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# Effects of polygenic risk score communication on short term health outcomes: systematic review and meta-analysis

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## ABSTRACT

**OBJECTIVE** To summarise the evidence so far from all randomised controlled trials on the efficacy of communication of polygenic risk scores in changing health outcomes.

**DESIGN** Systematic review and meta-analysis.

**DATA SOURCES** Cochrane Central Register of Controlled Trials (CENTRAL) and Pubmed, from inception to 1 March 2025.

**ELIGIBILITY CRITERIA FOR SELECTING STUDIES** Randomised controlled trials in human participants; articles published or accepted for publication in peer reviewed journals, or with available results on ClinicalTrials.gov, without time restriction in any language; and randomised controlled trials comparing the disclosure of inherited genetic risk obtained through the polygenic risk score for any phenotype (intervention group) with scenarios where no genetic information was provided (comparator group).

**RESULTS** Of 7830 articles retrieved, 27 randomised controlled trials were eligible for inclusion in the analysis. Polygenic risk scores mainly predicted risks for cancer (n=9 randomised controlled trials), cardiovascular diseases (n=8), and diabetes (n=6). 21 randomised controlled trials targeted mainly healthy populations, three targeted at-risk populations, and three trials targeted individuals who had already developed a disease and the polygenic risk score predicted complications. Most randomised controlled trials (15/27) concluded in their abstracts with favourable claims about the polygenic risk score, with only 5/15 trials justifying the score with any significant results. Nine of the 27 randomised controlled trials had a high risk of bias. Meta-analysis showed no significant effects on any of the 22 outcomes tested in two or more trials. Standardised mean differences for dietary outcomes were −0.11 (95% confidence interval (CI) −0.22 to 0.01) for daily energy intake, 0.03 (−0.18 to 0.25) for daily fat intake, and −0.11 (−0.28 to 0.06) for alcohol consumption. For physical activity, standardised mean difference was −0.01 (95% CI −0.13 to 0.11). Relative risks were 1.12 (95% CI 0.77 to 1.61) for screening attendance, 1.50 (0.98 to 2.29) for use of statins, and 0.95 (0.32 to 2.79) for incidence of disease. For psychological outcomes, standardised mean differences were −0.02 (95% CI −0.13 to 0.08) for anxiety, −0.06 (−0.23 to 0.10) for worry, −0.04 (−0.21 to 0.13) for perceived risk, and −0.05 (−0.23 to 0.13) for depression. For clinical outcomes, mean differences were −2.01 (95% CI −8.27 to 4.26) for total cholesterol, −3.64 (−7.88 to 0.60) for low density lipoprotein cholesterol, −0.21 (−2.65 to 2.23) for high density lipoprotein cholesterol, −1.88 (−4.17 to 0.42) for diastolic blood pressure, −1.26 (−4.44 to 1.92) for systolic blood pressure, −0.12 (−0.63 to 0.39) for body mass index, and −0.33 (−0.87 to 0.20) for weight. 80 outcomes were reported across multiple studies, with each outcome reported in a single trial only. 19 of 80 were primary outcomes, and of these two had significant results (P<0.05), as did three secondary outcomes.

**CONCLUSIONS** Overall, despite frequent promising claims, disclosure of polygenic risk scores did not result in meaningful changes in behavioural, psychological, or clinical measures for the outcomes examined. Although when interpreting the findings the heterogeneity and methodological limitations of the available trials should be considered, communication of polygenic risk scores did not

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Polygenic risk scores represent one of the most promising approaches of personalised medicine, where communication of genetic information is expected to improve behaviour and health outcomes

⇒ Previous reviews have evaluated the communication of genetic risk but none has evaluated the effect of disclosure of polygenic risk scores specifically

⇒ Because implementation of polygenic risk scores in clinical practice is being considered, rigorous evaluation of their impact is valuable for further implementation

## WHAT THIS STUDY ADDS

⇒ Polygenic risk score communication effects were close to the null for a large number of outcomes, showing no detectable improvement in preventive behaviours, including screening adherence or clinical measures

⇒ High heterogeneity was found in randomised controlled trials, with small sample sizes, short follow-up periods, and many self-reported outcomes

⇒ A gap was evident between the theoretical promise of polygenic risk score guided prevention and its lack of documented real world effectiveness

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ Based on the current evidence, disclosure of polygenic risk scores should not be assumed to produce meaningful behavioural or clinical changes in preventive settings

⇒ Research should explicitly evaluate whether, and in which contexts, polygenic risk scores provide added value beyond non-genetic risk factors

⇒ Better designed randomised controlled trials should be conducted to overcome the limitations of the current randomised controlled trials and further evaluate disclosure of polygenic risk scores

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show consistent improvements in preventive behaviours or risk factor modification.

