

A report from The Economist Intelligence Unit



Value-based Health Assessment in Italy

A decentralised model

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Introduction

Italy is an intriguing case study of how value-based healthcare can evolve. The country offers an interesting dichotomy between a pioneering approach to financing innovative treatments on the one hand, and a more complex and arguably less sophisticated institutional structure and measures for assessing healthcare outcomes on the other.

The structure of Italy's system for health technology assessment (HTA) reflects both its origins as a way of containing rising healthcare costs and the country's strong economic differences between the north and the south. Italy's population of 61m people is divided among 21 economically and culturally diverse regions and autonomous provinces, which in turn are subdivided into around 8,100 municipalities.¹

The lack of consistent co-ordination of HTA activities and inadequate communication between different agencies at both the national and the regional level has meant a lack of uniformity. This is aggravating existing regional health inequalities, making it difficult for Italy to establish a coherent system for assimilating data and evidence to back up its value assessments.

While the Italian government insists, as a matter of principle, on positive health outcomes when it negotiates price agreements with manufacturers, in practice its health technology assessment programmes focus squarely on cost control without regard to outcomes.²

"The rhetoric will say a decentralised system enables you to run a more customised system according to the needs of the population," says Federico Lega, professor of public management and healthcare management and policy at Bocconi University in Milan. "The downside of the system is that we have increasing variation among regions. The good ones are performing better and better, and the ones that are behind aren't making the leaps," he adds.

The uneven organisation of HTA structures at the national and the regional level contrasts with the country's leadership role in the area of financing innovative therapies, in which consultative and assessment structures are more varied and better established than in many other European countries.

¹ Ferré, F, de Belvis, AG *et al*, "Italy Health System Review", *Health Systems in Transition*, 2014, 16(4):1-168.

² Ciani, O, Tarricone, R *et al*, "Diffusion and use of health technology assessment in policy making: what lessons for decentralised healthcare systems", *Health Policy*, December 2012, 108(2-3):194-202.

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Chapter 1: Advantages and disadvantages of a unified national approach to value-based healthcare

³ Favaretti, C, Cicchetti, A *et al*, “Health Technology Assessment in Italy”, *International Journal of Technology Assessment in Health Care*, July 2009, 25(Suppl. S1): 127-133.

⁴ De Belvis, AG, Ferré, F, *et al*, “The financial crisis in Italy: implications for the healthcare sector”, *Health Policy*, June 2012, 106(1):10-16.

⁵ International Society for Pharmacoeconomics and Outcomes Research (ISPOR), ISPOR Global Health Systems Road Map. Available at: <https://www.ispor.org/HTARoadMaps/Italy.asp>; Ferré *et al*, “Italy Health System Review”, *Health Systems in Transition*, 2014, 16(4):1-168.

⁶ Garrido, MV, Kristensen, FB *et al*, *Health Technology Assessment and Health Policy-Making in Europe: current status, challenges and potential*. World Health Organisation and European Observatory on Health Systems and Policies, Study Series No. 14, 2008, p. 84.

In Italy the concept of value-based healthcare, which looks at health outcomes of treatment relative to cost, dates back to the 1990s, when a number of regions started to look more closely at the cost-effectiveness of expensive biomedical technologies.³ It has become a greater priority in the wake of the global economic crisis, as the government has sought to make the best use of stretched financial resources, including imposing a 12.5% reduction in the price of generic drugs.⁴ However, the development of an infrastructure to collect, analyse and share data has been a slower process.

A labyrinthine national framework

The Italian Medicine Agency (Agenzia Italiana del Farmaco—AIFA), which was established in 2003, is in charge of the country’s National Pharmaceutical Formulary (Prontuario Farmaceutico Nazionale—PFN). AIFA approves medicines that can be produced, used and marketed in Italy and assigns them to one of three classes for reimbursement purposes. Class A medicines, including essential medicines and those for chronic diseases, are fully reimbursed, while Class H products are only reimbursed for hospital use. All other products are classified as Class C, which must be entirely paid for by patients unless regional health departments include them in their reimbursement schemes.⁵ The agency’s

Technical and Scientific Committee (Comitato Scientifico e Tecnico) assesses new drugs for inclusion in the PFN, as well as undertaking health technology assessment (HTA) activities for pharmaceuticals. This classification system focuses entirely on cost reimbursement; the effectiveness of the drugs involved is not part of the scheme.

