The Jury, called to answer the question: Should the Health Service organize screening of the population with the aim of identifying healthy people who may have children with cystic fibrosis? unanimously expressed a vote of YES.

REASONS

In making this decision, the Jury carefully evaluated the viewpoints in favor and those opposed to the screening. The various motivations for the decision are presented here in the form of question and answer.

Why screening for cystic fibrosis and not for other diseases?
Cystic fibrosis is a genetic disease which, in the majority of cases, appears in early childhood and notably reduces quality of life and life expectancy. It has a considerable impact on family members and imposes high social costs. It is the most common serious genetic disease. In Italy about one person in 30 is a carrier of a genetic mutation capable of causing cystic fibrosis. The carrier of cystic fibrosis is a healthy individual who can transmit the mutation to his/her children. A couple of healthy carriers has a 25% probability (1 in 4) of having a child with cystic fibrosis who will then manifest symptoms of the disease at variable levels of severity. However, there is a non-invasive genetic test requiring only a simple blood sample that is able to identify the carriers of disease-causing mutations with high accuracy (around 85%). The test provides the couple with important information on which to base an informed reproductive decision. This screening will also serve as a model applicable to the detection of other genetic diseases.

Is there a risk of moving towards selective reproduction because of unforeseen consequences?
Screening for carriers of cystic fibrosis aims to provide people with additional information for more informed reproduction, without limiting personal freedom. Genetics has made long strides in the last few decades, and its application for preventive and curative purposes can be considered acceptable if it improves the health of the population.

Do we run the risk of provoking an excessive level of anxiety in a substantial part of the general population or of generating false illusions?
Because we are dealing with a frequent mutation, the screening will lead to the identification of a large number of healthy carriers. The diagnosis of “healthy carrier of cystic fibrosis” certainly has a psychological impact on those who receive it. But this impact is limited, according to health professionals. Valid, accurate information, combined with psychological support when necessary, can reduce the stress of a positive test result.
The test also produces a certain number, though limited, of false negatives - persons with a negative test result but who actually are carriers of the mutation; these people feel falsely reassured. No test is 100% accurate. The current carrier test is precise enough to find the overwhelming majority of healthy carriers, and its accuracy is bound to improve in the future thanks to progress in research. The margin of error is therefore small enough to be considered acceptable.
To improve the health of the general population, could the resources needed to organize the screening be employed more usefully by the National Health Service (Servizio Sanitario Nazionale)?

The decision to organize a population screening must not be driven by economic criteria, though this CF screening is sustainable from this point of view. The management and care of cystic fibrosis, which is a chronic illness, entails elevated costs for the Italian NHS and for families. Data collected in eastern Veneto, where the test is currently offered to all couples of reproductive age, indicate that the frequency of the disease markedly drops thanks to increased awareness of being a carrier and the risk of having a child with cystic fibrosis. It can therefore be reasonably presumed that the costs of the illness will continue to diminish, soon providing the resources necessary to cover the costs of screening.

Instead of offering screening to the general population, why not proceed with offering the test only to couples of reproductive age?

As opposed to active offering of the test, screening on a national level provides better guarantees of uniformity among the regions and therefore greater fairness. The complexity of the CF carrier screening and the experience - sometimes negative - with other screenings, should encourage the NHS to do better, especially in terms of information and educational interventions, rather than discouraging it.

The Jury was also asked to answer some sub-questions:

What information should the Health Service give regarding tests and CF to people of child-bearing age so they can plan children consciously and responsibly?

The Jury members believe that citizens should be informed of the fact that:

- One out of 30 people in Italy is a healthy carrier of cystic fibrosis and there is a test capable of determining carrier status;
- Healthy carriers are not ill and never will be, but they may pass the mutation on to their children;
- Two healthy carriers of cystic fibrosis have a 25% probability (1 in 4) of having a child with cystic fibrosis: in other words, a 25% chance of having a child who will develop the symptoms of cystic fibrosis in a more or less serious manner;
- The carrier test for cystic fibrosis has a sensitivity of 85%, but there is a residual probability (1 in 125) that a person who tests negative is actually a carrier of the mutation.

What aspects of the test on the carrier should be highlighted?

Citizens must know that:

- Taking the test does not entail risks, as it only requires a simple blood sample;
- The test is free, and is not compulsory;
- The test result will be delivered directly and confidentiality will be guaranteed;
- A positive result does not mean that the person is ill – simply that s/he may pass on the mutation to his/her children;
- The test has a very low margin of error for giving a negative result when the person is actually a healthy CF carrier.

Which aspects of cystic fibrosis should be highlighted?