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## Introduction

Personalised medicine based on genetic and genomic information has long promised a revolution in the prevention, diagnosis, and treatment of diseases.[1 2] Major advancements have occurred in genomic based testing on cancer tissue for guiding treatment[3 4] and in genetic testing applications for diagnosing rare diseases,[5 6] but genomic testing applications for prevention of common, multigenetic diseases are limited. Although guidelines that use genetic testing to prevent and risk stratify hereditary cancers and cardiovascular diseases have existed for decades,[7 8] the application of sophisticated algorithms that combine the effects of low to moderate penetrance genetic variants is still in the early stages, largely because of the lack of robust evidence on clinical use.[9 10]

Many studies have examined the relation between genetic variants and specific traits, such as diseases and specific conditions. Genome-wide assessments have detected large numbers of single nucleotide polymorphisms that occur more frequently in affected individuals, providing insights into genetic risk factors. Weighted sums, calculated from the identified single nucleotide polymorphisms, are usually referred to as polygenic risk scores (also known as genetic risk scores or polygenic scores).[11 12] These scores, which quantify an individual's genetic predisposition to a disease, are often presented as promising tools for personalised medicine, given their potential in the prediction of the risk of disease.[12 13]

Polygenic risk scores could identify high risk individuals who, in principle, could be targeted through personalised preventive strategies. Because polygenic risk scores can be constructed with a range of common genetic variants, from a large number, as in a genome-wide polygenic risk score, to only a few single nucleotide polymorphisms, known as a restricted polygenic risk score, their classification varies widely in the current literature.[14 15]

Several systematic reviews and meta-analyses have previously synthesised data from randomised controlled trials comparing groups who received and did not receive information on genetic risk.[16–20] These studies examined various outcomes, including smoking cessation, healthier dietary habits, increased physical activity, and changes in cholesterol levels or other risk factors for disease. Findings have been inconclusive, however, and each review included only 10 unique randomised controlled trials that used polygenic risk score genetic information that extended beyond one single nucleotide polymorphism or non-pathogenic variant.

In recent years, several randomised controlled trials have explored the effect of communication of polygenic risk scores on diverse outcomes, ranging from lifestyle changes to adherence to screening protocols. Moreover, more comprehensive polygenic risk scores have been used in recent trials and a wider range of polygenic risk scores have been assessed. The aim of this systematic review and meta-analysis was to summarise the evidence from all randomised controlled trials published so far on the efficacy of communication of polygenic risk scores in changing health behaviours, adherence to treatment, and psychological and clinical outcomes.

## Methods

We previously registered the protocol for this systematic review and meta-analysis on OpenScienceFramework.[21] This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.[22]

### Definitions

The National Cancer Institute defines polygenic risk scores as an assessment of the risk for a specific condition based on the cumulative influence of multiple genetic variants.[23–26] These scores are calculated by aggregating and quantifying the effects of common genetic variants, typically single nucleotide polymorphisms (ie, variations at a single base pair within the genome), classified as minor alleles with a frequency > 1%. Individually, these variants have small effects, but when combined can contribute to the overall risk score. The resulting polygenic risk score generally follows a normal distribution within the population, where higher scores indicate a greater risk of developing the condition. Single nucleotide polymorphisms included in a polygenic risk score can range widely, depending on the methodology used and the variants selection, from only a few to thousands.

### Search strategy

We conducted a preliminary search of Pubmed and Scopus to identify relevant keywords and previous systematic reviews on the same theme. We then used the terms identified during this process to build our search strategy. Firstly, we attempted to update previous systematic reviews by reusing their search strategies. Re-running the search strings from Horne et al,[19] from 2017 to the present, however, gave >70 000 results. Similarly, the search string used by Hollands et al,[18] restricted to records from 2016 onwards, returned 21 324 results only in Medline. Because of the large number of results in the literature, we decided that applying the previous search strategies was not efficient. Hence we extracted all of the unique trials in the systematic reviews previously identified during the preliminary search[16–20] and built our own search string from these terms:

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(polygenic*):ti OR (genetic*):ti OR (genomic*):ti OR (genotype-based*):ti.

