**Supplementary Materials and Methods**

Epigenetic risk assessment of female cancers: women’s information needs and attitudes

*Table A1.* Guideline for the focus groups

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| Initial questions and introductory sentences |
| Part One (1h 45min)Introduction/Purpose of the studyThis study asks about your attitude to and opinion on a novel testing method that is currently being developed. The purpose of this genetic test *with genome, epigenome, and metagenome analyses* is to determine the individual risk of developing certain female-specific cancers.* We first briefly introduce you to this novel testing method.
* Subsequently we would like to discuss a draft test information brochure with you.

Your personal opinion on the topic and the brochure is important to us because it will help us to develop and improve future information materials for the test, addressing possible knowledge needs as well as women's concerns.Please let us openly know about your thoughts. We would also like to let you know that there are no right or wrong answers. This is not a knowledge test and we are interested only in your honest opinion. If you don't want to say anything in regard to certain points, you don't have to. |
| Attitudes and arguments*I would like to briefly introduce the idea behind the novel test, which is being developed in a cooperation of several European research groups. The test is based on a smear. The analysis of cells in the smear targets your genome and how it was shaped in the past by the environment and your individual health behaviour.**This analysis of the sample will help to determine your personal risk of developing breast cancer, ovarian cancer, cervical cancer, and endometrial cancer.**The test result will tell you if you have a lower risk, an average risk, or higher risk of developing a particular cancer than the general population. Depending on a lower, an average, or a higher risk, the individual prevention strategy will be different: what can be done, should be done, or should not be done with regard to personal health behaviour, to further screening tests, or to preventive medical procedures.**The test is offered to both pre-menopausal women, when you can have children, as well as to post-menopausal women, when you can no longer have children.*What do you think about such a test? Do you personally see any tangible benefits / opportunities of such a test for you? Do you personally see any tangible risks / drawbacks of such a test for you? |
| Informational needs and intentionsImagine you are offered such a test. What would you need to know to feel confident that you know enough to decide for or against taking the test? What is information that you expect to get from your doctor before deciding for or against taking the test? |
| Hypothetical results: Informational needs and intentionsImagine you participate in the test and receive the result „*higher* risk of developing a certain cancer". Note that this is not yet a diagnosis, but instead a statement about the probability of developing this cancer.- What would you like to know next?- What would you do now?Imagine you participate in the test and receive the result „*lower* risk of developing a certain cancer".- What would you like to know next?- What would you do?Imagine you participate in the test and receive the result „*average* risk of developing a certain cancer".- What would you like to know next?- What would you do? |
| Test requirementsEvery test produces wrong results to a certain extent. For instance, a higher risk of developing a certain cancer could be indicated even though one’s cancer risk is in fact lower.- What are your thoughts on this?Vice-versa, the test could indicate a lower risk of developing a certain cancer even though one’s cancer risk is in fact higher.- What are your thoughts on this?At this point, do you have anything else to say about the risks and benefits of the test? Do you feel that your attitude has changed because of the information you received regarding the test quality and the test results?What other problems, apart from the possible disease, might crop up by classifying women's individual risk? |
| Informed intentionsWhat do you think: would you participate in such a test? Why/why not?Could you imagine that some women do not want to know their risk? If yes, what might be their concern? What could be the reason behind this concern? What is your opinion regarding women not wanting to know their risk?Do you think women should have the opportunity to opt out of certain test results?Imagine the test is provided for all women by the Health insurance - Do you think women may feel societal pressure to participate in testing?*Given that surgical options are available only for the “higher risk”-women with regard to a certain type of cancer, would you accept doing the test anyhow?**Given that no option to intervene is available for the “lower risk”-women, would you accept doing the test anyhow?* |
| 10 min break |
| Understanding and defining risksOut of 100 women in a ”lower risk group”, how many women do you expect to develop cancer during their lifetime?What risk level would you consider as lower risk? (e.g. x% risk; x-fold below pop. average)Out of 100 women in a ”higher risk group”, how many women do you expect to develop cancer during their lifetime?What risk level would you consider as higher risk? (e.g. x% risk; x-fold above pop. average)Implementation of the test- How do you feel about data protection and privacy?- Who should have party to the genetic information and the test results? Which use of the collected information should require your consent?- As an example, I would like to briefly introduce the procedure for mammography screening in Germany to you: Every two years, women from 50 years upwards receive an invitation for a screening at a fixed time and place. The recipient can either accept or cancel the appointment. Imagine you receive an invitation letter from your gynecologist to participate in the test discussed today for a specific date: What do you think?Epigenetics and responsibilityAs you just learnt, the cancer prediction test looks not only at the genome you inherited from your parents, but also at its changes due to external environmental factors, such as diseases, toxins, radiation, or general lifestyle. How do you feel about the fact that your own lifestyle contributes to the development of cancer?What would you like to know about that? |
| The leafletWhat do you expect from an information leaflet? Introduction + 10 min reading timeHow do you evaluate this leaflet?Do you think the information about the test in the leaflet can be easily understood?What was clear, what was not clear?What did not work?What information is missing? What is dispensable?Do you think women will be able to make an independent and well-considered choice? |
| FinishHow do you feel after this discussion?Is there something else you would like to discuss now and that was not yet covered? |

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*Table A2*. Final code assignment of “What information do women require on epigenetic cancer-risk assessment?”.

