MyPeBS breast cancer clinical trial: rigged up ?

MyPeBS is a randomized breast cancer screening trial organized in seven European countries. It has been presented as “a very ambitious project” that seeks to know whether screening tests based on “individual risks of cancer are as efficient or better than standard screening tests” (1).

A seemingly attractive proposition
The idea is quite bright: screening a higher number of women at a high risk of breast cancer and a smaller number of women at a low risk might decrease the overall number of deaths caused by breast cancer. At the same time, the adverse effects of screening might be reduced, especially the unnecessary diagnoses of non-progressive cancer (overdiagnosis) that lead to breast removal in women whose cancer would never have shown in her lifetime (overtreatment).

Incomplete implementation
Unfortunately, MyPeBS delivers inaccurate information to women and professionals. After more than 60 years of research, we still do not have evidence that breast cancer screening reduces ‘all-cause’ mortality. This is the paramount observation, at the core of the debates in the medical and scientific community. That leads to the following scenario proposed by the Civil and Healthcare Professionals Consultation organized by the French Health Minister: **stopping** breast cancer screening (2). Nevertheless, if people want to to know if a new screening method, based on individual risks, is more efficient than no screening, it would be important to compare it to…no screening. The MyPeBS protocol does not plan to do answer the important question.

A complex trial
A number of women will be selected at random. Some of them will be offered screening tests based on individual risks, starting from the age of 40, and the other will have “standard” screening tests.
Following a complex process, women from the screening-based-on-individual-risks-group will be divided into four subgroups. Women at low-risk will not undergo screening. Women at moderate risk will undergo screening every two years with mammography. Women at high-risk will undergo screening every year, and women at very high-risk will undergo an additional MRI scan every year. After four years, every women will then undergo mammography screening.
Women from the “standard screening” group will follow the local program organized in their geographical area, with some differences according to their countries: mammography screening every 1 to 3 years, from the age of 40 or 50.

It is so complex it is hard to see how reliable conclusions can be drawn: in the screening-based-on-individual-risks-group, mammography screening will begin at the age of 40, instead of 45 or 50 in the standard screening group. Screening programs organized in different countries will falsely be considered as identical. Paradoxically, in the screening-based-on-individual-risks-group, young women with low or moderate risk factors will undergo more mammography screenings than in the standard screening group. Conversely, some women over 50 will undergo fewer mammography screenings, and some others will undergo more. It will be very difficult to compare these heterogeneous groups and sub groups

Rigged comparison

The comparison methods are even more surprising. The protocol does not intend to find out if the new screening program is better than the former one, by looking at the change of breast cancer mortality. It intends to find out whether it is “not less efficient ” by looking at the number of new cases of stage 2 breast cancers: in other words, advanced and most serious forms of cancers (3). This method is referred to as “non-inferior“. In practice, if new cases of stage 2 breast cancers increase, but if that increase is smaller than 25%, then the “new method” will be considered as “equivalent“ to the former one: in other words, as efficient.
But there is a problem: the absence of all screening tests would probably lead to a stage 2 breast cancer incidence increase smaller than 25%.
This means that even if the “new screening test programme“ is absolutely inefficient, it will be considered as equivalent to the former one! Let's put it another way: the statistical calculation has been designed so that, whatever the results, the “new screening” will be considered equivalent to the old one. Even if there are 25% more advanced cancers in the new-screening-test-group with 25% more breast cancer deaths!

When the results of a trial are known in advance, you cannot call it a scientific trial: it is a marketing trial.
This poses a serious ethical problem. How could such a trial be approved, and receive grants. This is a mystery to us.

The Cancer-Rose group

1- S. Delaloge « Proposition de participation à une étude clinique » - courrier destiné aux futurs investigateurs, 28 août 2018, 2 pages.
2- Concertation citoyenne et scientifique « Ensemble, améliorons le dépistage du cancer du sein » Rapport du Comité d’Orientation, sept 2016, 166 pages. https://urlz.fr/4aI5
3- Unicancer - Protocole n° UC-0109/1805 de l’étude MyPEBS