This string, when applied to Pubmed with the filter for clinical trials and randomised controlled trials, identified 35 of 37 trials included in the previous systematic reviews, and review of the references of these 35 studies identified the other two missing trials. The string also captured all 10 unique trials that had been included in at least one previous systematic review dealing with polygenic risk scores that were eligible for our protocol. This string was then applied to identify articles in Pubmed, with the filters for randomised controlled trials and clinical trials, and in the Cochrane Central Register of Controlled Trials (CENTRAL), without restrictions on the publication year. Furthermore, we searched on ClinicalTrials.gov with the term combinations "Polygenic Risk Score" OR "polygenic score" OR "genetic risk score" OR "genetic score."

We retrieved articles up to 1 March 2025. We also examined the references of the retrieved eligible articles for any additional relevant randomised controlled trials. We searched ClinicalTrials.gov for each of the included randomised controlled trials for available study results.

### Study eligibility and selection

We evaluated each article against all of our eligibility criteria: randomised controlled trials in human participants; articles published or accepted for publication (ie, in press) in peer reviewed journals, or with available results on ClinicalTrials.gov, without time restriction in any language; and randomised controlled trials comparing the disclosure of inherited genetic risk obtained through the polygenic risk score for any phenotype (intervention group) with scenarios where no genetic information was provided (comparator group). Quasi randomised clinical trials, cluster randomised clinical trials, and all non-randomised studies were excluded. Studies focusing on highly penetrant genes or monogenic disorders, such as *BRCA1/2* mutations, were also excluded. We included all studies that defined a polygenic risk score as above, even if not explicitly referred to as a polygenic risk score (eg, genetic risk score, genetic score, or polygenic score). At least two single nucleotide polymorphisms were needed to classify a score as a polygenic risk score.

### Study selection

We uploaded the identified articles to the Rayyan platform, a software for systematic reviews. After deduplication, four reviewers (LR, AA, SF, and AC) screened the titles and abstracts and reviewed the full text, with each record assessed by two independent reviewers. Any discrepancies were dealt with by consensus or with a third reviewer. Articles that met the eligibility criteria were included in our systematic review. For included studies that did not report results (eg, abstracts or protocols), we contacted the study authors and principal investigators requesting data, if available.

### Data extraction

Three reviewers (LR, AC, and NL) independently extracted the data. Data extracted from each included study were: title, first author, doi (digital object identifier), name of journal, year of publication, country, eligibility criteria, personal characteristics of participants, study design, number of arms, type of information for each arm, number of participants in each arm, possible phenotypes predicted by the polygenic risk score, number of single nucleotide polymorphisms, risk of developing the phenotypes, target population of the intervention (eg, healthy or at risk), and outcomes of the study.

For each study, we extracted these outcomes: behavioural changes (ie, dietary behaviour, physical activity, smoking, alcohol consumption, attendance for medical visits, such as check-ups, cancer screenings, and follow-up visits, undergoing risk reducing surgery, or other behaviours aimed at reducing the risk of disease), adherence to treatment, incidence of the disease provided in the genetic information, quality of life, psychological effects (eg, depression, anxiety, emotional distress, worry, perceived efficacy, perceived risk, or other measured psychological change), incidence of other diseases (other than the disease linked to the genetic risk score), and any other measurable health outcome or result of the trial.

For each outcome, we extracted the measurement and the method used. When an outcome was measured subjectively, we referred to the self-reported data from the patient. For an objective measurement, we referred to the data obtained from tests, analyses, or medical evaluations. Although not prespecified in the protocol, we conducted a post hoc data extraction from the registry where the included randomised controlled trials were registered (eg, ClinicalTrials.gov, UMIN-CTR, or ISRCTN). For each trial, we collected information on the primary and secondary outcomes reported, and any available results. We also extracted the conclusions stated in the abstract and assessed whether, and how, the results of the studies supported these conclusions.

