Health Technology Assessment in France

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Abstract
Health Technology Assessment (henceforth, HTA) was originally defined as "a policy research that examines the short- and long-term social consequences of the application or use of technology" HTA plays an essential role in modern health care by supporting evidence-based decision-making in the health care policies and practices of many countries. In France, HTA has long been a key element of the government's health care policy. The French National Authority for Health (*Haute Autorité de S anté*, HAS), establishedin January 2005, is now the body responsible for conducting HTAs on behalf of the French public health insurance system.

In this paper, we review the history and current situation of HTA in France.

Key Words; France, health technology assessment

1. History of Health Technology Assessment

The term "technology assessment" came into use in the 1960s, especially in the United States, had has been used with regard to issues such as the implications of supersonic transport, environmental pollution, and the ethics of genetic screening (Banta, 2009). During a meeting of the Congressional Committee on Science and Astronautics in 1965, Chairman Daddario observed the need for policy makers to have information to facilitate the evaluation of the intended and unintended social, economic, and legal impacts of modern technology (Goodman 2004). As a result, the Office of Technology Assessment (OTA), an agency that provided the United States Congress with impartial assessments of technologies in the fields of medicine, telecommunications, agriculture, materials, transportation, and defense, was established. This agency contributed to many of the public policies that were created in the latter part of the 20th century. The OTA model was eventually adopted by Austria, Denmark, the European Community, France, Germany, Great Britain, The Netherlands, and Sweden (O'Donnell et al. 2009),

Health Technology Assessment (henceforth, HTA) was originally defined as "a policy research that examines the short- and long-term social consequences of the application or use of technology" (Office of Technology Assessment 1976). Subjects of assessment include evidence of safety, efficacy, patient-reported outcomes, real-world effectiveness, cost, and cost-effectiveness as well as social, legal, ethical, and political impacts (ISPOR 2003).

HTA plays an essential role in modern health care by supporting evidence-based decision-making in the health care policies and practices of many countries. In this paper, we review the history and current situation of HTA in France.

2. History of HTA in France

2.1. Background

France has a highly traditional culture; this characteristic has perhaps led to some ambivalence and scepticism regarding the attractions of modern medical technology. For the most part, however, technology innovation is greatly appreciated and sought after (Fuhrer, 1980). As health care technology progressed, the extent to which the national health insurance system should provide reimbursement for the use of such technology began to be questioned. In other words, the importance of analyzing the needs and benefits associated with technological advances was recognized, and awareness of this issue has gradually deepened. The first step in this process dates back to the late 1960s, when excessive equipment with scarce resources became a subject of discussion.

In 1970, the Health Facilities and Equipment Planning program (*carte sanitaire*) was implemented to regulate health facilities and services directly. The *carte sanitaire* was created by the Hospital Reform Act of 1970 and was used to regulate the allocation of resources on a regional and population basis from the viewpoint of equity. For this purpose, need indexes for equipment (*indices de besoins*) were calculated for each geographic area, but this process lacked transparency and sufficient analysis. The indexes were frequently accused of being manipulated because of budget restraints rather than medical needs; these accusations heightened calls for more scientific means of health planning (Weill and Banta 2009).

In parallel, in the late 1960s and early 1970s, the use of cost-effectiveness approaches entered the spotlight. A national movement for the rationalization of decision making within the limits of public

budget came into existence (*Rationalisation des choix budgétaires*). For example, to reduce the perinatal mortality rate, the Ministry of Health implemented the Perinatal Care Programme and set priorities for actions from the point of view of cost-effectiveness (Chapalain 1978). A similar study was conducted to decide whether psychiatric catchment areas were advantageous (Fuhrer 1980). Although the outcomes of these programmes by themselves were obscure, the experiences of the national movement rooted the notion that choices for new health care technologies should be discussed based on an evaluation of cost-effectiveness (Weill and Banta, 2009).

As an advisory agency for hospitals regarding investment in new technologies, the Committee for Evaluation and Diffusion of Medical Technology (*Comité d'Evaluation et de Diffusion des Innovations Technologiques*, CEDIT) was established in 1982 by the hospitals of Paris. The main task of CEDIT was to compile existing literature, but the committee also performed economic studies and prospective assessments to aid decision-making processes.