A separate organisation, the National Agency for Regional Health Services (Agenzia Nazionale per i Servizi Sanitari Regionali—AGENAS) was created to support the process of setting national priorities for medicine/technology, produce HTA reports on medical devices for the Ministry of Health, and provide technical and operational support for the development of HTA programmes in the regions in the absence of a national government HTA agency.

Italy’s health ministry began to fund HTA initiatives and the “promotion of multidisciplinary competencies in HTA” as early as 2002 and provided a grant to establish an Italian Health Technology Assessment Network (SIHTA) as an umbrella organisation for activities in the early years of HTA in Italy; the network includes HTA units in academic medical centres, research hospitals and regional and local health authorities.⁶

The term HTA was first used in the 2006–08 National Healthcare Plan, which emphasised the need to recognise HTA as a “priority”.⁷ AGENAS was only formally given a specific role to assess, adopt and manage technology in 2007,⁸ at which point it was required to support the planning and development of HTA initiatives at the regional and local levels and to disseminate the results of HTA at the central level in order to encourage consistency.

Since 2009 AIFA has also taken on HTA activities, including the evaluation of clinical efficacy, cost-effectiveness and budget-impact analyses. AGENAS is meant to be an evaluation agency producing reports as well as a co-ordination office or clearing house.⁹ However, “the multi-level structure of HTA in Italy has not yet provided a full co-ordination and harmonisation of practices and outcomes across the country”—and this consequently exacerbates inequality of access to services and technologies.¹⁰ That said, regional variation can also offer opportunities for innovation and the development of best practices.

According to Nino Cartabellotta, president and founder of the Italian group for evidence-based medicine, the GIMBE Foundation, “there is adequate co-ordination between the central bodies—AGENAS, AIFA and the Istituto Superiore di Sanita [the National Institute of Health, the country’s leading public technical-scientific body]—without any overlapping of functions or activities”. However, he adds that “these central bodies are unable to appropriately exercise their influence on regional health policies. Regions often only provide data streams for national reports and monitoring activities, but the two-way communication is largely insufficient.”

As Mr Cartabellotta points out, this results in many regions failing in their provision of healthcare procedures and treatment that previous assessments had deemed essential, including timely surgery for femoral neck fractures, overly high Caesarean section rates (up to 50% in the region of Campania), or lack of

home-care services and beds in hospices in most regions of southern Italy.

Regional variations and discrepancies

Italy’s centralised HTA activities are largely divided between AIFA and AGENAS. However, just five out of Italy’s 21 regions and autonomous provinces—Veneto, Emilia-Romagna, Lombardy, Piedmont and Tuscany, all of which are located in the wealthier northern half of the country—have established structures to include HTA in their healthcare decision-making process.¹¹

There is nevertheless a significant degree of variation in the way these regions have developed HTA. Many bodies play a role in HTA decision-making in Veneto, for example, while the other four regions have a more centralised structure for carrying out the evaluation process. Industry is involved in the process only in Emilia-Romagna, while patient involvement occurs only in Piedmont; the other three regions provide no role for either industry or patients.¹²

Meanwhile, Lombardy uses a broader definition of health technologies that are covered by HTA, including drugs, devices, procedures and clinical pathways, while Emilia-Romagna places the greatest priority on assessing devices and procedures. In addition, Veneto and Lombardy have put in place a formal set of prioritisation criteria for HTA, with Lombardy going so far as to set up a specific body to prioritise future HTA projects.¹³

This group includes some of the country’s regional “first movers”: the Emilia-Romagna region, working through its regional healthcare agency, contributed the first institutionally produced HTA reports supporting clinical practice and decision-making. Lombardy launched its own HTA programme in early 2010. Together with the Veneto region, Emilia-Romagna was involved in helping to build the first pan-European HTA network, now known as the EU-netHTA. The network was established in 2009 to facilitate crossborder collaboration between European HTA organisations and support the

⁷ Favaretti *et al*, *Health Technology Assessment in Italy*, p. 129.