### Screening and data extraction validation with otto-SR

As an additional validation step, we used an artificial intelligence platform, otto-SR,[27] to validate the retrieval of eligible articles and the correctness of the data extraction. otto-SR is a large language model based tool for automated screening and data extraction that was developed after our protocol had been posted. For the screening phase, otto-SR screened

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the search results from Pubmed and CENTRAL but not from ClinicalTrials.gov. The outputs generated by otto-SR were compared with those obtained by human reviewers, and concordance was calculated as the proportion of full text articles correctly identified by both approaches over the total number of studies included in the review. Discrepancies were classified as inclusion errors (articles included by otto-SR but not by the reviewers) or exclusion errors (articles missed by otto-SR but included by the reviewers). For the data extraction phase, the information independently extracted by otto-SR and the reviewers was compared across all predefined data fields. Concordance was defined as identical extraction between the two approaches. Discrepancies were categorised as extraction errors by otto-SR or by the reviewers, and overall concordance rates and error proportions were calculated for each dataset.

### Risk of bias assessment

Three authors (LR, SF, and AP) assessed the risk of bias of the included studies with the revised Cochrane risk-of-bias tool for randomised trials (RoB 2),[28] independently of each other, with each study assessed twice.

### Statistical analysis

The general characteristics of the studies are reported. For the quantitative analyses of the study results, we reported outcomes as mean (standard deviation (SD)) for continuous outcomes. We conducted a meta-analysis for studies that reported outcome measures at both the start and end of the trial, or the difference in value, allowing for a consistent quantitative comparison across studies in terms of outcome measures and reported data. If studies only provided the final value, the meta-analysis was conducted on the final difference between arms. To compare the control group (inherited polygenic risk score not disclosed to participants) and the polygenic risk score group (polygenic risk score disclosed to participants), we used the mean difference for continuous outcomes measured with the same method and unit across studies. When necessary, units were harmonised by appropriate conversion factors (eg, converting low density lipoprotein cholesterol, high density lipoprotein cholesterol, and total cholesterol from mmol/L to mg/dL, and weight from pounds to kilograms). When outcomes were assessed with different measurement methods or scales across studies that could not be similarly converted to the same units, we used the standardised mean difference, calculated with Hedges' method.[29] For binary outcomes, we used relative risk as the effect size, comparing groups at the end of the study. All effect sizes were reported with 95% confidence intervals (CIs).

We also conducted various sensitivity analyses, including a meta-analysis of final values restricted to studies reporting both baseline and final values, a meta-analysis of final values including only studies without baseline data, an analysis limited to randomised controlled trials with a low risk of bias, and an analysis restricted to studies conducted in healthy participants.

We used the group mean and SD of the change between baseline and the end of the study if a trial directly provided these values. Otherwise, we calculated the group mean difference and derived the SD by multiplying the standard error of the mean difference by the square root of the sample size (N), with $SD=SE \times \sqrt{N}$. When separate data for two groups within the same study arm (eg, low risk and high risk) were available but pooled data were required, we estimated the pooled mean and pooled SD or the pooled number of events, depending on the type of outcome. The pooled mean was calculated as the weighted average of group means based on their sample sizes. The pooled SD was derived from the standard formula for combining SD values of independent groups, weighted by their respective sample sizes. SD pooled = $\sqrt{((N1-1) \times SD1^2 + (N2-1) \times SD2^2)/(N1+N2-2)}$, where SD1 and SD2 are the SD values of the two groups, and N1 and N2 are their respective sample sizes.

When outcomes were reported as minimum, maximum, median, and first and third quartiles, we estimated the mean with the method of Luo et al[30] and SD with the method of Shi et al.[31] Before applying these estimations, we verified whether the data were significantly skewed from normality with the formula described by Shi et al.[32] If skewness was detected, we applied a logarithmic transformation to the summary data. After confirming that the transformed data were approximately normally distributed, we estimated the mean and SD on the log transformed scale and subsequently back transformed the results to the original scale. For binary outcomes, the pooled number of events was calculated as the sum of events across both groups (E pooled=E1+E2), and the pooled event rate was computed by dividing the total number of events by the total number of participants (E1+E2)/(N1+N2).

