Year 2006 Update of the Israel National List of Health Services

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Abstract

In Israel, updating of the National List of Health Services is performed on a yearly basis by means of a systematic and structured mechanism for almost a decade. The existence of such a mechanism is vital for keeping medicine up to date, since many innovative and breakthrough medical technologies continuously and frequently evolve. The 2006 update is unique in several aspects, relating both to the mechanism and to the decision-making process. In this article we describe notable issues that arose during the current process: modifications to the update mechanism, the four-phase increase in allocated resources to fund the addition of new medical technologies (including the addition of finances at the expense of the 2007 planned budget), and public funding for high-cost therapies. Finally, we discuss the impact of medical advances on healthcare costs and a suggested constant annual addition to the budget.

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In Israel since 1999, updating of the National List of Health Services is performed on a yearly basis by means of a systematic and structured mechanism. The existence of such a mechanism is vital for keeping medicine up to date since many innovative and breakthrough medical technologies continuously and frequently evolve. These include pharmaceuticals, devices, equipment, clinical and surgical procedures, and knowledge and support systems within which healthcare is provided.

As described in detail in previous papers [1-3], the Israeli mechanism for updating the NLHS is based on two main elements: health technology assessment and decision making. Health technology assessment serves as an analytical tool. It integrates clinical, epidemiologic and economic considerations, aiming to demonstrate the added value of each technology submitted for inclusion in the NLHS and its impact on the national budget. The decision-making process relies on the technologies' assessments and a set of predefined criteria together with ethical and legal considerations. Thus, it reflects the different ethical approaches, beliefs and personal experience of the members of the Public National Advisory Committee, which prioritizes the technologies recommended for inclusion in the NLHS.

Routinely, the update process begins each year, usually in May, with a Call for Proposals for new medical technologies to be included in the NLHS. The process is concluded when the government approves the list of prioritized technologies and receives a formal validity of an Act [3].

Modifications in the update mechanism of the NLHS

Unlike previous updates of the NLHS, the current process is characterized by several modifications made in the update mechanism. The most notable ones were conducted through the 2006 Economic Arrangements Law [4], aimed at stressing the economic weight of the whole process. Although the Law still held a draft-proposal status at that time, two amendments had already been enacted. The first relates to the mode of operation of the PNAC, i.e., members of the Committee are appointed by both the Minister of Health and the Minister of Finance, in contrast to the previous status in which they were appointed exclusively by the Minister of Health. In practice, two health economists were appointed to the PNAC, as well as the Israeli 2005 Nobel Prize laureate in the field of economy and game theory. The second amendment that the Economic Arrangements Law enacted is the appointment of a subcommittee to the PNAC that would provide the Committee with the anticipated overall cost on a national level of adding each technology to the NLHS. Members of the subcommittee include officials from the Ministry of Health, the Ministry of Finance and the non-profit health management organizations.

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NHLS = National List of Health Services

PNAC = Public National Advisory Committee

These changes indicate increased influence of the Ministry of Finance on the update process. Moreover, they placed an economic emphasis on the decision-making phase, which was not accepted readily. For instance, during its work, the subcommittee had debated the correct pricing of drugs submitted for inclusion in the NLHS. The correct pricing should balance between the actual costs (usually lower than the listed price) and the actual utilization (usually higher than anticipated) of these drugs. Since the debate has not been resolved, the Ministry of Health is currently evaluating the issue of drug pricing for inclusion in the list.

A continuum of these amendments to the mechanism is expected in the next update session, as the Israeli Prime Minister expressed his intention to revise both the composition and the functioning mode of the PNAC

Another important modification to the update mechanism is the Committee chairman's precedent to enable majority voting in specific cases when consensus cannot be reached. Although anecdotal, this issue is significant. On one hand, acting in consensus illustrates the deep moral dilemmas inherent in the Committee's decision-making task, and the need for broad consent in topics pertaining to human lives. On the other hand, a voting approach highlights the necessity for reaching resolutions in these issues, no matter how difficult they are. In effect, the voting approach was rarely utilized.

Issues in the 2006 update of the NLHS

In July 2006, the PNAC completed its task of prioritizing the medical technologies submitted for inclusion in the NLHS, and made recommendations regarding those to be added to the health services provided to Israeli residents through public funding. This update process, in particular, was accompanied by several fundamental issues.

