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OBJECTIVE

Feasibility and cost-effectiveness of returning validated genetic cancer risk information to female sample donors

ANALYSIS

Cohort simulation of women 20-79 years old with mutations associated with breast and ovarian cancer: compare recall to no recall over lifetime horizon

KNOWLEDGE GAINED

Recall was cost-effective for women with *BRCA1* and *BRCA2* variants aged 20-79 years, and with *PALB2* variants aged 30-59 years. Inclusion of relatives improved the results further

KEY MESSAGE

Returning genomic information to sample donors resulted in noteworthy health gains and was feasible and cost-effective

Lifetime Cost-Effectiveness of Hereditary Breast and Ovarian Cancer Prevention based on FinnGen and Biobank Data, Data Returning Process, and Prophylaxis

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BACKGROUND

- Germline mutations in the *BReast CAncer gene 1 or 2* (*BRCA1* or *BRCA2*)[1] and *Partner And Localizer of BRCA2* (*PALB2*)[2] are associated with a high lifetime risk of hereditary breast and ovarian cancer (HBOC).
- The FinnGen biobank study has genotyped >500,000 individuals and returned this data to biobanks. We screened the genotypes for pathogenic variants in *BRCA1*, *BRCA2*, and *PALB2* genes, and verified the pathological findings by sequencing. Reporting this risk information to donors and health care could enable prophylactic interventions or intensified screening to reduce HBOC burden. (Figure 1)

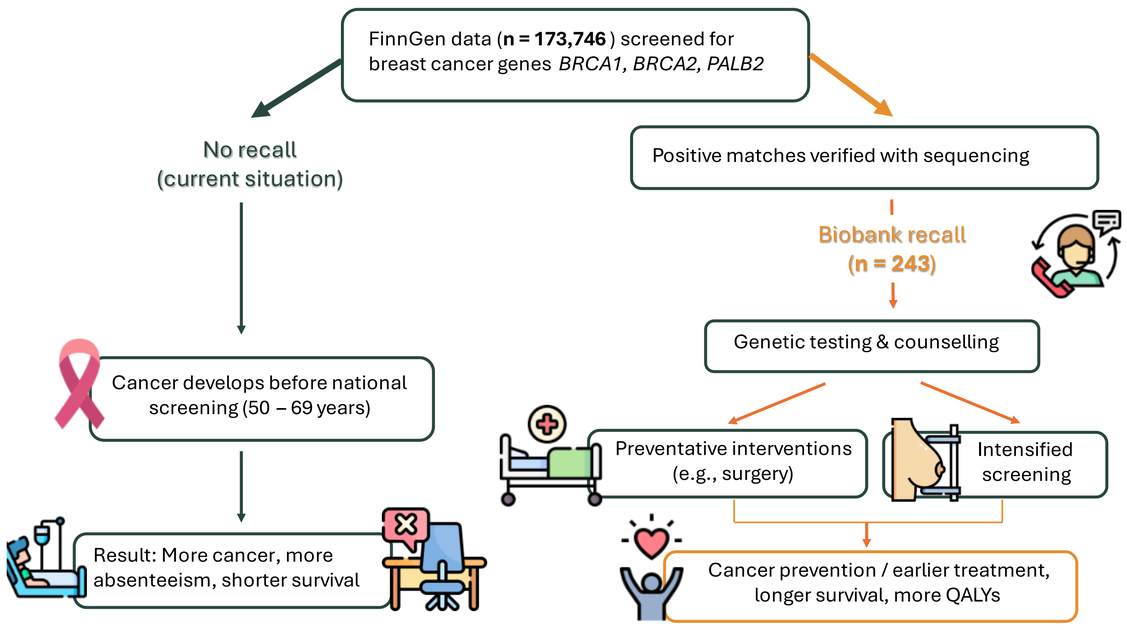

Figure 1. Comparison setting without and with the recall.

METHODS

The methods of the economic evaluation are summarized in the table below using the PICOSTEPS framework.[3]

COMPONENT	CONTENT
Patients	Women with germline mutations (*BRCA1/2*, *PALB2*) conferring **high risk of HBOC**, aged 20-79 years
Intervention	Recall by Helsinki Biobank, resulting in prophylactic interventions, intensified screening, or no change
Comparator	No recall
Outcomes	Number of HBOC cases, deaths due to HBOC, costs (euros in 2022), life-years (LY) and quality-adjusted life-years (QALY), and net monetary benefit (NMB) at a low prophylaxis willingness-to-pay (28,245 €/QALY gained)
Setting	**Cost-effectiveness** modelling using a cohort simulation model
Time	**Lifetime**. 3% per annum discounting for life-years, QALYs, and costs
Effects	Prophylactic bilateral mastectomy and risk-reducing bilateral salpingo-oophorectomy **reduce risk of HBOC**
Perspective	Finnish **societal perspective**
Sensitivity analyses	Type of mutation, age group, impact of relatives

CONCLUSIONS

- **Returning genomic information to sample donors with genetic counselling resulted in noteworthy health gains and was feasible and cost-effective. Inclusion of relatives further improved the results.**
- **Additional studies with men and clinical studies of patient decision making over time are warranted.**

ACKNOWLEDGEMENTS

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REFERENCES

1) *JAMA* 2017;317:2402–16. 2) *Nat Comms* 2020;11:6383. 3) *Clin Ther* 2017;39:537-57.