Mean difference was calculated for all outcomes; those with data from only one study were reported descriptively, whereas for outcomes with data from at least two studies, we conducted a meta-analysis. We combined studies with the inverse variance weighted method and used both fixed and random effect models.[33] We used the restricted maximum likelihood estimator to estimate variance between studies.[33] We tested for heterogeneity with Cochran's Q test and quantified heterogeneity with the $I^2$ statistic, interpreting values <50% as low, 50-75% as moderate, and >75%[34] as high heterogeneity. We created forest plots for graphical presentation of the data, including the point estimate, 95% CI, and study descriptors (first author and year of publication). We performed all statistical data analyses with R version 4.4.0 (24 April 2024) for Windows and used the meta package for the meta-analyses.

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### Patient and public involvement

Involving patients or the public in the design, conduct, and reporting of our research was not appropriate or possible. We plan to disseminate our findings to the public, patients, and clinical organisations through various ways, including social media, plain language summaries, and conference presentations. The findings will be communicated in accessible, non-technical language to ensure understanding among general audiences.

## Results

We retrieved 7830 articles and after deduplication, 5971 articles were assessed. After screening titles and abstracts, 204 articles were sought for retrieval. For 21 reports on protocols or registrations of unique randomised controlled trials, we contacted the principal investigators of these included eligible protocols, but only six replied. Five principal investigators responded that the data were not yet available because the study was still in the enrolment phase, and one responded that the article was submitted to a scientific journal but declined to share the results before publication. The remaining 15 authors did not respond. A total of 183 articles were assessed for full text review, and we included 33 reports[35–67] of 27 unique randomised controlled trials in the analysis.[37 42–67] Two more articles[68 69] were manually retrieved from the citations of an included randomised controlled trial, with a total of 35 articles included in the systematic review. We excluded 150 studies for various reasons: 12 studies were a secondary analysis of the included studies that did not provide any additional outcomes; 52 studies did not follow a randomised controlled trial design; in 22 studies, polygenic risk score disclosure was not randomised among participants; 30 studies focused on genetic testing of one gene pathogenetic (non-common) variant rather than polygenic risk scores; 13 studies used information from only one common single nucleotide polymorphism; and 21 were protocols of the included studies (figure 1).

### Validation of otto-SR

After reproducing the screening and extraction phases with the otto-SR outputs, we found a high degree of comparability between the results obtained by human reviewers and those generated by the large language model. For the screening phase, otto-SR identified 67 potentially eligible full text articles. Four studies were not retrievable by otto-SR; these studies had been identified through hand search of the main paper, starting from secondary publications included in the search string,[37 38 54] citation search,[68 69] and by screening of ClinicalTrials.gov.[49] Therefore, the total number of eligible and retrievable reports for assessment was 29. Of the 29 eligible reports, otto-SR correctly included 27 reports (93.1% sensitivity) and the reviewers correctly included 28 reports (96.5% sensitivity). Two articles[44 51] were incorrectly excluded by otto-SR because of misinterpretation of the ≥2 single nucleotide polymorphism threshold for polygenic risk score classification. One article[56] was incorrectly excluded by the reviewers but was captured by the otto-SR system. Of the remaining 40 records included by otto-SR, 36 were secondary analyses without outcomes, potentially eligible congress abstracts missing key information for inclusion, protocols of included trials, or protocols where we contacted the principal investigators. Thus otto-SR misclassified six articles (99.9% specificity) as eligible (false positive).

For the extraction of individual study data and general characteristics, 270 fields were analysed. Of these, 249 were correctly extracted by both the human reviewers and otto-SR, corresponding to a concordance of 92.2%. Among the remaining discrepancies, five fields (1.9%) were extracted incorrectly by the reviewers and 16 (5.9%) by otto-SR. For numerical outcome data extraction, 1415 fields were examined. otto-SR achieved a concordance of 98.6%, with 16 fields (1.1%) extracted incorrectly compared with four (0.3%) by the reviewers.

### Characteristics of the studies

Table 1 presents the characteristics of the 27 included randomised controlled trials. Median sample size was 207 (range 67-3177) participants. Most studies were conducted after 2017 (n=17 studies), with half conducted in the US (n=11), followed by Europe (n=5) and the UK (n=3). The median follow-up time of participants was six months (range 1-12 months). Twenty four studies were registered on a registry, with 17 on ClinicalTrials.gov and seven on other registries (eg, ISRCTN or ACTRN).