In 1984, the government unveiled a plan to support HTA. The designated objectives were to emphasize efficacy over utility and to establish an independent agency run by physicians to develop applied scientific research (Weill, 1995). Although the establishment of an agency was approved, it was not realized because of a lack of public financial support brought on by a change in political power. Moreover, since most of the people involved in HTA were not physicians but economists, sufficient attention was not attracted (Weil and Banta 2009).

2.2. Creation of ANDEM

In 1989, the government once again tried to develop HTA by legally establishing the *Agence Nationale de l'Evaluation Médicale* (ANDEM). ANDEM was an independent, nonprofit body responsible for all HTA, with the exception of pharmaceuticals. The agency performed systematic reviews of existing literature and was expected to serve as a resource center for national and international HTA. In total, ANDEM performed twenty-eight assessments (Fleurette and Banta, 2000). ANDEM consisted of 30 full-time staff members, mostly physicians and external scientific experts and health professionals. Its board of directors included representatives from the Ministries of Agriculture, Education, Health, and Research and others appointed by health insurance funds. ANDEM's budget was equally provided by the Ministry of Health and the National Health Insurance and sharply increased from US $1.5 million in 1990 to US $6 million in 1996 (Fleurette and Banta, 2000).

ANDEM's research on HTA, such as its assessment of excimer laser myopia corrective surgery in the field of ophthalmology, received financial support from the French National Health Insurance Fund (*Caisse Nationale d'Assurance Maladie des Travailleurs Salariés*, CNAMTS), etc. In 1994, ANDEM began to show active commitment to the development of clinical practice guidelines. This was triggered by the governmental decision to introduce compulsory clinical practice standards(*Références Médicales Opposables*,RMO).

(1) Development of Clinical Practice Guidelines

In 1993, CNAMTS agreed with the physicians' labor union on a plan to improve the quality of clinical practice based on the view that the best way of reducing medical expenditure was a quality-based approach. As an embodiment of this plan, a decision was made to develop a uniform electronic medical recording system and a coding for diagnosis and clinical practice services; the RMO was also introduced. In 1994, twenty-seven topics to be covered by the RMO were selected, and twenty-three additional topics were selected in 1995. ANDEM then began to prepare clinical practice guidelines covering these topics (Maisonneuve et al. 1997).

The first step taken by ANDEM was to conduct a mailed questionnaire survey of related professional societies and associations. Through this survey, ANDEM collected information on past studies related to these topics and a list of candidate members for the working group and the evaluation committee. In 1995, ANDEM asked 167 professional societies/associations about their interest in this plan, and 61 societies/associations expressed an interest (in an average of 5 topics per society) (Fourquet et al. 1997).

The next step was a literature search; literature in both English and French was sought through MEDLINE and EMBASE. In addition, PASCAL was used to search for literature in French. The key words used were clinical practice guidelines, consensus conferences, meta-analysis, literature review and decision analysis. Second-hand citations from review papers and papers by specialists were additionally collected. In this manner, 6,831 papers pertaining to 50 topics were collected. Of these papers, only 1,862 were cited in the final health care guidelines.

For each topic, a working group composed of 10-15 members (mean: 13.4 members) was formed. The transportation costs of each member were paid, and a financial reward corresponding to the cost of caring for 15 patients was given for the attendance

of each half-day meeting of the working group. At these group meetings, an equal opportunity was provided to specialists, non-specialists, general practitioners and hospital employees to voice their opinions. For example, the working group on common-type lower back pain was composed of 14 members (4 specialists in rheumatology, 3 pediatric surgeons, 3 radiologists, 1 neurologist, 2 general practitioners and 1 delegate from ANDEM) (Schott et al. 1996).

Each working group held three meetings. During the first two meetings, the strength level of the scientific evidence was assessed for the individual papers that had been collected. For papers lacking scientific evidence, the presence/absence of an extensive consensus among specialists was examined. In this manner, the draft guidelines were prepared. The draft guidelines were then sent to 20-40 evaluation committee members (32.8 members, on average) who were asked to use a checklist to evaluate the validity, ease of reading, and strength level of the evidence and applicability. The draft guidelines were then modified based on the results of this evaluation.

Between June and November 1994, guidelines on 27 topics were prepared, and 9,000 copies of the guidelines were distributed. Eleven of these guidelines were also published in medical journals. Between April and November 1995, guidelines on 23 topics were prepared, and 21 of these guidelines were published as supplements to medical journals and delivered to 50,000 physicians, while 2 guidelines remained unpublished. Of the 2 unpublished guidelines, one pertained to cesarean section. This guideline was not published because it was not based on a review of papers, but rather reflected the views of a group of specialists. The other unpublished guideline, pertaining to surgery for carpal tunnel syndrome, was not published because the working group and evaluation committee had not functioned satisfactorily because of conflicts of interests. The expenses needed to prepare, print, and deliver the clinical practice guidelines were reported to be about US $70,000 per topic (Grol et al. 1998).

