PROPHET
a PeRsOnalized Prevention roadmap
for the future HEalThcare

PROPHET FOR ALL - FACTSHEET#2

UNDERSTANDING CLINICAL UTILITY IN PERSONALIZED PREVENTION

WHAT IS "CLINICAL UTILITY"?

'Clinical utility' means how helpful a health test or practice is in improving patients' health or helping doctors make decisions. For tests that predict health issues, like genetic tests, clinical utility is about how useful the test is for the person to take action, such as starting prevention, changing lifestyle, undergoing closer monitoring, or receiving treatment. 'Clinical utility' has many meanings, depending on the situation. It's often connected to better health, but it's more than just how well a treatment works or whether a test works in a laboratory. It's about whether it makes a real difference in people's lives.

Clinical Utility covers ten areas, which are described by Erica Pitini, Medical Doctor at Sapienza University of Rome, and fellow researchers:

- **Analytic validity:** How well a test measures what it is supposed to measure.

For example: If a blood test is designed to measure cholesterol levels, it should give precise and consistent results each time it is repeated.

Clinical validity: How well a test can find or predict a health condition.

For example: If someone tests positive for a *BRCA* mutation, how strongly does that result actually predict a higher risk of breast or ovarian cancer?

Clinical efficacy: How much a test can improve symptoms, health, ability to function, quality of life, or survival rates.

For example: If knowing about a genetic risk leads to earlier and more frequent screening, and this allows cancer to be detected at an early stage, survival rates may improve.

Personal value: The benefits a person gets from knowing the test results.

For example: Someone who receives a negative genetic test result may feel relief and reduced anxiety. Another person who learns they are at higher risk may decide to adopt a healthier lifestyle, inform family members, or make reproductive choices based on that information. Even when there is no immediate cure, the information itself may have emotional, practical, or planning value.

Acceptability: How well a test meets the needs and expectations of patients and their families.

For example: A saliva-based genetic test may be more acceptable than an invasive procedure. People may also feel more comfortable if genetic counselling is provided to clearly explain the results and implications.

Feasibility: How practical it is to use the test and to overcome any challenges.

For example: If a test requires expensive equipment available only in major cities, it may be difficult to implement widely. If highly specialised professionals are required but scarce, this may limit access.

Equity: How fair a test is in the distribution of health for everyone.

For example: If a genetic test is only available privately and costs a lot of money, only wealthier individuals can benefit. A test has equitable utility when it is accessible regardless of income, education level, or place of residence.

Economic impact: The costs and financial benefits of the test.

For example: A genetic test may seem expensive upfront, but if it prevents advanced disease, major surgery, or long-term treatments, it may reduce overall healthcare costs in the long run.

Legitimacy: How well a test aligns with social values, ethics, norms, laws, and regulations.

For example: Is genetic data protected properly? Does the test comply with privacy regulations such as EU data protection laws?

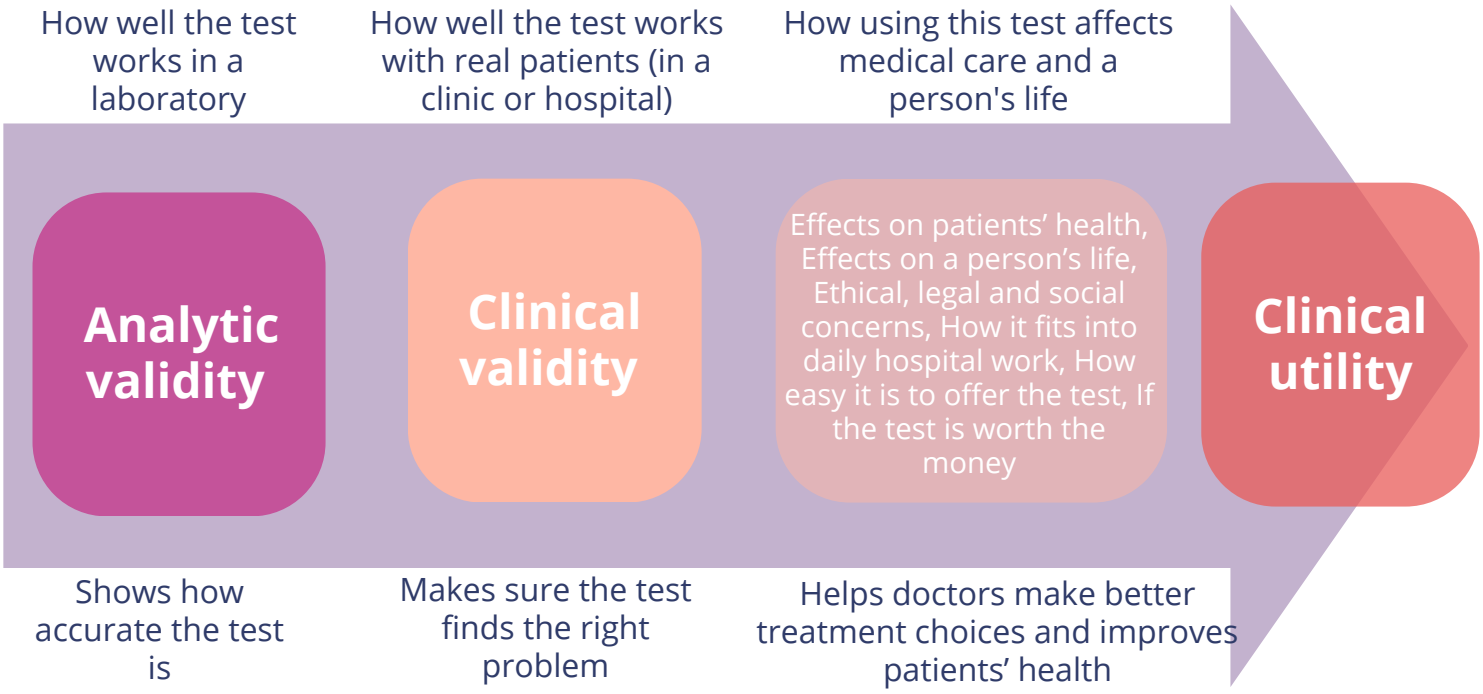
Context: Details about how the test is used, including: genetic variability (=differences in genes among different people), the health condition it targets, available treatment options, and recommendations to achieve the best outcomes.