Continuous budget increase

The predefined budget allocated by the government for the technology update of the NLHS designates the financial boundaries within which the PNAC provides their recommendations. This year there was a substantial budget increase concurrent with the PNAC meetings, mainly due to the difficulty of the PNAC to converge to the specified finances.

During the Committee's initial discussions, there was disagreement among members as to whether the Committee should venture beyond its authority and recommend a list of technologies at a cost higher than the allocated budget, or set its recommendations strictly within the budget allocated. The representative of the Ministry of Finance in the Committee held a minority opinion that the Committee should recommend a list of technologies not exceeding the original NIS 200 million (US$ 44 million) allocated. With the support of the majority of the Committee members, a list was compiled of 29 technologies that were considered essential, at an annual cost of NIS 467 million (US$ 103 million). This list was presented to the government for approval, despite the fact that this recommendation exceeded the budget considerably.

Following deliberations, in April 2006 the government announced that it would increase the budget allocation to NIS 310 million (US$ 69 million). Despite this increase, a gap of NIS 157 million (US$ 35 million) remained between the Committee's recommendation and the actual budget allocated. Consequently, several technologies recommended for inclusion were likely to be left unfunded, such as coverage for growth hormone for the treatment of short children, and omalizumab (Xolair®, Genentech Inc. and Novartis Pharmaceuticals), an anti-immunoglobulin E for treating patients with severe resistant allergic asthma. Furthermore, some technologies for treating patients with metastatic cancer were not included in the PNAC's recommended list. The public outcry, fueled by extensive media coverage of a hunger strike by a number of patients and family members, created massive public and political pressure for the inclusion of these technologies.

In efforts to resolve this problem and enable patient access to essential advances in healthcare, an additional NIS 40 million (US$ 9 million) were allocated to the update budget from the government's coalition agreement and a further adjustment of NIS 350 million (US$ 78 million) was added at the expense of the 2007 planned budget for the NLHS update. Overall, this four-stage increase yielded a total of NIS 700 million (US$ 156 million) to finance new medical technologies through the NLHS. To be noted, using next year's budget in advance implies that new technologies may not be included in the list until 2008. Table 1 summarizes the list of prioritized medical technologies included this year in the NLHS.

Public funding for high-cost therapies

For policy makers deliberating on the public financing of new treatments, their rising costs raise difficult questions. In recent years these questions have intensified, especially with the introduction of high-priced promising personalized biological treatments, such as monoclonal antibodies against molecular targets. The cost of such therapies may reach NIS 200,000 (US$ 44,000) for a single patient a year, as in the case of trastuzumab (Herceptin®, Genentech Inc.) for the adjuvant treatment of HER2-positive early breast cancer.

One of the underlying dilemmas of publicly funding high-cost medical technologies is whether to provide a large proportion of the public with low-cost treatments, or a small group of patients with high cost ones. Israel has never declared a definite position in this matter, as reflected in the diversity of health services that the government provides through public funding. However, a clear preference has been made by the PNAC in previous years towards the "much for few" category. A prominent example is the drug for Fabry disease, a rare life-threatening hereditary disorder. In the update of 2002, the drug agalsidase alfa (Replagal®, Transkaryotic Therapies Inc.) for the management of Fabry disease was included in the NLHS at an estimated cost of NIS 650,000 (US$ 144,000) per patient per year, for six patients only. The rationale behind this decision was that in the case of extraordinarily expensive drugs, not publicly funding them means determining the fate of the patients.