⁸ Ciani *et al*, *Diffusion and use of health technology assessment in policy making*, p. 196.

⁹ *Ibid.*, p. 197.

¹⁰ *Ibid.*, p. 194.

¹¹ Ferre *et al*, *Italy Health System Review*, p. 30.

¹² *Ibid.*

¹³ Ciani *et al*, *Diffusion and use of health technology assessment in policy making*, p. 197.

efficient production and use of HTA in European countries.¹⁴ Since 2013 the network has published seven joint assessments for national uptake.

Meanwhile, a few Italian regions have developed HTA models based around local, multidisciplinary hospital teams or appointed external experts to carry out evaluations.

“Theoretically speaking, the benefit [of regional diffusion of HTA] is that you can better control the provenance of use of therapy, one that takes into account the specific aspect of the hospital situation and the local patients,” says Paolo Daniele Siviero, senior adviser and fund manager at Principia SGR and former director of the Medicines Utilisation Monitoring Centre and Health Technology Assessment Office at AIFA.

He adds: “On the downside, this process sometimes takes too much time and could mean a delay in access. If we are talking about really advanced therapies, some hospitals might not be in a position to use them, but our system guarantees that a patient can move within the country and be fully covered for the costs of getting them.” Dr Siviero notes that many of the regions with the most developed HTA systems are also better organised and more efficient, with the result that they attract patients from other regions as well.

Regional programmes are nonetheless frequently constrained by a lack of sufficient data, which undermines transparency. “The feedback from the regional level—not only to national agencies but also to other regions—is not adequate,” highlights Dr Siviero. “If they take a decision on how to use a therapy in the process of treatment and aren’t able to share the basis of their decision-making, it’s often not clear what course of action has been taken. On the other hand, AIFA doesn’t publish the assessment reports that support decision-making.”

A less sophisticated system of measures

The national measures used for HTA in Italy tend to include demographic and cost-based factors,

such as disease relevance and burden, budgetary impact and relative effectiveness compared with existing methods, rather than focusing just on cost-effectiveness.

“The word ‘value’ isn’t on the agenda here in Italy—it’s relatively new”, Professor Lega of Bocconi University says. “We’re not yet at the point where we look at benefit and cost on a regular basis. The social and economic impact is not yet there. If we do have that, they are basically developing on parallel tracks. On one side are health systems using HTA techniques, and then the political side are doing health impact evaluation,” he explains.

Just three regions—Veneto, Lombardy and Campania—have their own list of priority criteria for determining the technologies considered “relevant for modifying clinical pathways”.¹⁵ Although wider social value is generally not a part of this discussion, in isolated cases public opinion has played a role in drawing attention to the relevance of certain therapies, according to Dr Cartabellotta and Oriana Ciani, a research fellow at Bocconi University. One example of this was the decision in 2013 of Italy’s health ministry to override AIFA’s ruling to block a controversial stem-cell procedure after coming under pressure from patient lobby groups.¹⁶

“As the budget for pharmaceutical products is separate from other healthcare expenditures, it’s not possible to directly consider the social costs, and not possible to get the benefit of global budgets,” says Dr Siviero, adding that up to now patient organisations have played no role in the decision-making process. Although AIFA uses quality-adjusted life years, or QALYs, as a “supportive element to the value proposition from a drug manufacturer”, it doesn’t base prices on the QALY threshold, according to Dr Siviero. Instead, he says, Italy’s central HTA agency has developed performance-based agreements with manufacturers to guarantee that even therapies for which the clinical benefit requires further evidence are immediately available, as will be shown in the next chapter.

¹⁴ Favaretti *et al*, *Health Technology Assessment in Italy*, p. 129.

¹⁵ Ciani *et al*, *Diffusion and use of health technology assessment*, p. 197.

¹⁶ “Researchers protest Italian government decision to life ban on controversial stem cell treatment”, *Stem Cells Translational Medicine*, March 2013. Available at: <http://stemcellstm.alphamedpress.org/site/misc/News124.xhtml>.

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Chapter 2: Evaluating outcomes and financing innovation

Like a number of other European countries, including Belgium and France, Italy takes into account the level of “innovativeness” when assessing new medicines in relation to existing therapies and looks at a range of health outcomes to determine whether they translate into improved health.

