Recommendations for Management of the Trastuzumab (Herceptin) among Iranian Breast Cancer Patients, a Policy Brief

ORIGINAL ARTICLE

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ABSTRACT

Background: Allocation of the new (expensive) drugs for difficult refractory diseases and financial protection of the patients is an important challenge in the national health systems worldwide especially in developing countries. Trastuzumab (Herceptin) as one of the effective but expensive drugs, put major financial burden for the Iranian patients and government. So the Ministry of Health and Medical Education (MOHME), decided to implement a national program for appropriate management of breast cancer and regulation of Trastuzumab in I.R of Iran (NPMBCT). In this policy brief we evaluated this issue and provided necessary recommendations.

Methods: We designed a conceptual model consisting of the goals, main and supporting processes for management of Trastuzumab in the national program. Five macro-processes selected as the main concerns. Then an expert panel including different scientific disciplines discussed the different aspects of the issue and provided the necessary recommendations. We determined the link between the suggested recommendations and the objectives of the program.

Results: Based on the five selected main processes, the experts provided 10 recommendations including: 1) balance in the resource allocation, 2) appropriate modeling for the subsides allocation, 3) avoiding "poor subsidize the rich" phenomenon, 4) development and updating the clinical guidelines, 5) cost-effectiveness analysis on accepted guideline, 6) Quality improvement of diagnostic tests, 7) standardization of the laboratory kits, 8) brand management and lowering the drug cost, 9) improving the patient registry system by ICT infra-structure, 10) development of expert systems to empower the diagnostic laboratories.

Conclusion: Given these recommendations, the NPMBCT program will be a successful model for the appropriate management of the expensive drugs and treatment of breast cancer in I.R. of Iran and other developing countries.

Keywords: ***Trastuzumab, Breast Cancer, Iran, management, New High-Cost Cancer Drugs (NHCCD).***

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Introduction

Policymaking and management of new high-cost cancer drugs (NHCCD) has been one of the most complex and challenging issues of health system in I.R of Iran and other countries. According to the principles and ethics in health systems, it is necessary to spend several health expenditure per capita for a small population, which will impose the financial burden of the treatments to the patients. Trastuzumab (Herceptin) is one of those drugs whose effectiveness in treatment of HER2 positive breast cancer has been proved.

The Iranian Ministry of Health and Medical Education (MOHME) began a national program to regulate the prescription and use of Trastuzumab in I.R. of Iran in 2010 named NPMBCT. The program considered different parts including diagnosis of eligible patients, distribution and administration of Trastuzumab and subsidization the drug for breast cancer patients. Establishment of an electronic data registry as a regulatory mechanism is the strategic initiatives in this program beyond the improvement of diagnostic procedures, and developing a national treatment guideline for Trastuzumab prescription through the country.

This study has addressed the comprehensive integrated strategies that must be made for policymaking of the expensive oncology drugs. Here we introduce the factors that affect strategic decision and establishment of the processes in NPMBCT.

A- Main factors

• **Incidence and prevalence of breast cancer in Iran and proportion of HER2+ cases of the disease:** Breast cancer is the most common cancer among Iranian women. Every year, about 10,000 new cases of the breast cancer occur in I.R of Iran,[1] of which, 20%-25% are expected to be HER2+. In addition, according to the expert estimation about 500 prevalent patients who are referred with a recurrent and metastatic cancer needs Trastuzumab in the country. Therefore, we estimated that about 2500 breast cancer patients need to take Trastuzumab in Iran each year.

• **Limitation of governmental subsidy resources to support refractory diseases:** The cost of treating 2500 breast cancer patients with Trastuzumab per year would be over 1,250,000,000,000 IRR (12,000,000 USD), which is more than total subsidy resources of the government allocated for hard to treat diseases (HTDS) in 2010.

• **Lack of stable and integrated management of new high-cost drugs in the national health care system and health insurance organizations.**

• **Lack of targeted drug subsidies:** According to the National Pharmaceutical Statistics (NPS), over 310,000,000,000 IRR (30,000,000 USD) was spent for Trastuzumab in 2010. Generally based on the supportive subsidy regulations, in the years following the execution of the program, one third of patients' treatment cost has been paid by the state subsidy and the rest of the cost must be paid by the patients themselves. Although covering the two third of the cost by patients was considerably high and many patients who could not afford the expense stop their treatment in the middle of their treatment plan. This issue leads to the fact that wealthy patients can take the most benefit from the supportive subsidy and lead to inequity.