For the phenotypes predicted by the polygenic risk score, cancers (n=9) and cardiovascular diseases (n=8) were the most common, followed by diabetes (n=6). In two studies, the polygenic risk score predicted both diabetes and cardiovascular diseases. Other predicted phenotypes included metabolic alteration (n=4), including high body mass index and abnormal lipid profile, metabolic responses, obesity related response, and alcohol metabolism. One study predicted the development of renal complications of diabetes. Among cancer related studies, melanoma (n=5) was the most frequently investigated.

Twenty four studies focused on healthy (n=21) or at-risk (n=3) populations, whereas three studies targeted individuals who had already developed a disease. In these three studies,[46 48 59 68 69] the polygenic risk score was used to predict disease complications. Specifically, in Ma et al,[59] the polygenic risk score predicted the risk of developing complications related to diabetes, particularly kidney disease. In the study of Doménech et al,[46] the score predicted the risk of cardiovascular disease in patients who already had a diagnosis of hypertension, and in the

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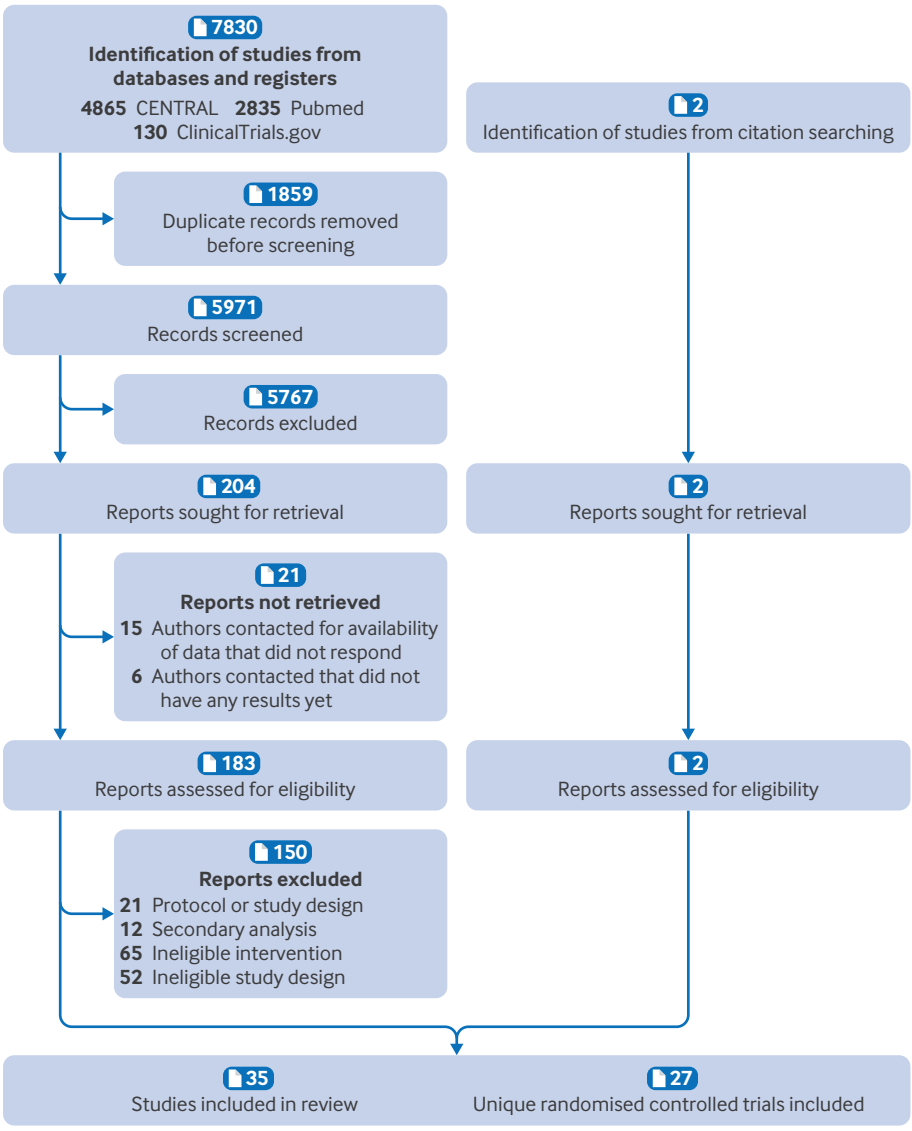



**Figure 1 | Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the study search and selection process**

study of Horne et al,[48 68 69] the score predicted the response to weight loss and physical activity in individuals with obesity. Online supplemental table 1 shows the outcomes included in each study.

