MyPeBS is a clinical trial which compares the incidence of advanced breast cancers in a group of women subjected to breast cancer risk-based screening tests and in a control group undergoing current standard planned screening tests.
Stratified screening on risk factors is an interesting project in itself, and carrying out a clinical study can only be favorable in order to confirm whether it is or not.
This study, however, would have to be carried out with appropriate methodology, which appears not to be the case of MyPeBS.

**1st point: the choice of using standard screening as a control arm is contestable.**
3 options can be considered for future screening programs: changing to stratified screening tests, continuing current standard screening tests, or discontinuing all screening tests.
Comparing the stratified screening arm to a current standard control arm could hopefully provide the answer to the question: Is stratified screening more efficient or less efficient than standard screening?
The answer to this question would only enable to make a choice between changing to a risk based strategy and continuing with the standard screening strategy. It will not provide any additional information to enable to make a choice between screening; stratified or standard, and no screening.
It is all the more regrettable that planned screening does not seem as adequate in 2018 as when it became the standard strategy. In terms of benefits, the 20% relevant mortality risk reduction is based on old studies and has not been found in recent studies. In terms of risks, overdiagnosis has possibly been underestimated, as recent studies have evaluated it nearer to 40% than to 10% as initially forecast. It should not be forgotten that overdiagnosis = unnecessary treatment, side effects - sometimes serious- with no benefits in return.

MyPeBS therefore represents a missed opportunity: the opportunity to provide the answer, with current data, to the question: Should planned screening tests be discontinued, be continued or be changed to risk-based?
To achieve this, including 3 arms in the study: one risk-based screening arm, one standard screening arm, and one with no screening would have been sufficient.
Of course this would mean accepting to reconsider the importance of screening if the study did not demonstrate superiority of screening compared to no screening. The sponsors of MyPeBS do not appear to be ready to call into the possible question.

**2nd point: a lax approach as to non-inferiority.**
The main objective of MyPeBS is to demonstrate non-inferiority of risk-based screening, as compared to standard screening.
Contrary to what one might believe, A non-inferior to B does not mean that A is at least as performant as B. A non-inferior to B, means in effect that A can be inferior to B but that this inferiority does not exceed a certain threshold.
In the case of MyPeBS, this threshold of non-inferiority is set, arbitrarily, to -25%.
In other words, it is easy to think that at the end of the study, risk-based screening is certainly less performant than standard screening with, for example, performance loss somewhere between -5 and -20%; however, as the performance loss does not reach -25%, non-inferiority is confirmed, when in fact at best, the loss is of -5%, and at worst, this performance loss could reach -20%.
Supposing your employer were to inform you that your salary scale was going to be revised downwards or upwards. Would you be truly reassured if your boss specified that in any case, if your salary were to decrease, this decrease would not be inferior to -25% ?
And would you consider that a decrease of -25% of your income is insignificant? Well, this is exactly what MyPeBS puts forward. Simply replace “employer” by “study protocol” and “salary” by “screening efficiency”.

**3rd point: deceitful information.**

In the information leaflet, large-scale studies which showed that screening had reduced the mortality rate of breast cancer by around 20% are mentioned in the part of the text “Advantages and disadvantages of standard breast cancer screening”. Indication that those studies are old and probably obsolete or that a significant decrease of mortality by screening has not been found in recent studies[1,2] has been carefully omitted.

Concerning overdiagnosis, the leaflet merely mentions 10%, failing to specify that the frequency of overdiagnosis is not well known, with rates of up to 50% in some studies [3,4].

Furthermore, there is no mention of overtreatment that occurs with overdiagnosis. Nevertheless, they are indeed unnecessary treatments, with multiple side effects, which represent the major risks of screening tests.

Present scientific uncertainties make the presentation of benefits and harms of screening difficult. However, no information should be withheld, or for the purpose of clarity, should only convenient statistics be presented and others overlooked.

Studying the interest of stratified screening on risk factors might seem useful, but not haphazardly and certainly not with the main intention of promoting mammography screening one way or the other. This intention is clearly mentioned in Dr Balleyguer’s statement, page 14 in the press folder MyPeBS, 28 September 2018: "MyPeBS will probably encourage more women to enter national screening programs. Today, barely one out of two are taking part” [5].

1. Autier P., Boniol M., Koechlin A., Pizot C, Boniol M. (2017), Effectiveness of and overdiagnosis from mammography screening in the Netherlands: population based study. BMJ 2017;359:j5224 doi:10.1136/bmj.j5224

2. Møller M.H., Lousdal M.L., Kristiansen I.S., Støvring H. (2018), Effect of organized mammography screening on breast cancer mortality: A population-based cohort study in Norway. Int J Cancer. doi:10.1002/ijc.31832

3. Junod B., Zahl P.-H., Kaplan R.M., Olsen J., Greenland S. (2011), An investigation of the apparent breast cancer epidemic in France: screening and incidence trends in birth cohorts. BMC Cancer. 2011 Sep 21,11(1):401.

4. Welch H.G., M.P.H., Prorok P.C., O’Malley A.J., Kramer B.S. (2016), Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness. N Engl J Med 2016; 375:1438-1447. doi: 10.1056/NEJMoa1600249

5. http://www.unicancer.fr/sites/default/files/MyPeBS-DP.pdf