(2) Introduction and influence of RMO

In 1994, RMO were introduced covering 14 topics, including the "prescription of non-steroidal anti-inflammatory drugs" and the "prescription of antibiotics." The RMO for these topics were prepared by CNAMTS and physicians' labor unions, and were independent of ANDEM's clinical practice guidelines. The following year (1995), RMO covering 26 topics were introduced. In 1996, RMO on 14 topics were introduced. The RMOs introduced after 1995 were based on ANDEM's clinical practice guidelines. Several banned practices were listed for each topic in these ROM, and 90 (61%) of the 147 banned practices were based on the clinical practice guidelines published by ANDEM. For each banned practice, a penalty was set on the basis of the healthcare index, financial index and frequency of violation, with the amount ranging from 1,562 to 11,250 francs. When the penalty was analyzed in relation to the frequency of the violation, the penalty was the most severe for the violation of banned practices related to the prescription of non-steroidal anti-inflammatory drugs, and at least 3 violations during a period of 2 months resulted in a penalty. The least severe penalties pertained to hematological testing, 3 or more sessions of ultrasonography for women during normal pregnancy, multiple sessions of thyroid tests for symptom-free cases, multiple sessions of electrocardiography for patients with moderate hypertension, etc., for which a penalty was imposed once 13 violations had been accrued (Durand-Zaleski et al. 1997).

The restrictions set forth in the RMO have been frequently corrected or deleted. For example, a restriction on "uterine cervix smear testing during routine clinical practice" imposed a penalty for violation of the rule that a smear test should not be performed more than once in 3 years for women who were free of symptoms, did not have a history of gynecological disease, and had no risk factors or abnormalities upon examination of their latest smear test result. However, this restriction caused controversy in the major newspaper Figaro and some other media, which criticized it from the viewpoint of the physicians' freedom of choice and the need for frequent testing, etc. As a result, the penalty for the violation of this restriction was lifted in early 1998 (Moss? 1998). In the November 1998 version of the RMO, there were 242 banned practices pertaining to 58 topics.

Inspections were performed by 3,000 physicians who were appointed as inspectors by the *Caisse Primaire de l'Assurance Maladie* (CPAM). Physicians who failed to observe the RMO were required to justify their practices. During the first 2 years after the introduction of the RMO, 13,000 physicians (about 10% of all clinical practitioners) were inspected, and 1,278 of these physicians were audited by other physicians. Of these audited physicians, 186 were prosecuted and 75 were ultimately penalized (Lalardrie 1996).

It is understandable why the RMO was not easily accepted by clinical physicians. According to a survey conducted by a medical association and sent to more than 62,000 physicians, 38% of the physicians resented the RMO penalty system (Fourquet et al., 1997). The percentage of physicians who

observed the RMO or who even were aware of the RMO was also reported to be inadequate. Durieux et al. (2000) conducted a questionnaire survey of general practitioners asking them to select 4 RMO topics from 8 clinical practices and to select 8 practices banned by the RMO among the 16 clinical practices. Of the 321 respondents, 80% indicated that they occasionally read the RMO; however, none of the physicians were able to provide correct answers to all the questions. The correct answer rate was 55.8% for questions on clinical topics and 50.5% for questions on RMO-banned practices. Because the correct answer rate was expected to be 50% if the answers were randomly chosen, the results of this survey seemed to indicate that the RMO had not been extensively understood by the physicians. In fact, when prescriptions issued by 2,300 physicians during the four-year period from 1992 to 1995 were investigated, the percentage of prescriptions abiding by the RMO rules was highest for antibiotics and non-steroidal anti-inflammatory drugs (40-45%) and lowest for antihypertensive agents, steroids and antidiabetic drugs (5-15%) (Le Fur and Sermet 1996).

A major limitation of RMO-based inspections is that the electronic filing system for the information is inadequate. The above-mentioned survey also involved manual checking of RMO compliance, which required as much as 300 - 350 hours to check the prescriptions made by each physician over a 2-month period (Le Fur and Sermet 1996). Thus, inspecting all the prescriptions and tests issued or conducted by individual physicians was practically impossible.