Table 2 reports the details of the interventions and outcomes of the randomised controlled trials. Twenty one studies were two arm randomised controlled trials (77.8%), and the remaining studies were three (n=1) or four (n=5) arm trials, including comparisons with other estimated phenotypic risk or other information, such as web based advice. The studies evaluated interventions involving the communication of polygenic risk score, either alone (n=3) or combined with additional or combined strategies, including personalised booklets or educational materials (n=7), genetic counselling (n=5), lifestyle advice (n=2), or behavioural programmes, such as stopping smoking or preventing diabetes (n=2). Specifically, the behavioural programmes were also given to the control arm. The information in the control arms was usually traditional risk assessment (n=7), standard of care (n=12), or no information or intervention (n=4). In six of the two arm randomised controlled trials, the intervention group was further classified into intervention low risk and high risk groups.

### Risk of bias evaluation

Figure 2 shows the results of the risk of bias evaluations. Overall, nine studies (33.3%) were assessed as having a high risk for overall bias, 11 (40.7%) raised some concerns, and seven (25.9%) were at low risk. Missing outcome data was the most frequent domain contributing to a high risk of bias.

### Outcomes with meta-analysis

Table 3 reports the results of the meta-analysis for 22 outcomes; forest plots are available in the online supplemental material. In the meta-analyses,

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**Table 1 | Characteristics of the 27 randomised controlled trials included in the systematic review**

| First author and publication year | Country | Registration No | Possible phenotype predicted by polygenic risk score | No of single nucleotide polymorphisms | Target population | Follow-up time (months) | Sample size | No of women (%); mean (SD) age (years) |
|---|---|---|---|---|---|---|---|---|
| Halmesvaara 2025[54] Halmesvaara 2022[35] | Finland | NR | Diabetes and coronary heart disease | GWAS polygenic risk score (7 million variants for type 2 diabetes and 6.6 million variants for coronary heart disease) | Healthy | 3 | 3177 | 56.0; 55.1 (15.4) |
| Owaki 2024[56] | Japan | UMIN000044148 | Alcohol metabolism alterations and alcohol use disorder | 2 | Healthy | 6 | 196 | 56.6; 22.6 (NA) |
| Wu 2023[53] | USA | NCT03979872 | Skin cancer | 7 | Healthy | 1 | 92 | 70.7; 22.4 (5.3) |
| Lee 2023[57] | Korea | KCT0004650 | High body mass index and abnormal lipid profile | 14 | Healthy | 6 | 100 | 50.0; 28.1 (2.1) |
| Wolever 2022[52] | USA | NCT01884545 | Diabetes and coronary heart disease | 4 | Healthy and at risk | 12 | 200 | 49.0; 47.7 (11.6) |
| Viigimaa 2022[58] | Estonia | NCT04291157 | Cardiovascular diseases | GWAS polygenic risk score (49 000 variants) | Healthy | 12 | 1018 | 62.2; 52.2 (9.8) |
| Ma 2022[59] | Hong Kong | NCT02364323 | Renal complications of diabetes | 5 | Non-healthy (diabetes) | 12 | 420 | 49.4; 59.3 (7.8) |
| Lacson 2022[51] | USA | NCT03509467 | Melanoma | 47 | Healthy | 9 | 920 | 70.8; 46.1 (15.4) |
| Watanabe 2021[50] | Japan | UMIN000031709 | Breast and cervical cancer | 4 | Healthy | 12 | 144 | 100; 47.3 (1.49) |
| Smit 2021[62] | Australia | ACTRN 12617000691347 | Melanoma | 40 | Healthy | 12 | 1025 | 51.0; 46.9 (14.6) |
| Lacson 2021[49] | USA | NCT03509467 | Melanoma | 38 | Healthy | 12 | 1134 | 50.4; 48.1 (15.9) |
| Horne 2020[48] Horne 2020[68] Horne 2020[69] | Canada | NCT03015012 | Obesity related response | 6 | Non-healthy (obesity) | 12 | 140 | 87.1; 55.0 (12.9) |
| Silarova 2019[61] | UK | ISRCTN17721237 | Coronary heart disease | 46 | Healthy | 3 | 956 | 44.3; 56.6 (8.9) |
| Wu 2017[47] | USA | NCT00849563 | Diabetes | 4 | Healthy | 12 | 391 | 69.6; 50.1 (13.2) |
| Knowles 2017[55] | USA | NCT01406808 | Coronary heart disease | 19 | Healthy | 6 | 94 | 42.6; 57.5 (9.1) |
| Smit 2017[60] | Australia | ACTRN 12615000356561 | Melanoma | 42 | Healthy | 3 | 118 | 50.0; 53.0 (13.6) |
| Nichols 2018[63] | UK | NCT01176383 | Lung cancer | 20 | Healthy | 6 | 127 | 54.5; 49.4 (NA) |
| Kullo 2016[64] Naderian 2025[41] | USA | NCT01936675 | Coronary heart disease | 28 | Healthy | 6 | 207 | 52.2; 59.4 (5.1) |
| Doménech 2016[46] | Spain | NR | Coronary heart disease | 9 | Non-healthy (hypertension) | 4 | 67 | 25.4; 54.6 (9.3) |
| Livingstone 2016[37] Celis-Morales 2017[38] | 7 European countries | NCT01530139 | High body mass index, weight, and waist circumference, and metabolic responses (omega 3, fat, and folate) | 5 | Healthy | 6 | 1540 | 58.5; 39.9 (13.0) |
| Turner 2016[65] | USA | NCT02381015 | Prostate cancer | 46 | Healthy and at risk | 3 | 700 | 0; 44.9 (2.9) |
| Godino 2016[66] | UK | ISRCTN 09650496 | Diabetes | 23 | Healthy | 2 | 569 | 52.9; 48.7 (7.3) |