A complete overview of the pathology will need to be provided. In particular, the problems regarding the respiratory system and the pancreas will need to be explained. The efforts required of parents of sick children, both in everyday management and in case of acute episodes, must also be explained. The consequences of the illness and its treatment on the child’s quality of life and that of
the family should be reported. In addition, it must be specified that the disease has different degrees of severity and that though people may have many symptoms, some only find they are ill in adulthood because of sterility. For this reason, it would be useful to have the percentages of people in whom the disease appears in severe, moderate, or mild forms.

Who should do the informing, in what context and how?
The information will certainly have to be conveyed through the usual channels of mass communication: TV as well as national and local press, coordinated by national public institutions, not tied to partial interests. General practitioners, gynecologists, family counselling services, women’s health centers, and volunteer associations should all have a primary role in promoting information regarding the screening. The involvement of secondary level schools should also be considered. A frank, but not alarmist communicative style is recommended.

Are there unknown issues that should be researched scientifically regarding the test for the healthy carrier?
Research should be directed towards a better forecast of the disease’s severity on the basis of the type of mutation, in order to establish more precisely the mutations that cause the most severe forms from those that cause milder ones. The Jury members hope that research will improve the test’s ability to correctly identify healthy carriers.

The current document was read and approved by the Citizens’ Jury.
The Jury was asked: Should the Health Service organize screening of the population with the aim of identifying healthy people who may have children with CF? It did not reach agreement, but it deliberated by a majority (9 to 7) in favor of screening.

**REASONS**

The jurors, regardless of the final choice, agreed unanimously on the need for the Health Service to do more to inform the public about cystic fibrosis (CF), and enable individuals/couples to make informed reproductive choices. The jury, however, was split on how to achieve this: a majority was in favor of population screening and a minority in favor of a campaign to actively offer the CF carrier test to couples of childbearing age. According to most of the jurors, screening provides the general population with greater social justice on the national level, while an active campaign jeopardizes the citizens of some regions and the most vulnerable population. Based on the experience in Eastern Veneto, screening is an effective tool to help reduce the incidence of the disease, with considerable advantages in human - avoidance of suffering to families and potential patients - and economic terms, considering both direct and indirect costs of the disease, and the increasing costs as new treatments become available.

Although aware that the organization of population screening involves important economic and organizational efforts by the Health Service, the majority of jurors believes that the cost-benefit balance is positive and that nation-wide population screening would also lead to a reduction in the cost of the test. Moreover, the recommendation for population screening with the related information campaign would achieve the aim of launching a warning about genetic diseases and informed reproductive choices. Considering the complexity of the concepts to be conveyed, all the jurors agreed on the critical importance of the informative phase.

For some jurors the limits of the CF carrier test are unacceptable, but the majority believes that sensitivity around 85% is good enough, although they hope that research will produce a test with better sensitivity and specificity, to predict the severity of the disease more accurately.

The Jury was also asked to answer some sub-questions:

**What information should the Health Service give regarding tests and CF to people of childbearing age so they can plan children consciously and responsibly?**

People must be informed that in Italy one in 3,000 newborns has cystic fibrosis, one in 30 persons is a CF carrier, and CF is an inherited disease, not contagious in any way. It must be made clear that carriers are people who will never develop the disease but people must be informed that two carriers have a 1 in 4 probability of having a sick child.

**What aspects of the test on the carrier should be highlighted?**

It must be explained that this test is a blood test, aimed at women and men of childbearing age; it is free and participation is the discretion of each person invited. It should also be specified that the test can identify 85% of healthy carriers, but that a negative result does not provide absolute certainty of not being a CF carrier, even if this likelihood is greatly reduced. It should be explained that the test is notable to predict the severity of the disease.

**Which aspects of cystic fibrosis should be highlighted?**
It must be explained what CF is, its symptoms, the available therapy, life expectancy and quality of life of patients and their families. It should be specified that the disease has different degrees of severity.

Who should do the informing, in what context and how?
Health services and health professionals must be required to inform the population; schools and voluntary associations must also be involved. The invitation to the screening must give all the necessary information, and the information campaign should involve radio, television, institutional websites and social networks. Instead of physicians using their own initiative, guidelines are required to outline what to say and how to say it.

Are there unknown issues that should be researched scientifically regarding the carrier test? Research should focus on: (1) the reduction of the uncertainty of the test, increasing its sensitivity and specificity, and (2) increasing the predictive power of the test regarding the severity of the disease, depending on the mutations found in the couple or fetus.

The current document was read and approved by the Citizens' Jury.