Questions have also been raised as to the usefulness of RMO as a means of decreasing medical expenditure. When the efficacy of 18 RMOs related to drug prescriptions was evaluated, significant efficacy (not transient, but continuing) was noted. However, the effect on actual drug cost savings was reported to be minimal (La Pape and Sermet 1998). At present, the RMO is essentially considered to be non-functional.

2.3 Creation of ANAES and AFSSAPS

With the creation of ANDEM, HTA started to take root in France. Hospitals other than those joining CEDIT began to develop activities related to HTA. INSERM, The national health research institute (*Institut National de la Santé et de la Recherch Médicale*, INSERM) that funds most health-related research, began to fund technology assessments, especially those related to preventative medicine. Physicians also made efforts to disseminate the HTA results. In parallel, the National School of Public Health (*Ecole Nationale de la Santé Publique*, ENSP) started to pay more attention to HTA.

Despite ANDEM's contribution to the dissemination of HTA, however, the government was dissatisfied with the overall development of HTA, as many physicians and hospitals continued to ignore evidence of efficacy, safety and cost-effectiveness and proceeded with no changes to their clinical practice. At the same time, ANDEM began to be lobbied by physicians and high-ranking civil servants, and produced poorly organized technology assessment of medical devices. Hence, the government tightened its regulation by establishing a new agency in 1999.

In the Health Care Reform (*Juppé* reform) of 1996, the Agency for Accreditation and Evaluation of Health Care (*Agence Nationale d'Accréditation et d'Evaluation en Santé*, ANAES) was established as the successor to ANDEM. The most important change in the new agency's responsibilities was the accreditation of health care organizations, for which guidelines were developed. The government mandated that health care organizations must incorporate HTA to obtain accreditation. Although ANAES was originally given a role in HTA, it has invested little in this endeavor.

In March 1999, the National Agency for Health Products (*Agence française de sécurité sanitaire des produits de santé*, AFSSAPS) was established to provide premarketing approval for some medical devices to guarantee the safety of patients and ensure postmarketing surveillance of the products. Since its establishment, with an expectation formore systematic evaluation, AFSSAPS, as well as ANAES, has been responsible for establishing clinical guidelines. Since patient involvement in the safety and quality of care was imposed by law in 2002, both physicians and hospitals have been expected to practice in a more evidence-based manner.

3. Current HTA activities

3.1 Creation of HAS

In January 2005, an independent scientific body of the French National Authority for Health (*Haute A utorité de Santé*, HAS) was founded as a result of the National Health Insurance Reform Act of 2004 to provide better care with less spending. The HAS was given expanded powers and a mandate. The disintegration of HTA activities in several programmes was behind this move. By establishing the HAS, the government attempted to consolidate all HTA-related activities under a single body.

The HAS is a public organization with financial autonomy and acts independently from the Ministry of Health. The government first estab-

lished the organization in August 2004 to integrate all HTA-related activities within the health care system under a single roof.

The HAS is mandated by law to report to the French Government and Parliament and to serve as a technical consultant to *Union Nationale des Caisses d'Assurance Maladie* (UNCAM), the Ministry of Health, and other authorities. In particular, the HAS is responsible for the assessment of drugs, medical devices and equipment, diagnostic and therapeutic procedures, and biological tests. Based on assessments of the benefits to patients and to public health, the HAS provides its opinion (which may be either positive or negative) to health authorities regarding the coverage of services and reimbursement. Though the HAS provides information, the decisions on pricing and coverage are made by other agencies. In addition to offering its opinions, the HAS also makes decisions regarding reimbursable chronic diseases, publishes clinical guidelines, performs hospital accreditations, and certifies doctors.

The HAS is comprised of one chairperson and 7 members; each of the members in turn heads a committee of specialists. The chairperson and members are appointed by the President of the Republic, the National Assembly, the Senate and the Ministries of Economic and Social Council. The seven specialist committees are responsible for pharmaceuticals (CT), medical devices and related services (CEPP), interventional and diagnostic procedures (CEAP), economic and public health evaluation (CEESP), health care coverage for long-term conditions, medical information quality and dissemination, and the accreditation of health care organizations. The first four committees are responsible for HTA.

The HAS supports the development of HTA in other countries including the National Institute for Clinical Excellence (NICE) in the UK and the *Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* (IQWiG) in Germany, as these efforts underlie reimbursement decisions in Europe.