Table 1. Technologies added to the NLHS in the 2006 update

No.	Technology	Indications	Cost/patient/ year (US$)	No. of patients	Total cost (million US$)
1	Ezetimibe (Ezetrol®)/ rosuvastatin (Crestor®)	Treatment of patients with hypercholesterolemia and a high risk for a cardiovascular event who have not reached target LDL level of 100 m/dl while being treated with maximal doses of statins	526	28,000	14.7
2	Angiotensin-II receptor antagonists: losartan (Ocsaar®)/ candesartan (Atacand®)/valsartan (Diovan®)	Treatment of patients with high blood pressure or congestive heart failure who have developed side effects or sensitivity reaction to ACE-inhibitor therapy	175	24,175	4.2
3	Long-acting insulin analogues: insulin glargine (Lantus®)/insulin detemir (Levemir®)	Expansion of eligibility criteria: Treatment of patients with diabetes mellitus not reaching target blood glucose levels with regular long-acting insulin therapy	258	7,000	1.8
4	Short-acting insulin analogues: insulin glulisine (Apidra®)/ insulin lispro (Humalog®)/insulin aspart (Novorapid®)	Expansion of eligibility criteria: Treatment of diabetes mellitus patients not reaching target blood glucose levels with regular insulin therapy	98	3,000	0.29
5	Oxaliplatin (Eloxatin®)	Adjuvant treatment for patients with stage III (Duke's C) colon cancer	7,556	800	6.0
6	Capecitabine (Xeloda®)	Adjuvant monotherapy for patients with stage III (Duke's C) colon cancer	616	200	0.1
7	Trastuzumab (Herceptin®)	Adjuvant treatment for patients with HER2-positive early breast cancer with a high risk for recurrence	43,519	350	15.2
8	Adefovir (Hepsera®)	Treatment of patients with chronic hepatitis B resistant to interferon and lamivudine	2,144	700	1.5
9	Fosamprenavir (Lexiva®)	Treatment of HIV infection in adults	474	150	0.1
10	Tenofovir (Viread®)	Expansion of eligibility criteria: first-line treatment of HIV infection	1,790	360	0.6
11	Tobramycin for inhalation (Tobi®)	Treatment of cystic fibrosis patients with *Pseudomonas aeroginosa* infection	15,902	250	4.0
12	Pneumococcal 7-valent conjugate vaccine (Prevnar®)	Vaccination against *Streptococcus pneumoniae* for high risk children	127	2,500	0.3
13	Rituximab (Mabthera®)	First-line treatment for follicular non-Hodgkin's lymphoma	22,170	250	5.5
14	Olanzapine (Zyprexa®)	Second-line treatment for bipolar disorder	1,392	5,000	7.0
15	Quetiapine (Seroquel®)	Second-line treatment for bipolar disorder	214	5,000	1.1
16	Levetiracetam (Keppra®)	Fourth-line treatment for patients with severe epilepsy	1,884	500	0.9
17	Vagal nerve stimulation	Treatment for patients with severe epilepsy resistant to drug therapy	23,888	50	1.2
18	Deferasirox (Exjade®)	Treatment of patients with chronic iron overload due to blood transfusions	16,488	250	4.1
19	Clopidogrel (Plavix®)	Reduction of atherothrombotic events for patients in whom recurrent stroke occurred while being treated with aspirin	656	3,000	2.0
20	Growth hormone	Treatment of short children (SDS < 2.6)	9,624	670	6.4
21	Clopidogrel (Plavix®)	Reduction of atherothrombotic events for patients with acute coronary syndrome who are unsuitable for a percutaneous intervention. Eligibility is for 3 months treatment.	164	5,000	0.8
22	Zoledronic acid (Zomera®)	Treatment of patients with bone metastases from prostate cancer	3,701	300	1.1
23	Omalizumab (Xolair®)	Treatment of patients with severe allergic asthma resistant to all other treatments	20,902	400	8.4
24	Bortezomib (Velcade®)	Second or third-line treatment for patients with multiple myeloma	28,745	230	6.6
25	Pulsed radiofrequency neurotomy	Treatment of patients with chronic resistant pain	667	1,000	0.7
26	Tetrabenazine (Xenazine®)	Treatment of patients with movement disorders	924	250	0.2
27	Xphen tyr tyrosidone	Special food for patients with tyrosinemia	7,067	5	0.0
28	Ketocal	Special food for the treatment of epilepsy	8,680	33	0.3
29	Trastuzumab (Herceptin®)	Adjuvant treatment for patients with HER2-positive early breast cancer with a low risk for recurrence	43,721	235	10.3
30	Letrozole (Femara®)	Extended adjuvant treatment of early breast cancer in postmenopausal women who have received prior standard 5 year adjuvant tamoxifen therapy.	2,048	4,300	8.8
31	Cetuximab (Erbitux®)	Erbitux in combination with radiation therapy for patients with locally advanced squamous cell cancer of the head and neck	12,259	180	2.2
32	Bevacizumab (Avastin®)	First-line treatment for patients with metastatic carcinoma of the colon or rectum, and to be used in combination with intravenous 5-fluorouracil-based chemotherapy	35,565	500	17.8

Table 1. (Cont.)

