use of economic evaluation in decision making and, where it is used, benefits are more often assessed in terms of clinical added value. In these countries, however, no distinction is made between health technologies and policy decisions on coverage and reimbursement of medical devices are generally not subject to any type of economic analysis. This part of the research provided useful insights into the potential for increasing the use of economic evaluation in various EU member states (Torbica *et al.*, 2016).

The second part of the research, reported in the fifth paper of this supplement (Tarricone *et al.*, 2017a), used two case studies of implantable cardiac devices in order to demonstrate current, and possible future approaches to the use of economic evaluation. The case studies, implantable cardioverter defibrillators (ICDs) and transcatheter aortic valve implantation (TAVI) were chosen in order to explore a wide range of device characteristics, including the significance of irreversible decisions and the complexity associated with evolving technologies. Most of the published economic evaluations and HTA reports located in the literature review did not take account of the special features of medical devices (i.e. learning curves, incremental innovation, dynamic pricing and organizational aspects) in the base case analysis, but were sometimes considered in sensitivity analyses. Overall, the conclusion was that the existing economic evaluations did not pay enough attention to the specific characteristics of devices explored in the MedtecHTA project.

Finally, building on the findings of both WP3 and WP4, the impact of the learning curve on effectiveness and cost was estimated for endovascular aneurysm repair (EVAR) and fenestrated EVAR (fEVAR). This research is reported in the sixth paper in this supplement (Varabyova *et al.*, 2017). It was found that in the case of EVAR there was a moderate, but significant effect of learning on both in-hospital mortality and hospital length of stay. The same impact was not found for fEVAR, one reason for which could be its similarity to EVAR, meaning that much of the learning in EVAR was transferable to the new procedure

2.5. UNCERTAINTY IN THE ECONOMIC EVALUATION OF MEDICAL DEVICES

Work Package 5 focused on characterizing uncertainty in the economic evaluation of medical devices and determining future research needs. This research, reported in the seventh paper in this supplement (Rothery *et al.*, 2017), sets out a number of conceptual issues when dealing with uncertainty and the value of research in the context of some of the specific characteristics of devices such as learning curve effects, incremental device

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innovation and dynamic pricing. It uses value of information analysis to explore the optimal timing of reimbursement decisions and the suitability of conditional coverage decisions, such as 'only in research' and 'approval with research'.

Such conditional reimbursement policies are now becoming popular in a number of countries, given the growing recognition that, for medical devices, there will always be considerable evidence gaps, particularly in evidence on effectiveness. As in the other WPs, a case study is chosen to illustrate the use of methods at different stages of device development and diffusion. The example chosen is enhanced external counterpulsation (EECP), a device used to provide symptomatic relief from chronic refractory angina, where the existence of substantial irrecoverable costs and price changes have a substantial impact on coverage decisions.

2.6. ORGANIZATIONAL IMPACT OF MEDICAL DEVICES

The final methodological issue investigated in the MedtecHTA project was the organizational impact of medical devices. In this part of the project, the aim was to propose a methodology that will allow for incorporating organizational issues in a broader HTA framework. A systematic review of the literature was conducted, which was used to develop a large (54 item) survey of cardiologists, conducted in collaboration with the European Society of Cardiology. The objective was to explore the role of physicians' motivation and organizational factors in the adoption and diffusion of medical devices. The survey focused on seven different catheter-based or implantable cardiovascular devices. Multivariate hierarchical modeling was used to determine the associations between the various motivational and organizational factors and device diffusion and use. This research is reported in the eighth paper in this supplement (Hatz *et al.*, 2017).

3. DISSEMINATION OF PROJECT FINDINGS

In the final phase of the project (Part III), the findings and results from the previous phases were collated into a final report (WP7), which provides recommendations for decision makers, in formulating health policy, within the medical devices industry, as well as in the management of health care organizations. In addition, recommendations on developments in methodology were made for the scientific community. These recommendations are summarized in the final paper in this supplement (Tarricone *et al.*, 2017b). These are divided into recommendations for policy, recommendations for methods and recommendations for further research.

Taken together, the papers in this supplement represent a comprehensive report of all the main findings of the MedtecHTA project and give references to other published outputs for the project. It is intended to be the main source for researchers and policy makers requiring information on the project.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest relevant to the contents of this paper.

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REFERENCES

Boriani G, Biffi M, Martignani C, Diemberger I, Valzania C, Bertini M, Branzi A. 2009. Expenditure and value for money: the challenge of implantable cardioverter defibrillators. *QJM* **102**(5): 349–356. DOI:10.1093/qjmed/hcp025.

Boriani G, Maniadakis N, Auricchio A, Vardas P. 2010. Health economics and outcomes research: a new challenge and field of action for the European Heart Rhythm Association. *Europace* **12**(5): 601–603. DOI:10.1093/europace/euq028.

Ciani O, Wilcher B, Blankart CR, Hatz M, Rupel VP, Erker RS, Taylor RS. 2015. Health technology assessment of medical devices: a survey of non-European union agencies. *International Journal of Technology Assessment in Health Care* **31**(03): 154–165. DOI:10.1017/s0266462315000185.

Ciani O, Wilcher B, van Giessen A, Taylor RS. 2017. Linking the regulatory and reimbursement processes for medical Devices: the need for integrated assessments. *Health Economics* **26**(Suppl.1): 13–29.