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| **Final code family for “What information do women require on epigenetic cancer-risk assessment?”** | **Code** | **Number of participants under 40 years****(n =12 )** | **Number participants over 55 years****(n=13)** |
| Disease-related information requirements | Epidemiology | 4/-3 | 7 |
|  | Genome–environment interplay  | -/-1 | 1 |
|  | Mortality and treatability | 6 | 4/-2 |
|  | Pathology of diseases | 2/-6 | 2/-1 |
|  | Personal history | 2 | 2 |
| Technical background of the test | Epigenomics in practice | 3 | 8 |
|  | Medical procedure | 2 | 3 |
|  | Analytical details | 1/-3 | 1 |
| Implementation information requirements | Conditions | 2 | 5 |
|  | Costs | 2 | - |
|  | Counseling | 1 | 5 |
|  | Measures to deal with a result | 6 | 5 |
| Evaluative information requirements | Benefits-to-harms ratio | 1 | 2 |
|  | Risk category definitions | 4 | 2 |
|  | Test quality general | 6 | 3 |
| Informational requirements given result | Psychological impact of testing | 2 | 1/-2 |
|  | High risk – disease knowledge | 3 | 1 |
|  | High risk – follow-up pipeline | 9 | 5 |
|  | High risk – monitoring | 2 | - |
|  | High risk – support | 1 | - |

Negative numbers after “/” indicate women’s statements that were explicitly excluded from information needs.

*Table A3*. Final code assignment of beliefs about benefits and concerns about testing, which were provided as arguments.

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| **Final code family for beliefs** | **Code** | **Number of participants under 40 years****(n =12 )** | **Number participants over 55 years****(n=13)** |
| In favor of testing | Guidance on medical strategy | 3 | 2 |
|  | Reducing concern about cancer | 1 | 1 |
|  | Increasing survival | 1 | 1 |
|  | Curiosity | 1 | - |
|  | Development of coping strategies (Empowerment by risk knowledge) | 1 | 5 |
|  | Increased control of life by facing the risk as a chance | 1 | 2 |
|  | Motivational push to more conscious living  | 2 | 2 |
|  | Responding to familial cancer burden | 1 | 3 |
|  | Strategic use | 1 | 1 |
|  | Being similar to established and accepted health tests | 1 | 1 |
| Against testing | Aleatory uncertainty | 3 | 2 |
|  | Lack of benefits | - | 3 |
|  | Pressure to change life | 1 | 1 |
|  | No need to know | - | 2 |
|  | Unnecessary worry | 6 | 3 |
|  | Waiting for cancer | 1 | 3 |

*Table A4*. Final code assignment of risk communication.

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| **Final code** | **Number of participants under 40 years****(n =12 )** | **Number participants over 55 years****(n=13)** |
| Risk definition | 7 | 10 |
| Result communication | 2 | 6 |
| Test quality | 12 | 13 |

*Table A5*. Final code assignment of responses to hypothetical test results.

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| **Final code family for result responses** | **Code** | **Number of participants under 40 years****(n =12 )** | **Number participants over 55 years****(n=13)** |
| Given a higher risk result | Higher risk: desire for care | 7 | 5 |
|  | Higher risk: intending healthy lifestyle | 5/-2 | 5/-3 |
|  | Higher risk: child-related behavior | 6 | 2 |
|  | Higher risk: conscious living | - | 2 |
|  | Higher risk: responsibility | 4 | 2 |
|  | Higher risk: no response | 1 | 4 |
|  | Higher risk: support | 2 | 2 |
|  | Higher risk: test repetition | 3 | 2 |
|  | Higher risk: role of worry | 2 | 6/-2 |
| Given an average risk result | Average risk: intended behavioral change | 7 | 1 |
|  | Average risk: stable intention | 2 | 3 |
|  | Average risk: use of monitoring | 3/-1 | - |
|  | Average risk: evaluation | 7 | - |
|  | Average risk: reducing worry | 2 | 1 |
| Given a lower risk result | Lower risk: satisfaction | 3 | 5/-3 |
|  | Lower risk: less care desired | 2/-6 | 2/-3 |
|  | Lower risk: stable intention | 7 | 4 |

Negative numbers after “/” indicate women’s statements that rejected intended actions.