• **Controversial statistics about the percentage of patients with HER2+ breast cancer:** Although scientific evidence showed that about one fourth of patients with breast cancer are HER2 positive,[2] some surveys reported the prevalence of HER2+ is higher than that the expected rate and in some report it approached to more than 50% and lead to a high rate of Trastuzumab prescription and notable increase in the treatment cost of breast cancer treatment in I.R of Iran.[3] This variation could be mostly related to technical problems and the use of non-standard kits to perform IHC tests.

• **Lack of uniform approach to pharmacological treatment among Oncologists:** Although specialists are interested in to follow the international clinical guidelines, including the recommendations provided by National Comprehensive Cancer Network (NCCN) in U.S.[4] and National Institute for Health and Clinical Excellence (NICE) in UK,[5] because of expensive treatment with Trastuzumab, there is proposals to consider the short-term and low dose regimens (9 courses, 4mg/kg at first and 2mg/kg for the next) instead of long term and high dose (18 courses, 8mg/kg at first and 2mg/kg for the next) regimen.[6]

B- Contextual factors

• **Lack of appropriate information technology infrastructure for establishment of effective communication among sections involved in the management of expensive drugs:** These infrastructures have major deficiencies in terms of both inter-organization information system (IOIS) and patient electronic data.

• **Lack of awareness among general population and patients and unrealistic expectations about effectiveness of the expensive drugs:** lack of the appropriate awareness has caused patients to be misled by the media and non-scientific bodies and magnify the effectiveness of the expensive drugs. Patients may overestimate the effect of the drug and believe overall survival of disease is increase and disease will cure with an expensive drug. These problems make patients and their relatives urge the physicians to prescribe the drug even when it is not necessary.

• **Failure to make policies and decisions based on the local cost-effectiveness and economic analyses:** Generally, these types of economic analyses are not performed in many developing countries and decision-makers has to decide without such evidence.[7]

• **Lack of scientific priority setting due to economical restrictions and ethical considerations:** The priority setting and consideration of all aspect of cancer control which is usually done in the developed countries is an important tool for appropriate decision making. It is not usually available in Iran and high likely many developing countries.

C- Intervening factors

• **The pressure on the MOHME by politicians** for providing supportive subsidies to the some particular groups of patients.

• **The pressure of mass media:** the mass media do not have enough information about the monitoring processes of providing supportive subsidies for the drug.

• **Advertisements by pharmaceutical companies:** the pharmaceutical companies advertise only the effectiveness and cost-effectiveness report provided in the high income countries. The patients and even clinicians may misled by those advertisements.

The aim of this policy brief is to analyze the goals, strategies, and processes that are developed for the above-mentioned factors. Besides being integrated to the overall goals of the health system, it will complement the strategies and processes considered in the NPMBCT program.

Methodology

The steps through which this policy brief was developed are as follows:

A. Assessment of the factors affecting the issue: having been familiar with generalities of NPMBCT program, we established a working group and assess factors (main, contextual, and intervening factors) influenced on the program (**Fig. 1**).