Cohen D, Billingsley M. 2011. Europeans are left to their own devices. *BMJ* **342**(may13 2): d2748–d2748. DOI:10.1136/bmj.d2748.

Directive 2007/47/EC of the European parliament and and of the Council of 5 September 2007 2007. *Official Journal of the European Union, 21 September 2007* http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:247:0021:0055:en:PDF; accessed July 23rd 2016].

Drummond M, Griffin A, Tarricone R. 2009. Economic evaluation for devices and drugs—same or different? *Value in Health* **12**(4): 402–404. DOI:10.1111/j.1524-4733.2008.00476_1.x.

EUnetHTA (2015). Therapeutic medical devices [https://eunethta.fedimbo.belgium.be/sites/5026.fedimbo.belgium.be/files/Therapeutic%20medical%20devices_Guideline_Final%20Nov%202015.pdf; accessed July 23rd, 2016].

European Commission, DG Growth 2016. http://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework/revision_en [accessed 23rd July 2016].

Fattore G, Maniadakis N, Mantovani LG, Boriani G. 2011. Health technology assessment: what is it? Current status and perspectives in the field of electrophysiology. *Europace* **13**(suppl 2): ii49–ii53. DOI:10.1093/europace/eur083.

Fraser AG, Krucoff MC, Brindis RG, Komajda M, Smith SC Jr. 2011. Commentary: International collaboration needed on device clinical trials. *British Medical Journal* **342**: d2952.

Hatz M, Schreyögg J, Torbica A, Boriani G, Blankart CR. (2017). Adoption decisions for medical devices in the field of cardiology: results from a European Survey. *Health Economics* **26**(Suppl.1): 124-144.

National Institute for Health and Care Excellence (NICE) 2011. Medical Technologies Evaluation Programme. Methods Guide. London: NICE https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-medical-technologies/Medical-technologies-evaluation-programme-methods-guide.pdf accessed July 23rd 2016]

Ramsay CR, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT. 2001. Statistical assessment of the learning curves of health technologies. *Health Technology Assessment* **5**(12). DOI:10.3310/hta5120.

Rothery C, Claxton K, Palmer S, Epstein D, Tarricone R, Sculpher M. (2017). Characterising uncertainty in the assessment of medical devices and determining future research needs. *Health Economics* **26**(Suppl.1): 109–123.

Schreyögg J, Bäumler M, Busse R. 2009. Balancing adoption and affordability of medical devices in Europe. *Health Policy* **92**(2-3): 218–224. DOI:10.1016/j.healthpol.2009.03.016.

Schnell-Inderst P, Hunger T, Conrads-Frank A, Arvandi M. 2016a. Comparative effectiveness of medical devices. [www.medtechta.eu accessed 9 December 2016].

Schnell-Inderst P, Iglesias CP, Arvandi M, et al. 2017. A bias-adjusted evidence synthesis of RCT and observational data: the case of total hip replacement. *Health Economics* **26**(Suppl.1): 46–69.

Sorenson C, Tarricone R, Siebert M, Drummond M. 2011. Applying health economics for policy decision making: do devices differ from drugs? *Europace* **13**(suppl 2): ii54–ii58. DOI:10.1093/europace/eur089.

Tarricone R, Drummond M. 2011. Challenges in the clinical and economic evaluation of medical devices: the case of transcatheter aortic valve implantation. *Journal of Medical Marketing: Device, Diagnostic and Pharmaceutical Marketing* **11**(3): 221–229. DOI:10.1177/1745790411412242.

Tarricone R, Callea G, Ogorevc M, Rupel VP. (2017a). Improving the methods for the economic evaluation of medical devices. *Health Economics* **26**(Suppl.1): 70–92.

Tarricone R, Torbica A, Ferré F, Drummond M. 2014. Generating appropriate clinical data for value assessment of medical devices: what role does regulation play? *Expert Review of Pharmacoeconomics & Outcomes Research* **14**(5): 707–718. DOI:10.1586/14737167.2014.950233.

Tarricone R, Torbica A, Drummond M. 2017. Key recommendations from the MedtecHTA project. *Health Economics* **26** (Suppl.1): 5–11.

Taylor RS, Iglesias CP. 2009. Assessing the clinical and cost-effectiveness of medical devices and drugs: are they that different? *Value in Health* **12**(4): 404–406. DOI:10.1111/j.1524-4733.2008.00476_2.x.

Torbica A, Banks H, Valzania C, Boriani G, Fattore G. 2017. Investigating regional variation of cardiac implantable electrical device implant rates in European healthcare systems: what drives differences?. *Health Economics* **26** (Suppl.1): 30–45.

Torbica A, Drummond M, Ferré F, Tarricone R, Fattore G. (2016). Economic evaluation and health technology assessment in Europe and USA. [www.medtechta.eu accessed 9 December 2016].
Valzania C, Torbica A, Tarricone R, Leyva F, Boriani G. 2015. Implant rates of cardiac implantable electrical devices in Europe: a systematic literature review. *Health Policy*. DOI:10.1016/j.healthpol.2015.11.001.
Varabyova Y, Blankart CR, Schreyögg J. (2017). The role of learning in health technology assessments: an empirical assessment of endovascular aneurysm repairs in *German hospitals: Health Economics*. **26**(Suppl. 1): 93–108