The HAS has approximately 350 permanent staff members including health professionals and health economists. In addition to its full-time staff, the HAS can call upon an additional 3000 external experts. In 2008, it has an annual budget of €60 million, of which the largest income sources are 10% of proceeds from a tax on pharmaceutical companies' advertising expenditures (47%), followed by funding from the health insurance fund (33.5%) , fees from manufacturers (8%), government subsidy (6%). (HAS 2009)

The HAS liaises closely with government health agencies, national health insurance funds, scientific societies, research organizations, unions of health care professionals, and patients' representatives. Its staff members sit on committees and working groups so that the expectations of these organizations are reflected in the HAS' opinions.

(1) CT

The Transparency Committee (*Commission de Transparence*, CT) is a subordinate body of the HAS. After the accreditation of market authorization, the CT works together with health professionals to assess and appraise the actual clinical benefits of pharmaceuticals. To be assessed by the CT, drug manufacturers must perform clinical trials to assess the safety and the efficacy of a new drug. Information on the positive benefit/risk ratio, risk management plan, and a detailed summary of the product characteristics based on international randomized controlled trials is necessary for an assessment.

In 2008, the CT issued a total of 664 opinions, of which 225 were for newly assessed products (HAS 2009).

(2) CEPP

The Commission for the Assessment of Devices and Related Services (*Commission d'Evaluation des Produits et Prestations*, CEPP) was created within the HAS in March 2001 under the auspices of the Ministries of Health and Social Security. The CEPP ascertains the clinical benefits of medical devices and associated services and aids as well as health care products. The CEPP consists of one chairperson representing the HAS, two deputy chairpersons appointed by the HAS, and twelve scientific experts. In addition, representatives from the statutory health system and representatives of manufacturers and distributors act as consultants.

In 2008, the CEPP issued 176 opinions (HAS 2009).

(3) CEAP

The Commission for the Assessment of Professional Acts (*Commission d'évaluation des actes professionnels*, CEAP) is an HAS committee that was established in March 2005. It consists of one president and vice-president and 13 members. To foster good practices and the proper use of health services, the CEAP serves to assess techniques and methods used by health professionals for prevention, diagnosis or therapy in cooperation with other committees, such as the CEPP. It produces clinical practice guidelines based on systematic literature reviews and expert opinions.

In 2008, the CEAP issued 47 opinions (HAS 2009).

(4) CEESP

The Commission of Economic Evaluation and Public Health (*Commission d'Evaluation Economique et de Santé Publique*, CEESP) was newly established as a sub-organization responsible for HTA in June 2008 with the objective of re-evaluating pharmaceuticals. Its first task was to re-evaluate the use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, proton pump inhibitors, etc. CEESP is composed of one chairperson, two vice chairpersons, and 25 members, including health professionals, patients' representatives, and experts representing several disciplines such as economics, public health, management and epidemiology.

3.2 From Marketing Authorization to Drug Pricing

Agencies Involved in the Process of Market Authorization to Price Setting are shown in Table 1. HTA is a prerequisite for new drugs, devices, or medical procedures to be placed on the NHI reimbursement list. In this section, the process of proceeding from marketing authorization to drug pricing and the role of the HTA will be explained.

(1) Market Authorization

Since 1972, market authorization has been a prerequisite for all drugs sold in France, with a few exceptions including the temporary authorization of pharmaceuticals for rare diseases, etc. (Paris 2005). Market authorization can be obtained through an assessment performed by Committee for Medicinal Products for Human Use (CHMP), the European Medicines Agency (EMEA) or AFSSAPS. An EU level market authorization can also be obtained through a centralized procedure within the EMEA for the evaluation of medicinal products. Once a drug has already received a market authorization in one member state, a decentralized procedure exists for mutual recognition aimed at granting an EU level market authorization.. A national level of market authorization for any drug sold in France can be assessed by either the EMEA or the AFSSAPS. Either of these organizations can then give the European Commission or AFSSAPS marketing authorization for the product. In either case, to obtain market authorization, a drug must meet three criteria: pharmaceutical quality, safety and effectiveness.

An exception to the requirement for market authorization is the Temporary Authorization of Use (ATU), which can be granted by the AFSSAPS to drugs that have not yet received market authorization. Pharmaceuticals entitled to ATU status are covered by the NHI with restricted conditions.

(2) Single Technology Assessment

After being granted marketing authorization, a new drug still requires a further assessment, known as a Single Technology Assessment (STA), to be used in France under the national health care system. Assessment at this level has some commonalities with the underlying principles of market authorization, but several country-specific factors are also included, making the decision country-specific.