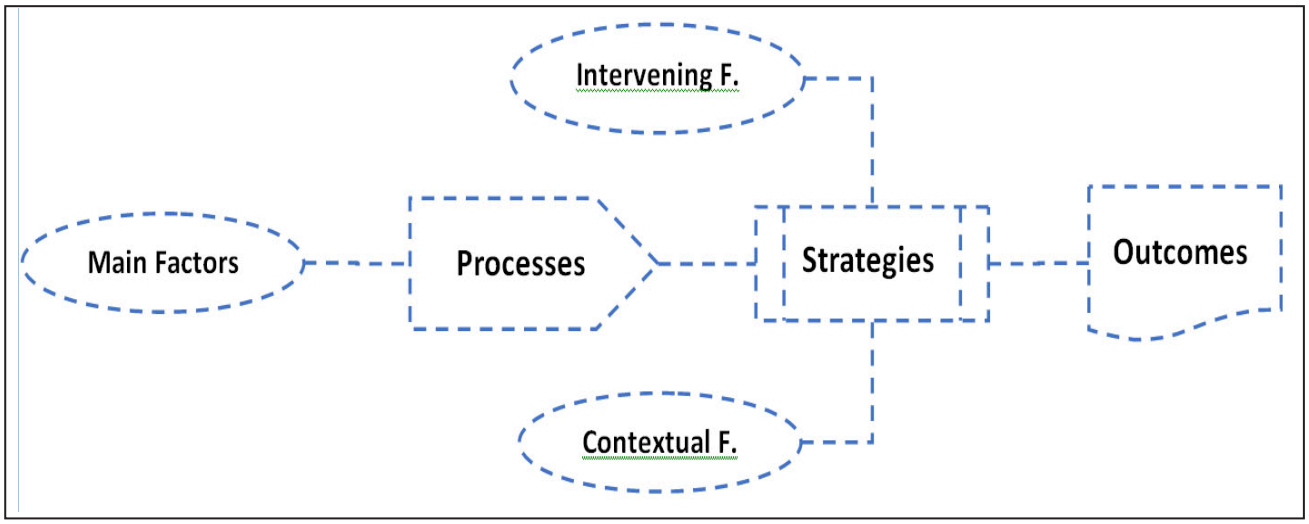

Figure 1. The Factors make influence on the processes and strategies that system develop to approach the outcomes.

B. Designing the conceptual framework: this conceptual framework was designed based on a top-down approach in order to demonstrate conceivable goals of the national program and main processes. The model dealt with optimal allocation of a (high-cost) new drug in refractory diseases in general.

C. Establishment of an expert panel: to establish the expert panel, we invited experts and clinicians from different disciplines. In this respect, the panel consisted of specialists in medical oncology, pathology, surgery, radiation oncology, epidemiology, cancer immunology, management and information technology, and health policy research. The panel started working by holding a 90-minunte meeting to get familiar with the subject matter and factors affecting it and comply with the conceptual model that had been designed by the working group. The panel members selected five essential (main) processes in the NPMBCT program.

D. Development of policy options (strategies): Based on the discussions by the invited experts, ten policy options and were provided to the authorities and the executive group of the national program.

Results and Discussions

A. The conceptual model: as mentioned in the methodology, the conceptual model was primarily composed of the objectives. The five conceivable objectives of the model are shown in **Table 1**. This table also defines the correlation between these objectives and the final impact of the health care system, namely, equity, effectiveness, efficiency, financial stability, and satisfaction.

According to the presented conceptual model (Figure 3), a set of core and supportive processes were determined to accomplish the above objectives. The core processes refer to a set of processes necessary for accomplishment of the objectives, and absence of any of them may make achievement of the objectives impossible. In the conceptual model, three core processes were considered to reach the objectives: 1) Appropriate treatment including appropriate selection of patients eligible for Trastuzumab treatment, use of the drug, and follow-up and monitoring of the patients for side effects, especially cardiovascular complications, disease-free survival in the primary breast cancer and overall survival in metastatic patients, 2) Supply and distribution of the drug, and 3) financial support and reimbursement through insurance or supportive subsidies.

In addition, in this model we considered the support processes that refer to the set of processes for improvement of the efficiency of the system. The support processes in this example include research and development, continuous education, information technology, budget management, etc.

From all the processes (both core & support), we prioritized the following ones:

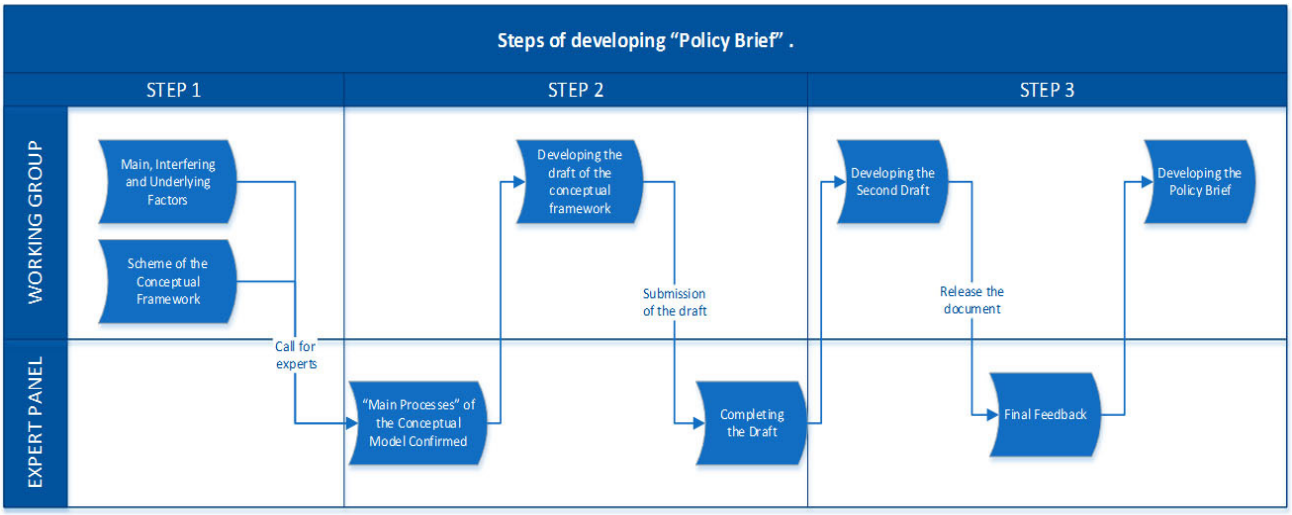

Figure 2. The steps through which the policy brief was developed.