No.	Technology	Indications	Cost/patient/ year (US$)	No. of patients	Total cost (million US$)
33	Bevacizumab (Avastin®)	Treatment of rectal cancer with local recurrence	35,565	50	1.8
34	Docetaxel (Taxotere®)	Treatment of patients with hormone-refractory prostate cancer	10,000	350	3.5
35	Alemtuzumab (Mabcampath®)	Treatment of patients with CLL who have been treated with alkylating agents and who failed to achieve a complete or partial response or achieved only a short remission (less than 6 months) following fludarabine phosphate therapy	17,376	20	0.3
36	Gemtuzumab (Mylotarg®)	Treatment of patients with CD33-positive acute myeloid leukemia in first relapse who are 60 years old or more and who are not considered candidates for cytotoxic chemotherapy. The safety and efficacy of Mylotarg in patients with poor performance status and organ dysfunction has not been established.	13,279	50	0.7
37	Ibritumomab + yttrium) (Zevalin® + Ytracis®)	Treatment of adult patients with rituximab relapsed or refractory CD20+ follicular B cell non-Hodgkins lymphoma	22,462	25	0.6
38	Duloxetine (Cymbalta®), gabapentin (Gabapentin-Teva®), pregabalin (Lyrica®)	• Cymbalta: second-line treatment of neuropathic pain associated with diabetic peripheral neuropathy. • Gabapentin Teva: second-line treatment of neuropathic pain in diabetic neuropathy or post-herpetic neuropathy (neuralgia). • Lyrica: treatment of peripheral neuropathic pain resistant to Cymbalta or Gabapentin.	222	50,000	11.1
39	Tenofovir + emtricitabine (Truvada®)	In combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults over 18 years old.	2,376	200	0.5
40	Sildenafil (Revatio®)	Treatment of patients with pulmonary arterial hypertension	–		–
41	Iloprost (Ventavis®)	Treatment of patients with pulmonary arterial hypertension	–		–
42	Trastuzumab (Herfeptin®)	Neo-adjuvant (pre-surgical) treatment for HER2-positive early breast cancer	–		–
43	Alglucosidase alfa (Myozyme®)	Treatment of patients with Pompe disease	263,636	11	2.9
44	Capsule endoscopy	• Recurrent gastrointestinal bleeding from unknown origin • Suspected IBD not diagnosed by all other means	844	1,000	0.8
45	Insertable loop recorder (ECG)	Patients suffering from recurrent fainting for which etiology was not revealed with other diagnostic methods	2,031	100	0.2
46	Cochlear implant for adults	Adults over 18 years old suffering from deafness in both ears in whom hearing devices are not helpful	23,215	50	1.2
47	PGD	Couples undergoing IVF who carry genes for severe genetic diseases or chromosomal aberration that can be diagnosed by the PGD procedure	1,202	50	0.1
48	PGD + IVF	Repeated abortions due to chromosomal aberrations	8,000	50	0.4
	Total			**146,594**	**156.7**

$1 US = 4.5 NIS

LDL = low density lipoprotein, ACE = angiotensin-converting enzyme, CLL = chronic lymphocytic leukemia, HIV = human immunodeficiency virus, IBD = inflammatory bowel disease, IVF = in vitro fertilization, PGD = pre-implantation genetic diagnosis, SDS = standard deviation score

The same rationale guided the PNAC members to place trastuzumab – for the adjuvant treatment of 350 breast cancer patients classified as high risk for recurrence of the disease – in the top ten of the prioritization list in 2006. As mentioned earlier, the estimated cost of this therapy reaches NIS 200,000 (US$ 44,000) per patient per year. In contrast, the lipid-lowering drugs ezetimibe (Ezetrol®, Merck and Schering-Plough) and rosuvastatin (Crestor®, AstraZeneca Pharmaceuticals), which were ranked this year by the Committee as top priority, are intended to treat 28,000 patient at a cost of NIS 2400 (US$ 530) per patient per year. To emphasize the dilemma, the overall annual cost of trastuzumab for 350 patients equals the approximate annual cost of ezetimibe/rosuvastatin for 28,000 patients. Thus, in an era that necessitates priority setting in healthcare, the social, moral and ethical values of the nation should assist in accomplishing this task.