RESULTS

- FinnGen data freeze 7 consisted of 173,746 female donor samples, of which 243 individuals were estimated to proceed to recall.
- The recall resulted in an average additional lifetime cost of € 1,310/recalled woman (€ 1,418 result disclosure process, € 5,335 screening and prophylactic interventions, and € 5,443 cost offset for avoided HBOC treatments), Figure 2.

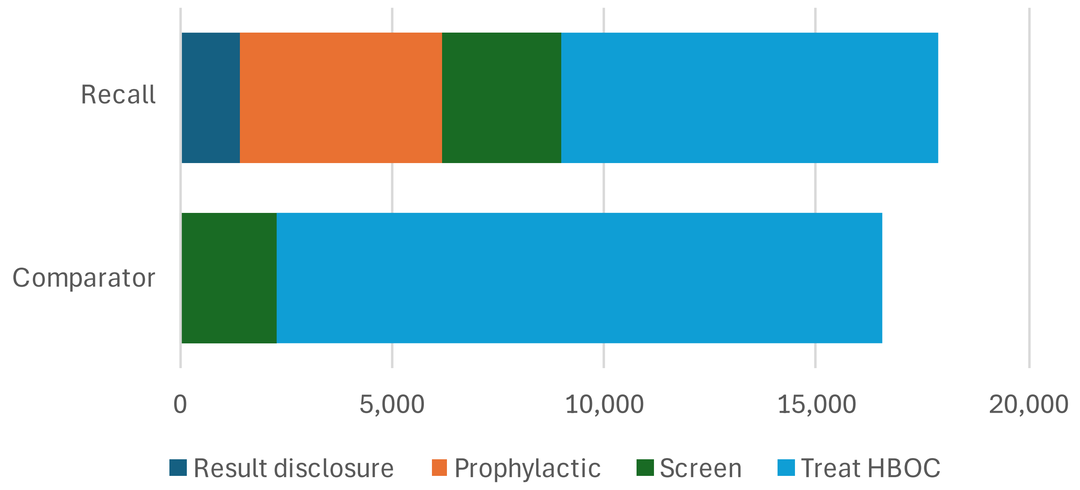

Figure 2. Expected discounted average lifetime costs (€) per patient.

- With the recall, 47 (40%) HBOC cases and 15 (40%) HBOC deaths could be avoided. This would generate 117 additional life-years and 59 additional QALYs, clearly favoring recall.
- NMB was positive for women with *BRCA1* and *BRCA2* aged 20-79 years, and with *PALB2* aged 30-59 years. (Figure 3)

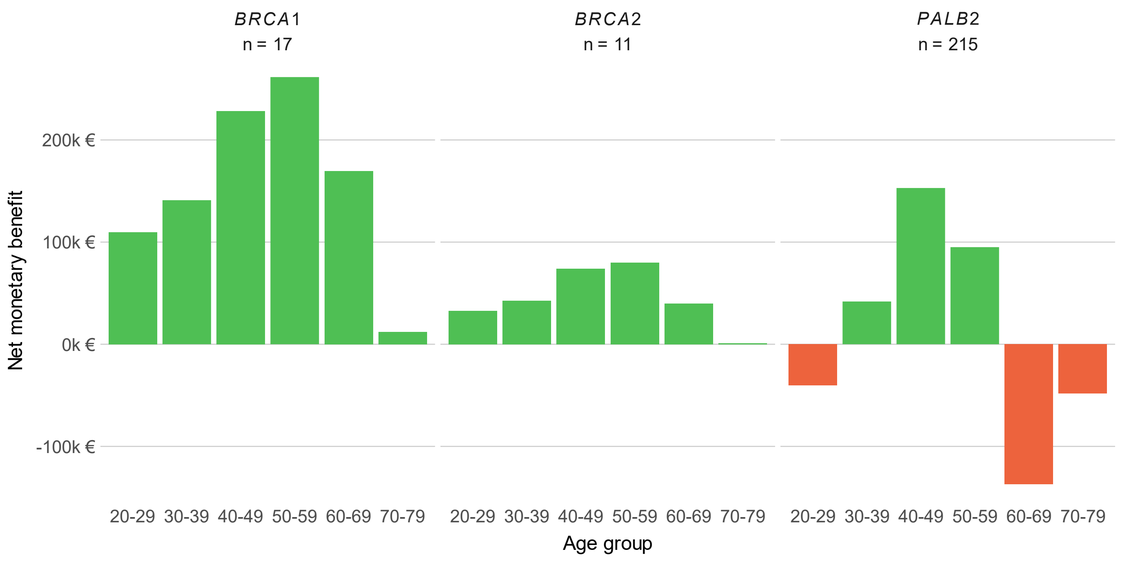

Figure 3. Expected discounted lifetime net monetary benefit by mutation and age.

- In sensitivity analysis, **first-degree relatives of the sample donors** agreeing to screening were included. 259 relatives with high risk of HBOC were identified:
  - The age distribution of relatives was assumed to match that of the sample donors, as no data were available from Finland.
  - Biobank costs do not apply to the identification of relatives, resulting in slightly better cost-effectiveness.
  - An additional 125 LYs and 63 QALYs can be gained in relatives, at a cost of € 1,107/identified relative.