For example: A genetic test may be highly useful for someone with a strong family history of cancer, but less useful for someone without any known risk factors.

WHAT DOES IT MEAN FOR A MEDICAL TEST TO HAVE 'CLINICAL UTILITY'?

To check if a genetic or medical test is useful, it must pass several tests. We first check its ability to accurately identify its intended purpose (**Analytic Validity**). Then, we check if it works well in a real hospital or clinic (**Clinical Validity**). Lastly, we look at wider use of a test for patient care like how easy it is to offer the test, if it is worth the money, if it is practical to use in daily hospital work, and if it's safe and effective.

The picture below shows this process from start to finish. This is how we check if a medical test is useful:



There are different ways to **prove** that a test is useful. Large studies called randomized controlled trials (RCTs) are often viewed as the best: one group receives the test or treatment, and another group does not, without persons knowing to which group they belong, to measure improvements. But these trials are not always possible, especially for rare diseases or long-term results. There are also other types of proof. This includes studies that show changes over time, tests for accuracy, computer model analyses, and expert opinions. Smaller studies or expert reports can help when clinical trials are not practical.

In the end, we decide if a test is useful by looking at many different factors, for example: personal experiences, and how many people had better results, and if the test helps doctors in decision-making, is easy to use and accepted in hospitals and clinics.

UNDERSTANDING HOW GENETICS HELPS PREVENT BREAST CANCER

BRCA Testing as an example

So-called *BRCA* tests check for mutations in the *BRCA1* and *BRCA2* genes. If someone has these mutations, they have a higher risk of getting breast or ovarian cancer. Knowing this can help make choices about prevention and treatment. BRCA testing is available in many countries.

For instance, a person with a known *BRCA* mutation might get screenings more often. They can also choose surgery to remove their breasts or take medicine to prevent cancer. These options are recommended by health experts worldwide.

This can help save many lives. So, understanding genetic risks is very important for breast and ovarian cancer prevention.

Breast cancer risk can come from a combination of factors: This includes when you began and stopped having periods. It also includes if you've had children and when. Your lifestyle choices, hormone levels, and genes matter too. The two genes *BRCA1* and *BRCA2* can sharply raise your life-time risk of breast and ovarian cancer if they have specific mutations.

Here's how *BRCA* testing meets the "clinical utility" standards:

- **Analytic validity:** Does it accurately find changes in *BRCA1/2* genes? Yes - the technology used for *BRCA* testing is very accurate.
- **Clinical validity:** Does having changes in *BRCA* genes mean you are more likely to get the disease? Yes - changes in *BRCA1/2* genes are strongly linked to a higher risk of getting breast cancer.
- **Clinical efficacy:** Does the test lead to effective ways to prevent or treat the disease? Yes - having surgery, taking specific medication (for instance Tamoxifen), or getting regular screenings (MRIs/mammograms) can help.
- **Personal value:** Does the information from the test help the person emotionally? Yes - many patients feel less worried after testing and feel more in control.
- **Acceptability:** Does the test match what patients want and value? Generally, yes - while some people may choose not to know or to avoid surgery, many people accept the test when they have received good genetic counseling.
- **Feasibility:** Can the test and follow-up actions be done in practice? Yes - *BRCA* testing is part of preventive care in many health systems, but there can be challenges with logistics and resources.

- **Equity:** Does the test make health differences between population groups better or worse? Mixed - the test is available in many places, but not everyone has equal access and especially ethic minorities or low-income groups may struggle to get it.
- **Economic Impact** Is the test affordable? Yes – Economic modelling shows that for instance in groups with a high risk, such as family members of a patient, adds value for money or saves costs.
- **Legitimacy** Does the test align with social values, ethics, norms, laws, and regulations? Yes – *BRCA* testing is regulated by national laws and European frameworks.
- **Context** Is the test part of a clear clinical pathway? Yes – *BRCA* testing is part of care pathways with follow-up, including surveillance, surgery, and chemoprevention.

WHY IS 'CLINICAL UTILITY' IMPORTANT FOR REAL-LIFE MEDICAL CARE & POLICYMAKING?

Doctors and health workers need clear proof and advice to help them decide if they should use genetic tests to prevent, find, or treat diseases. The goal is to use tests that make patients better and can be easily used in hospitals and clinics.

People who make policies also need strong proof of how useful these tests are. This helps them make good decisions about using the tests, paying for them, and regulating them.

Right now, we don't always have enough proof that some genetic tests help prevent diseases, but it is very important to have more proof. For instance, we may know the test identifies people at increased risk, but we may not always know if this would lead to better health for the whole population. It may take years to find out, or treatments may not be available. That is why we need clear definitions and evaluation frameworks to make sure everyone understands and agrees on how to use these tests. This helps doctors and people who decide on policies to make fair and transparent choices.

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