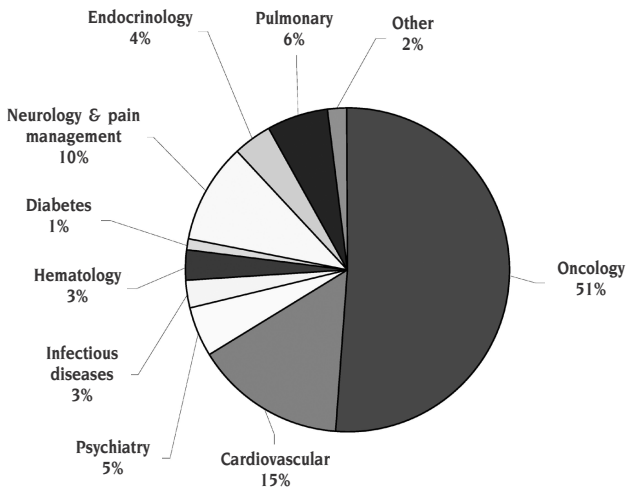

Figure 1. Cost of medical technologies included in the 2006 NLHS update.

Implementation of ethical precepts in priority setting of medical technologies

Budget constraints that characterize all health systems, globally, require that priorities be set to determine "worthy" preferences between new candidate medical technologies each time public funding is considered. Resolving issues of how to prioritize and according to what criteria is extremely complex, since apart from clinical and economic considerations, ethical and moral dilemmas also lie at the core of the process.

The Israeli model for setting priorities in heathcare defines a list of guiding criteria derived from ethical theories [3]. One of the most fundamental criteria is "life-saving," generally defined as a substantial prolongation of life. Its position as a major overriding criterion is derived from the Jewish belief in the sanctity of life, meaning that all resources should be devoted to saving lives. Accordingly, Israel is considered an early adopter of new and emerging medical technologies, especially those considered "life-saving," through acceptance into standard care despite immature data or substantial experience in the non-investigational setting.

The most recent example of early adoption of a new therapy is the PNAC's decision to provide public funding for the drug Myozyme® (alglucosidase alfa, Genzyme Corporation), a truly "life-saving" therapy indicated for use in patients with the rare neuromuscular genetic Pompe disease. Committee deliberations concerning the inclusion of this therapy in the NLHS focused on the high uncertainty regarding projected prevalence of the disease and future spending on the drug (which significantly escalates in accordance to body weight increase). Furthermore, alglucosidase alfa was only recently granted marketing approval in the United States (April 2006, under a priority review process), and it is currently in its final stage of approval in Israel. However, substantial clinical evidence on the drug has not yet been collected. Recognizing the severely debilitating nature of the disease, which is usually fatal, while bearing in mind that this is an extremely costly medication beyond the reach of the individual, members of the Committee decided to support the provision of this treatment at an annual cost of NIS 13 million (US$ 2.9 million) for 7 patients.

Another recent example is the ongoing deliberation on the drug trastuzumab for the adjuvant treatment of HER2-positive early breast cancer. In October 2005, an interim analysis of four large-scale independent prospective studies reported that adjuvant trastuzumab reduces the risk for disease recurrence by almost 50%, even at less than 2 years of follow-up [5,6]. Given that metastatic breast cancer is almost always incurable, reducing the risk of recurrence means fewer metastatic patients and, therefore, improved survival rates. Because of the magnitude of the benefit afforded by the drug and the consistency of the results across the studies, this treatment option was considered positively. This is despite the fact that these were only interim results and this indication was not approved at that time by any health regulatory agency worldwide. Eventually, this treatment, as well as alglucosidase alfa, was recommended for inclusion in the current update of the NLHS under a prior condition that it be approved by the Ministry of Health.