In France, the assessment of new drugs is performed in two steps. First, internal assessors review the available literature and other data sources as well as a dossier submitted by the pharmaceutical company. Then, members of the CT, which is a subordinate body of the HAS, and health professionals discuss and appraise the drug from two viewpoints: the medical benefit (*Service Médical Rendu*, SMR), and the improvement in medical benefit (*Amélioration de Service Médical*

Table 1. Agencies Involved in the Process of Market Authorization to Price Setting

	Pharmaceuticals	Medical Devices	Diagnostic & Therapeutic Procedures
Marketing Authorization	EMEA/AFSSAPS (Benefit/risk assessment; Validation of risk assessment plan)	Notified bodies for CE marking AFSSAPS	NA
Assessment of Medical Benefit	CT at HAS (SMR; ASMR - medical benefit, added value, importance for public health, target population)	CEPP at HAS	CEAP at HAS
Reimbursement Decision	Ministry of Health (Registration on the reimbursement list)	Ministry of Health (Registration on the reimbursement list)	UNCAM (Registration on the reimbursement list)
Price Setting	CEPS (Commitment on price, volume and post-market studies; reimbursement price) UNCAM (Reimbursement rate)	CEPS	UNCAM (Reimbursement tariffs; reimbursement rates for procedures)

Rendu, AMSR).

The target timeframe of an STA from the initial application to the final opinion is stipulated by law. This timeframe is 90 days for medical devices and drugs and180 days for procedures. In 2008, the mean delay was 73 days for drugs, which was reduced from 100 days in 2006 (HAS 2009).

Overall, STA accounts for roughly 80% of all drug assessments, 20% of all medical device assessments, and 50% of all procedure assessments (Rochaix and Xerri, 2009).

SMR

The medical benefit of a product is assessed based on the severity of the disorder, the clinical effectiveness of the medicine, and the impact on public health. This is called *Service Médical Rendu* (SMR), which provides recommendations to the Ministry of Health on whether a drug should be placed on the positive list for reimbursement. Since October 1999, an SMR assessment has been compulsory for the inclusion of any drug on the reimbursement positive list. An SMR assessment can be initiated upon the request of a drug or device manufacturer or, in the case of a procedure assessment, the request of a professional association.

SMR is assessed according to five criteria: effectiveness and possible side effects of the drug; therapeutic superiority in relation to existing alternatives; seriousness of its indications; curative, preventive or symptomatic properties; and its importance to public health. Following an evaluation of the degree of clinical utility, pharmaceuticals are classified into three SMR categories: "major or important", "moderate", or "weak". A drug can be placed on the reimbursement list for five years, after which time it must be re-evaluated. Those drugs that do not fall into one of the three categories, i.e., that are classified as "insufficient", are not covered by national health insurance. Based on the SMR result, the reimbursement rate for the product, and thus the copayment, is determined by UNCAM (Table 2). Currently, most products submitted for SMR assessment are fully reimbursed (HAS 2009).

In addition, pharmaceuticals that are used for life-threatening conditions and that are not substitutable and are particularly expensive, are reimbursed at a rate of 100%. Drugs that fall into this category are labelled with a white bar and include cancer drugs and anti-HIV drugs. Moreover, HAS classifies 30 chronic conditions that require lengthy and expensive treatment as a long-term disease (ALD). Patients with diseases listed on ALD receive all medications for the disease without requiring copayment.

According to HAS's annual activity report (HAS 2009), among the new drugs that underwent SMR accreditation for the first time in 2008, 205 were major or important, 19 were moderate, 12 were weak, and 8 were insufficient. Among those that underwent SMR accreditation for the extension of their indications in 2008, 41 were major or important, 4 were moderate, 1 was weak, and 2 were insufficient.

