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How to Best Define Target Populations of Medicines in View of Their Coverage by the National Health Insurance Scheme?

Françoise F. Hamers[1], *Jacques Massol*[2], *Patricia Maillère*[3] *and participants of Round Table n°5 of Giens XXV*[⋆]

1 Service Évaluation Économique et de Santé Publique, Haute Autorité de Santé, Saint-Denis La Plaine Cedex, France
2 Hôpital Saint Jacques, Besançon, France
3 IRIS, Groupe Servier, Courbevoie, France

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Abstract – The target population of a medicine may include different populations that may partially overlap including the population that has been evaluated in the clinical trials, the population for which the medicine provides an actual benefit (SMR), that for which the drug provides an improvement of the actual benefit (ASMR), etc. The definition of the target population in both qualitative and quantitative terms has key public health and economic implications. Recommendations are made to shed light on the definitions, to clarify the requests of the public decision makers and to improve the methods and the sources allowing the quantification of target populations.

1. Introduction

Round Table n°5 was devoted to the definition of target populations for medicines with a view to their coverage by the national french health insurance scheme. The qualitative and quantitative definition of target populations is associated with major public health and economic stakes for the different parties involved – the pharmaceutical industry, payers, decision makers, evaluation agencies, and patients. Several of the parties involved have expressed their dissatisfaction regarding both the quality of the target population estimations or the data allowing their estimation, and the lack of transparency about the manner in which this information is being used at the different levels of the reimbursement decision process.

2. Definitions

A major part of the debates involved the definition of the term "target population" itself. This term is widely used in marketing and refers to a section of the population for which a product or service is intended. In the evaluation of a medicine, in particular with reference to its reimbursement, this term encompass different populations that partially overlap and that are defined and used for different ends by the different players [pharmaceutical industry, Ministry of Health, Economic Committee for Health Products (CEP), Transparency Committee, European Medicine Agency (EMA)] at different moments of the process, from the development of a medicine to its market launch and its coverage.

At the time of the introduction on the market, the target population is defined based on the results of clinical trials of the therapy administered for a given therapeutic objective. Although the population of these trials is supposed to represent the target population of the treating physician, it is only a sub-group of it (figure 1). One can never be entirely sure that the administration of the same therapy, under the same conditions, but to other individuals, would give the same results, precisely because those individuals are different (in particular, the patients included in trials are often at a lower risk). However, everyday medical practice is based on the

⋆ For the list of participants, see the end of the article.

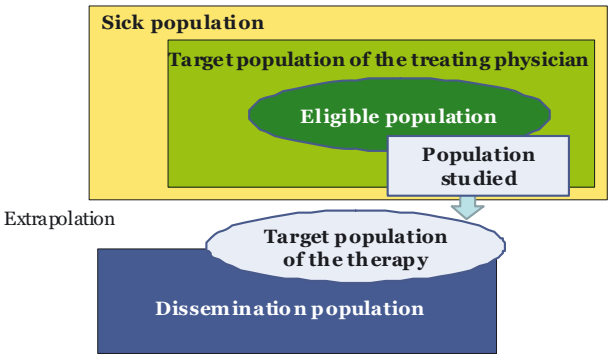

Fig. 1. Populations of interest. After Collet *et al.*[3]

inference of the efficacy of treatments on people who are different from those on whom they were tested.[1]

With regard to coverage status, Article R 163-18 of the French Social Security Code defines the target population as follows: "The estimation of the number of patients falling within the therapeutic indication(s) for which the TC deems the inclusion in the coverage list justified, according to the epidemiological data available. If necessary, the evaluation will mention the impossibility of carrying out precise estimations."

The standard coverage application documentation[2] identifies the populations to be described in the following manner:

"Define all patients falling within the therapeutic indication(s) and likely to derive a benefit from the treatment, excluding specifically:

- *The patients for whom a benefit has not been demonstrated.*
- *The patients presenting with a contraindication.*

Then describe the sub-groups of patients deriving a particular benefit from the proprietary medicine, for example those for whom an ASMR (improvement in actual benefit) is requested, if this is not the case for the entire target population.

Estimation of the target population falling within the indication(s).

Estimation of a sub-population able to benefit more particularly from the treatment".

It has also been emphasised that the target population of a product is not defined once and for all but that it may evolve over time according to various factors including changes in diagnostic techniques, screening strategies, available treatment strategies and treatment recommendations.

3. Current situation

3.1. Process for producing target populations

The opinions (evaluation reports) of the TC are prepared at the outset by the project manager of the given dossiers at the French National Authority for Health (HAS) in the form of a preparatory document supported by the opinions of two or three clinical experts, which is then discussed, approved and finalised by the TC (figure 2).

Table I. Examples of target populations estimates extracted from the Transparency Committee opinions published on the website of the HAS in the period January to July 2009.

Medicine	Target population
N...	14 000 to 18 000
E...	180 000 to 580 000
E...	56 000 to 500 000
R...	Maximum 15 000
T...	900
L...	796 000 (758 000 to 910 000)

3.2. Revues of estimated target populations

A systematic review of the paragraph entitled "target population" of all the opinions of the TC published on the HAS website from January to July 2009 has been performed.

Of the 130 opinions containing a "target population" paragraph, the target population could not be estimated at all in 15 (12%) and could only be estimated partly in nine (7%). In one third of the cases (n=42), the Transparency Committee opinion explicitly relied on expert opinion to estimate either the size of the target population as such or one of the key parameters used for this estimation (see examples below).

- Example 1. "The sub-population of resistant patients who may benefit from a treatment with [...] could, according to the experts, reach a maximum of 3000 patients in France".
- Example 2. "The percentage of patients presenting a contraindication to metformine accounts for about 10% of the population (expert opinion)".

It is noted that in 30% of the cases, the target population was estimated to be less than 10 000 people. The way target populations estimates are formulated and their levels of precision are highly variable, which reflects, at least partly, the quality of available data (table I).

Also, at the time of listing for coverage, in over 85% of cases, the population defined by the medicinal product's marketing authorisation (MA) corresponds to the population for which the TC had considered the actual medical benefit (SMR) of the drug as sufficient to justify its coverage, and also corresponds to the population for which the TC has established the level of improvement in medical benefit (ASMR). In some cases, the reimbursement population (SMR) is more restricted than that of the MA (figure 3). In such cases, the estimation of this population is of particular importance.