Table 1. The default goals of NPMBCT program in alignment with main goals of the national health system, namely, equity, effectiveness, efficiency, financial protection, and satisfaction. The objective has been considered in developing the conceptual model.
G1. All the patients who need the drug can receive it with minimum problem (in cost, availability, etc.).
G2. The drug is not prescribed for patients who have not shown the effectiveness of the drug, and these patients are informed of not using the drug.
G3. Ensuring of the effectiveness of the drug in patients who receive it and use it optimally.
G4. Ensuring of the fact that all eligible patients take the drug optimally.
G5. Ensuring of the fact that all the above four objectives are fulfilled at any time.

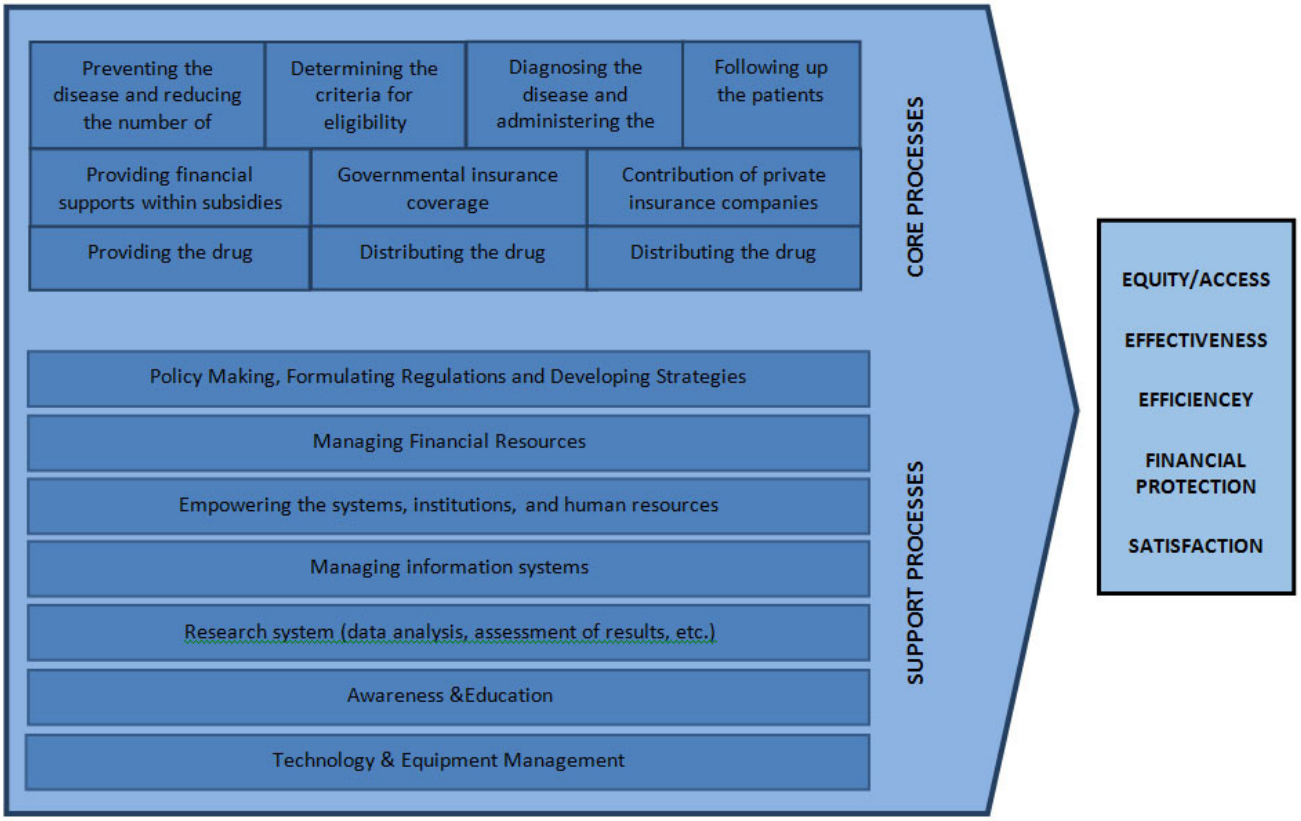

Figure 3: A model for management of new drugs for HTDS in Iran; final goals and core/support processes.