Since the Italian government negotiates price and reimbursement in a single process, this has helped the country take the lead in experimenting with a range of innovative financing approaches, as well as introducing a greater emphasis on outcomes.

Once AIFA has completed its assessment of a medicine, committees with representatives from several ministries and health insurance funds conduct price negotiations with manufacturers.¹⁷

These processes are beginning to have an impact on drug development itself, according to one recent article, as agencies and pharmaceutical companies make use of three groups of activities: managed market entry agreements; horizon scanning and early HTA; and bipartite and tripartite early dialogue between manufacturers, regulators and HTA assessors.¹⁸

Italy has been ahead of other European countries in establishing managed entry agreements

(MEAs) with pharmaceutical companies that share risk and allow for the greater collection of clinical evidence once new drugs are already in use.¹⁹ The arrangements are designed to help reduce the likelihood of health systems adopting treatments that end up not being cost-effective, while allowing pharmaceutical companies to recoup some of the cost of their investment.²⁰

The use of MEAs is one of the clear differences between Italy and other European countries, such as the UK. While the UK makes a decision whether or not to recommend a medicine before deciding how to make it accessible, in Italy most new drugs are approved with an MEA already attached.

“Italy has been taken as a case study for this type of approach, and it has been shared with other European countries as a very effective way to manage the introduction of innovation,” Dr Siviero says. “The intention is to have in place registries that not only provide data about the product, but about real outcomes.”

Looking at price and outcomes

MEAs fall into a number of different categories. The earliest, which predate the trend towards value-based healthcare, focused on costs, in an effort to control health budgets.

¹⁷ Paris, V and Belloni, A, *Value in Pharmaceutical Pricing*, OECD Health Working Papers No. 63, OECD 2013, pp. 14, 20.

¹⁸ Ciani, O and Jommi, C, “The role of health technology assessment bodies in shaping drug development”, *Drug Design, Development and Therapy*, November 2014, 10;8:2273-81.

¹⁹ Garratini, L and Curto, AI, “Italian risk-sharing agreements on drugs: are they worthwhile?” *European Journal of Health Economics*, January 2015, 16(1):1-3.

²⁰ Ibid.

Cost-sharing agreements involve a simple price discount that is usually limited in term and in the form of a payback. Other conditional agreements include price-per-volume, with discounts to the user for reaching a specified volume of patients treated, and price ceilings, where the number of patients likely to benefit from the treatment is defined in advance, with the manufacturer paying if that number is exceeded.

One example of the latter is dabigatran, which is used to prevent deep-vein thrombosis and pulmonary embolism as well as to reduce the risk of stroke. The Italian authorities have approved reimbursement for the drug for its first indication only and for use in hospitals. AIFA has set a cap of €3.2bn (about US\$3.59bn at current exchange rates) to be paid in the 24 months immediately after the entry into force of the contract, with manufacturer Boehringer Ingelheim agreeing to fund any excess above this amount.²¹

By contrast, recent MEA models have sought to build on the accumulation of HTA evidence and are driven by outcomes: they most commonly take the form of payment-by-result (PbR) or risk-sharing schemes. The agreements require manufacturers to pay back the full price (in the case of PbR agreements) or part of the price (in the case of risk-sharing) for each patient who fails to respond to the new treatment. One recent example is Lucentis, a drug used to treat macular degeneration, which was the subject of a PbR arrangement,²² although PbR and risk-sharing agreements are most frequently used for oncological drugs, according to Dr Ciani of Bocconi University.