Table 2. The reimbursement rate based on the SMR result

SMR rating	Reimbursement rate (severe illness)	Reimbursement rate (non-serious illness)	Label color
Major or important	65%	35%	White
Moderate or weak	35%	35%	Blue
Insufficient	0%	0%	NA

ASMR

Following the SMR evaluation, a product is compared to existing treatments to assess the improvement in the medical service rendered (*Amélioration de Service Médical Rendu*, ASMR). ASMR evaluates the medical benefit relative to the therapeutic value of other drugs in the same therapeutic classification; five ASMR significance levels are possible (Table 3). Specifically, among the other drugs in the same therapeutic category, the most popular drug, the cheapest drug in defines daily dose (DDD), and the newest drug are selected for comparison. The

Table 3. ASMR evaluation and reimbursement price

ASMR significance level	Evaluation of product	Reimbursement price
I	Major therapeutic advance	Free pricing based on average prices in other EU countries (Germany, Italy, Spain, UK) but should not exceed the highest price in above countries
II	Important improvement in terms of efficacy and/or safety	
III	Moderate progress in terms of efficacy and/or safety	
IV	Minor progress in terms of efficacy and/or safety	Equivalent/higher price to /than domestically available comparators
V	No clinical improvement	Only listed if cheaper than that of domestically available comparators

ASMR level for pediatric and orphan drugs is set at one stage higher, as per an agreement with the French Pharmaceutical Companies Association (*Les Entreprises du Médicament*, LEEM).

If a drug fulfils the following three criteria (Table 4), it is considered "innovative" and receives an ASMR classification of I, II, or III. Upon a request from the manufacturer, innovative drugs can be eligible for faster assessment. Under such conditions, the HTA assessment starts before market authorization has been granted, and an opinion can be issued a few weeks after market authorization has been received.. Furthermore, innovative drugs have another advantage. Pharmaceutical companies can set a price and submit an application to the *Co mité Economique des Produits de Santé* (CEPS) as long as the set price is equivalent to or lower than the highest price available in Germany, Italy, Spain or the UK. If the CEPS do not object within two weeks, the price will be accepted. If the CEPS do not agree with the submitted price, the ordinary price setting process is initiated. However, to be covered by national health insurance, products with an ASMR classification of V must be less expensive than competitor drugs to ease the financial burden on social security funds. Thus, the price is directly related to the ASMR rating.

Table 4. Three criteria required for a drug to be considered innovative

1	Novel disease treatment • new pharmacological class; • new target; • effective for a specific population; • new method of administration
2	Clinical trial results predict an improvement compared with available standard of care because of improved efficacy, tolerance, or administration route.
3	Serves an unmet medical need because available commercial drugs do not have the same specific indications, have a low efficacy, or do not exist.

Source: Adopted from Jeunne, 2009

Since July 2003, drugs that receive an ASMR classification of III have had the additional condition of not exceeding sales of ?40 million in the third year after the launch of the product. If this condition is not met, a rebate must be paid. However, this condition was abolished in 2006, when the agreement between the CEPS and the LEEM was extended.

According to the HAS's annual activity report (HAS 2009), among the new drugs that underwent ASMR accreditation for the first time in 2008, 1 was classified as level 1, 4 were classified as level II, 3 were classified as level III, 5 were classified as level IV, and 209 were classified as level V. Among those that underwent ASMR accreditation for the extension of their indications in 2008, a total of 1, 1, 0, 13, and 30 were classified as level I, II, III, IV, and V, respectively.

(3) Reimbursement Decision

Before a final version is issued, the HAS submits all its guidance reports to the product manufacturers. The companies have the right to an appeal and can either send written comments or a request for a hearing within eight days. In addition, after a decision has been made by an authority based on the HAS's opinion, the companies may file a lawsuit with the French Supreme Administrative Court.

Reimbursement decisions are made by the Ministry of Health for pharmaceuticals and medical devices, and by the UNCAM for procedures and biological tests. While the HAS recommendations are advisory, they have a considerable impact on the decisions of the Ministry of Health and the UNCAM, as more than 95% of all positive STA opinions lead to reimbursement decisions. Also, negative recommendations are followed in almost all cases (Rochaix and Xerri 2009).

(4) Pricing

Since 1994, CEPS has set the reimbursement prices for drugs for outpatient services in agreement with pharmaceutical companies through negotiations that must be completed within 180 days after the submission of a dossier to the AFSSAPS. The price determination takes into account the ASMR level evaluated by the CT within the HAS, the sales forecast or recorded sales volumes, the prices of comparable drugs, and the foreseeable and actual conditions of the use of the drug. If the drug sales exceed the expected volume, the public authorities can either obtain a refund from the manufacturers or lower the price.

