Polygenic scores for cancer

Chantal Babb de Villiers*[1], Sowmiya Moorthie[1, 2], Laura Blackburn[1], Mark Kroese[1]

[1]PHG Foundation, Cambridge, United Kingdom, [2]Cambridge Public Health, University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom

PHG FOUNDATION

making science work for health

Polygenic scores (PGS) could contribute significantly to the prevention, identification and management of cancer. There is substantial PGS research and development underway in a variety of cancers.
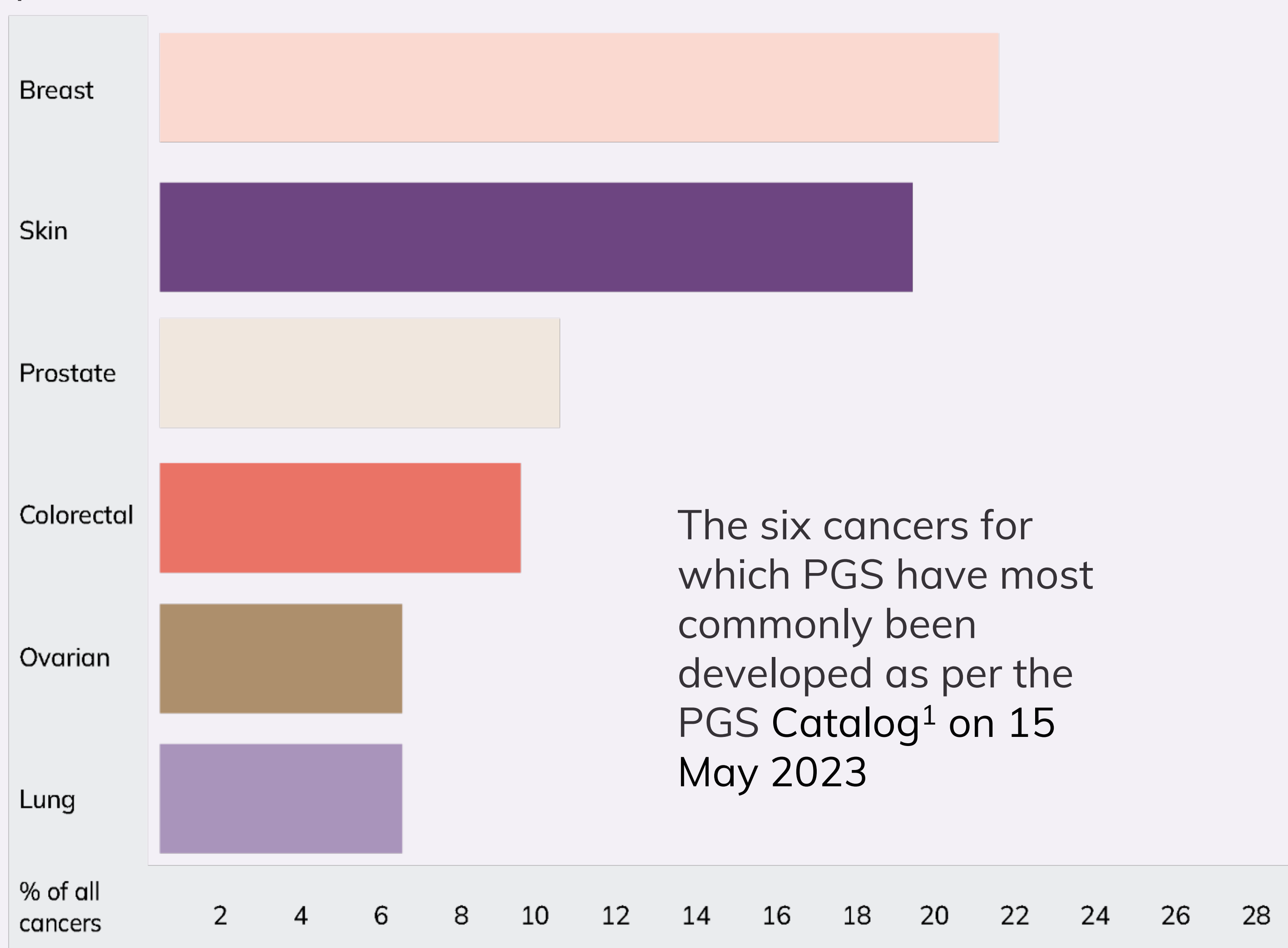
Methods

We reviewed the literature including grey literature, databases, and identifying ongoing clinical trials, then appraised the research and development of PGS based applications for cancer, their potential use in healthcare, and policy and implementation considerations.

Results

There is considerable research ongoing to determine if PGS can contribute to stratified screening strategies for cancer screening programmes, by improving their clinical effectiveness and efficiency.

Trials are underway to determine the role that stratified screening using comprehensive, integrated risk prediction models (that include PGS) could have in such programmes. PGS for rarer cancers are also being developed, including those with a limited number of known risk factors and biomarkers.

Whilst there are significant issues still to be addressed, such as generalisability, there are indications that PGS can improve risk prediction in some cancers and in some clinical contexts.

The six cancers for which PGS have most commonly been developed as per the PGS Catalog[1] on 15 May 2023

Conclusion

The development, validation and regulation of new tests, as well as infrastructure needs and evidence of clinical utility are required before implementation becomes possible.

PGS could have potential in specific contexts and for specific purposes but further sustained research and translation efforts are required to adequately assess their potential role in improving cancer prediction, prevention and management.

Contact: chantal.babbdevilliers@phgfoundation.org

Key points

- Cancer is a highly variable and complex disease, and each cancer has multiple factors – e.g. genetics, environment – that contribute to its development. The genetic component of different cancers, and their subtypes, varies.

- Between a third and a half of cancer cases could be prevented if current knowledge about risk factors was translated into effective public health actions.

- Comprehensive risk prediction models that bring together information across a diverse range of factors can inform prevention strategies. The extent to which such models are used in clinical practice varies.

- Polygenic scores are considered a measure of genetic contribution to the risk of developing cancer. They are now being considered as a factor for risk prediction which could be used independently or as part of risk prediction models for cancer.

- Polygenic scores can improve risk prediction in some cancers and in some clinical contexts, but the magnitude of the improvement varies between cancers and populations.

- Any use of polygenic scores in cancer management will be specific to the cancer and the clinical context. This is not a one size fits all solution.

- Wider implementation of risk prediction using polygenic scores requires sufficient understanding of how they will affect clinical care, as well as wider infrastructure considerations for delivery.

- Continued effort is needed to gather the appropriate evidence for evaluation and demonstration of utility that would support implementation efforts.

- Premature implementation of polygenic scores in cancer risk estimation approaches could undermine these efforts, and risk loss of confidence in this potentially valuable area of population health improvement.

Access our report on **Polygenic scores for cancer**[2] and related reports with the QR code.

References:
1. Lambert, S.A. et al. The Polygenic Score Catalog as an open database for reproducibility and systematic evaluation. Nat Genet 53, (2021). https://doi.org/10.1038/s41588-021-00783-5
2. Babb de Villiers C et al. Polygenic scores and clinical utility. PHG Foundation report (2022)

UNIVERSITY OF CAMBRIDGE

www.phgfoundation.org