These types of MEAs, which are similar to patient-access schemes in the UK, use web registries to allow hospitals to track patient eligibility and monitor the use of participating drugs and their outcomes. They are also driving closer co-operation between regulators and manufacturers, according to a 2014 article by Dr Ciani and Claudio Jommi, which noted: “From early stages of clinical research up to

post-authorisation studies, there is a trend towards increased collaboration between parties, anticipation of market access evidence collection and post-marketing risk-sharing.”²³

AIFA agreed to the first MEA contract in 2006, making it the first regulatory agency to design such an arrangement; 25 drugs have been subject to outcome-MEA contracts,²⁴ including everolimus, which was approved subject to a PbR contract requiring maker Novartis to make a payback to hospitals for patients who did not respond after 3–6 months’ of treatment with the drug for certain kinds of renal and breast cancers. A report by the London School of Economics in 2013 found that while around 43% of all MEA agreements in Italy were focused on the budgetary impact of the treatment, “improving the use of medicines emerges as the main objective overall”.²⁵

However, an editorial in the *European Journal of Health Economics*, quoting an AIFA report on MEA revenues from September 2013, found that the country’s health system was successful at clawing back only two-thirds of an estimated €46.3m in paybacks it was owed as a result of disputes with pharmaceutical companies or late requests by hospitals. By comparison, the study considered cost-sharing agreements to be “more efficient”.²⁶ However, Dr Siviero notes that AIFA reshaped its web tools substantially in 2013 to make them more effective at collecting payback from companies.

Long-range impact

Horizon-scanning systems (HSSs) help to evaluate the possible impact of new technologies to anticipate policy, development, access and health-service provision. Technologies are given priority based on expected benefits or financial impact, variation of use across the country and effect on other health policies, such as a reduction in inequalities.

In theory, HSSs can help drug developers anticipate potential difficulties that patients

²¹ Paris, V et al, *Value in Pharmaceutical Pricing*, p. 43.

²² *Ibid.*, p. 54.

²³ Ciani, O and Jommi, C, *The role of health technology assessment bodies in shaping drug development*, p. 2273.

²⁴ *Ibid.*, p. 2279.

²⁵ Ferrario, A and Kanavos, P, *Managed entry agreements for pharmaceuticals: the European experience*. The London School of Economics and Political Science, April 2013. http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/mea_report_en.pdf.

²⁶ Garattini et al, *Italian risk-sharing agreements on drugs: are they worthwhile?*

may experience in accessing certain drugs and work to overcome them. Although AIFA funded an HSS demonstration project in 2008, in which it produced an annual list of drugs in the pipeline with accompanying results on the epidemiology of the target patients, clinical evidence and comparators, there are few data available on how and whether it has used the results of the project.

In the case of medical devices, manufacturers use early HTA to make a provisional evaluation of safety, effectiveness and cost-effectiveness, based largely on evidence from bench and animal tests.

In 2011 AIFA introduced a programme to provide early scientific advice and HTA, with guidelines available on the agency's website. Guidance is given for the most appropriate comparator,

endpoints used, relevance of disease severity and drug budget impact on price/reimbursement negotiations. Fees range from €10,000 to €40,000, according to the questions asked. While data availability on the current uptake is limited, some 21 enquiries were processed in 2011-13, most of them relating to Phase II and Phase III studies.²⁷

Tripartite dialogue between regulators, HTA bodies and industry could reduce delays by allowing all parties to discuss differing data needs and learn about HTA requirements in the early stages. The process can also help to avoid the duplication of resources, as HTA advice may come from one or more reimbursement agencies and different HTA bodies.²⁸

²⁷ Ciani, O and Jommi, C, *The role of health technology assessment bodies in shaping drug development.*, pp. 2277-2278.

²⁸ Ibid.



Conclusion

Italy's approach to implementing value-based healthcare offers both room for improvement and clear areas where it can be a model for some of its European neighbours.

While the country's decentralised healthcare structure provides a significant degree of regional autonomy, the lack of uniformity undermines consistency in decision-making, something which helps to contribute to inequalities. Similarly, a degree of overlapping responsibilities and inadequate communication of the decision-making process between the centre and the regions leads to both duplication of efforts and a lack of transparency.

At the same time, the country is increasingly taking a leading role on the continent when

it comes to innovative forms of financing new treatments. Although a significant percentage of managed agreements between AIFA and manufacturers continues to be shaped by cost considerations, a growing number reflect efforts to measure cost-effectiveness and outcomes. This trend is driving the agency and manufacturers to work more closely together to help gather evidence about the impact of new technologies and treatments.

A further streamlining of Italy's HTA structure at the regional level and better communication and dissemination of data could help to move this process along and allow the country's health system to benefit from treatments that offer the greatest amount of long-term value. ■

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