Due to the lack of transparency of the negotiation mechanism and its insufficiency to regulate pharmaceutical expenditure, this pricing mechanism has been criticized.. In addition, pharmaceutical manufacturers also complain about the relatively low drug prices, compared with in other EU countries. They are especially dissatisfied with the lack of freedom to set prices for innovative drugs. In 2003, after lobbying by the pharmaceutical industry, the current system of giving limited freedom to set drug prices for innovative products with ASMR classifications of I, II, or III was started as part of an agreement between the CEPS and the LEEM. Consequently, the prices of drugs with ASMR classifications of I to III can be set similar to the prices in other EU countries, though the CEPS still has the power to veto the price requested by the

manufacturers.

As to pharmaceuticals for hospital use, once a decision for reimbursement has been made, the price can be negotiated between each hospital and the pharmaceutical company. Trying to lower prices for the sake of its budgets, each hospital invites competitions among manufacturers. Under such conditions, cost-effectiveness data is utilized as a key determinant.

In summary, for outpatient drugs in France, the relative therapeutic value of a pharmaceutical as evaluated in the SMR and ASMR assessments is the principal determinant of a drug's price. It is neither absolute therapeutic value of the drug nor cost-effectiveness, but the degree of improvement in the medical benefits that underlies HTA in France.

3.3 Multiple Technology Assessments

In addition to assessment performed for new entries, the HAS performs another kind of HTA called multiple technology assessment (MTA) or reassessment. MTA, which is conducted by the CEESP in HAS, applies to all drugs already on the reimbursement list that must be reviewed for the renewal of coverage within 5 years at the latest or sooner if significant new information is available, using the same criteria as those used for the SMR and ASMR assessments.

Unlike STA, which focuses on one drug or treatment and assesses it within a short time period, MTA reviews an entire class of drugs, devices or procedures. Such reviews also take into account non-clinical considerations such as societal and ethical factors as well as cost-effectiveness (Table 5).

MTA may be initiated by the HAS but usually arises from requests by other public agencies, academic societies or patients' associations. The following list contains examples of MTA projects recently conducted by the HAS.

Alzheimer's drugs review
Medical devices: total hip prostheses, wound dressings, self-monitoring glycemia devices, cochlear implants, implants for wall repair in genito-urology and digestive surgery, cardiac pacemakers
Third-generation oral contraceptives
Strategy for the management of carotid stenosis: indications for revascularization techniques
Cardiac surgery with or without extra-corporeal circulation: role of the second surgeon
Dental prostheses with a ceramic structure
Sleeve gastrectomy for morbid obesity
Tension-free vaginal tapes
Lumbar disc prosthesis

4. Implications for Japan

Many payers around the world rely on some form of HTA to determine how new health technologies are effective or cost-effective relative to comparable established treatments. HTA is applied especially for pharmaceutical policy. Faced with rising prices for many branded drugs on the one hand, and the availability of a growing range of inexpensive generic drugs on the other hand, healthcare payers around the world are becoming much more selective with regard to the branded drugs they reimburse. Increasingly, reimbursement of new drugs is conditional upon evidence of innovation.

In Japan, the application of HTA to health policy has been quite limited, although the need for such consideration has often been pointed out. Japan does not have an HTA agency at present, and a large number of healthcare technologies have been diffused and used without critical evaluations.

The Ministry of Health, Labour, and Welfare (MHLW) of Japan has sometimes attempted to use HTA results when making policy decisions. For example, since August 2003, the Ministry has allowed pharmaceutical companies to submit cost-effectiveness data for new pharmaceutical products at the time of price negotiations, possibly in search of evidence-based pricing decisions. However, because the rules for reflecting cost-effectiveness data in the pricing of new drugs have not been clearly stated and no explicit influence on pricing

Table 5. Differences between STA and MTA

	STA (Single Technology Assessment)	MTA (Multiple Technology Assessment)
Target	All new drugs	All products
Timeframe	Less than 90 days	Variable
Evaluation aspects	Mainly clinical	Clinical, ethical, economic, societal
Outcome	• Positive/negative opinion • Added clinical value • Target population • Recommendation for optimal best use • Request for post-marketing study	• Recommendation for most effective strategy • Consequences of reimbursement price

Source: Adopted from Jeunne, 2009

has been observed so far, the submission rate has gradually decreased: it was only about 5% in recent years. (Ikeda, 2009).

Even if a new health technology is approved for a very broad range of conditions, it is unlikely to prove cost-effective for every possible indication. HTA has strong political support in many countries such as France, where agencies in this field have been established.

Resources for health care are limited. Hence, choices must be made, and rational, evidence-based choices are needed. To promote evidence-based health policy and clinical decision-making in Japan, an independent HTA agency such as that existing in France, is needed.

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