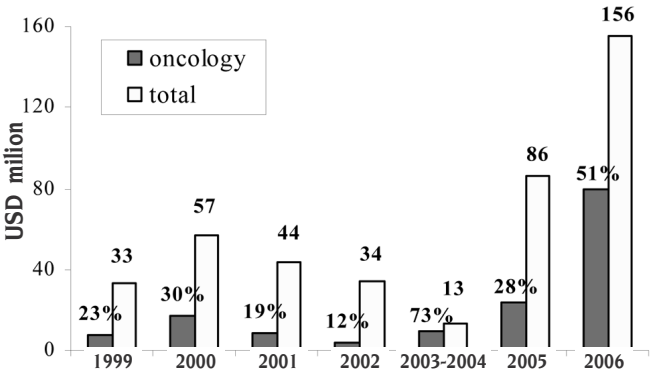

Figure 2. Resource allocation for oncology treatments 1999–2006: percentage of the overall funding appropriation each year.

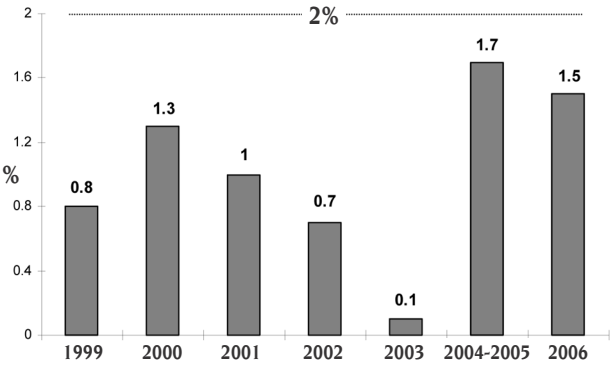

Figure 3. Funding appropriation for the NLHS update 1999–2006: percentage of the HMOs' budget.
* Estimate, based on combined 2006-2007 update budget

The addition of oncology drugs with each update of the NLHS [Figure 2] demonstrates the impact of social and ethical values of life prolongation.

The impact of medical advance on healthcare costs

The continuous progress in medicine is reflected in the development of new and innovative medical technologies. Not only does this medical advance exert an upward impact on healthcare costs, it is also a major factor driving these costs.

A report prepared in the U.S. in 2001 by Project HOPE (Health Opportunities for People Everywhere) [7] examined the role of medical technology relative to other factors in influencing spending on healthcare. The examination of the technology-expenditure link was based on nine case studies of new and emerging medical technologies. Using the "residual" approach, the authors projected the contribution of medical technology to future healthcare costs to be 1.5– 2.2% per annum (for the years 2001–2005). Another study, published in 2002, was conducted for the UK Office of Treasury in order to identify the key drivers of health need and cost in Britain in the future [8]. This report presented estimates of the historical contribution of technology to health spending growth in the UK, suggesting that medical technology contributed around 2 percentage points to the annual health spending over the past 20 years. Forecasts for the years 2002–2022 predicted that technological advance would account for 1.3 to 3.95 percentage points of the annual average increase in expenditure on health.

These studies support the enactment of a predefined mechanism for monetary allocation in order to sustain an adequate level of healthcare. Over the past years in Israel, the resources designated for the purpose of financing medical advances have been far below the recommended allocation of 2–4% [2,9] of the national public healthcare expenditure (the HMOs' annual budget), as presented in Figure 3. The authors would like to point out that so far neither Israel nor other western countries has enacted an automatic mechanism for budgeting medical advance.

HMO = health management organizations

Summary

The management of the NLHS involves many diverse issues and its complexity grows over time. The case of the 2006 update in particular demonstrates many repercussions involved in the process, and illustrates the problematic nature of the current situation in which there is no systematically defined procedure for resource allocation towards the addition of new medical technologies to the NLHS.

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Erratum

In the Table of Contents of the August issue, the article by Kaufman et al. appeared incorrectly. The word "indications" was written instead of "implications." The correct title is: "Estimating the usual prevalence and incidence of acute illness in the community: implications for pandemic influenza and bioterrorism preparedness." This mistake occurred only in the Contents page and not in the article itself (page 563) or online.