1. Identification of the patients required the drug;
2. Rational use of the drug;
3. Optimized supply and distribution of the drug;
4. Using information technology infrastructure for regulation and monitoring of the program
5. Equity-based distribution of the supportive subsidy.

B. Strategic recommendations: The study continued through the above prioritized processes and ten recommendations were provided as follows:

Recommendation 1: The supportive subsidies related to Trastuzumab should be determined proportionately as compared to other priorities in control of breast cancer (like screening, diagnosis, and other therapeutic regimens).

Recommendation 2: Financial support should be based valid data and distribution of the patients across the country.

Table 2. The default goals of NPMBCT program in alignment with main goals of the national health system, namely, equity, effectiveness, efficiency, financial protection, and satisfaction. The objective has been considered in developing the conceptual model.

Processes in priority	Strategic Recommendation	GOALS				
		G1	G2	G3	G4	G5
Identification of the patients required the drug	1. Appropriate and balanced allocation of subsidies					☐
	2.Allocation of subsidies based on valid data	☐				
	3.Prioritization of patients for receiving the drug subsidy	☐				
Rational use of the drug	4.Developing guidelines for treatment and administration of the drug		☐	☐	☐	
	5.Assessing the effectiveness of the treatment instructions		☐	☐	☐	
Optimized supply and distribution	6.Developing guidelines for diagnostic tests		☐	☐		
	7.Standardizing IHC laboratory kits		☐	☐		
Using ICT for regulation and monitoring	8.Brand management for reducing drug cost	☐				☐
Equity-based distribution of the supportive subsidy	9.Program management in the electronic system and proper record of patients' information	☐	☐	☐	☐	☐
	10. Utilizing expert systems to enhance the quality of laboratories		☐	☐		

Table 3. Short-term outcomes and final effects of the priority processes and the recommended strategies for management of Trastuzumab in patients with breast cancer in Iran.

Processes	Strategies (Recommended)	Outcomes	Final Impact
Systematic distribution of the supportive subsidy for the drug	Allocation of the subsidy based on the effectiveness, cost-effectiveness, and budget impact analysis	Increased accessibility of eligible patients to the drug	Justice
Systematic administration of the drug	Development and implementation of the instructions based on the available resources	Approaching to the standard care	Effectiveness, efficiency, and financial stability
Diagnosing patients eligible for the drug	Increasing sensitivity and specificity of diagnostic tests	Reduction of the false positive and false negative errors in identification of eligible patients	Effectiveness and efficiency
Optimal supply and distribution of the drug	Brand management	Reduction of treatment cost	Justice, financial stability and satisfaction
Expanding the information technology infrastructure	Designing and operating a comprehensive system for drug management	Optimum management of the treatment process	Justice, effectiveness, efficiency, financial stability and satisfaction

Recommendation 3: To avoid the phenomenon named "subsidy of the poor to the rich patients", it is important to provide financial support to all patients equally. All treatment options should be included in the criteria for financial support.

Recommendation 4: It is necessary to develop and update national treatment guidelines with Trastuzumab on the basis of scientific evidence, international protocols, and local cost-effectiveness analyses.

Recommendation 5: The cost-effectiveness of

Trastuzumab should be studied in both long and short regimen.

Recommendation 6: It is necessary to develop standards of immunohistochemistry (IHC) test for HER2 assessment. Training of the specialists, and laboratories would be necessary to get the valid response.

Recommendation 7: The IHC kits of the HER2 test should be evaluated and standardized in the laboratories throughout the country.

Recommendation 8: new brands of Trastuzumab will be produced after 2013. It is necessary to consider solutions such as "brand management" to prepare the low price of the drug in the country.

Recommendation 9: Development of an inter-organization information system (IOIS) for management of the work-flow based on the approved clinical guideline could assure the success and evaluation of the program. In addition, data from this system can be used for future clinical and epidemiological research.

Recommendation 10: the expert systems should be designed and implemented in order to empower laboratories for accurate and proper use of the national laboratory protocols.

We believe that the consideration of the mentioned recommendations, this program will be a successful model for the appropriate management of the Trastuzumab and other high-cost drugs in Iran and other low resource countries.

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