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**Table 1** Continued

| First author and publication year | Country | Registration No | Possible phenotype predicted by polygenic risk score | No of single nucleotide polymorphisms | Target population | Follow-up time (months) | Sample size | No of women (%); mean (SD) age (years) |
|---|---|---|---|---|---|---|---|---|
| Voils 2015[45]<br>McVay 2015[36]<br>Raghavan 2020[40] | USA | NCT01060540 | Diabetes | 3 | Healthy | 6 | 601 | 19.6; 54.1 (8.7) |
| Hietaranta-Luoma 2015[44] | Finland | NR | Cardiovascular disease | 2 | Healthy | 12 | 113 | 69.2; 47.0 (12.1) |
| Weinberg 2014[43] | USA | NCT00087360 | Colorectal cancer | 2 | Healthy and at risk | 6 | 783 | 58.6; 58.4 (7.3) |
| Nielsen 2014[42] | Canada | NCT01353014 | Metabolic responses | 5 | Healthy | 12 | 138 | 76.8; 26.7 (3.0) |
| Grant 2013[67]<br>Vassy 2018[39] | USA | NCT01034319 | Diabetes | 36 | Healthy | 3 | 177 | 40.5; 58.7 (10.5) |

GWAS, genome wide association study; NA, not available; NR, not reported; SD, standard deviation.

we found no significant effects for the outcomes assessed. Outcomes included lipids, weight, blood pressure, physical activity, dietary and sun related behaviours, and clinical and psychological outcomes. Moreover, the point estimates were close to the null, with standardised mean difference estimates ranging from −0.11 to 0.04, relative risk estimates ranging from 0.95 to 1.5, and relatively small mean differences in lipid, weight, and blood pressure outcomes. Meta-analyses of the final value and the sensitivity analyses did not show any major modifications (online supplemental tables 2–6). Online supplemental material has the meta-analysed forest plots of the final values.

### Narrative description of outcomes reported in single studies

Online supplemental table 7 reports the analysis for 80 outcomes across multiple studies, with each outcome reported only once. Of these, 19 were presented as primary outcomes in the respective randomised controlled trials, and the remainder as secondary outcomes. For the 19 primary outcomes, two reported a significant change. Ma et al[59] reported a moderate improvement for the only primary outcome, change in composite treatment target score for diabetes (relative risk 0.84, 95% CI 0.70 to 0.99). This score was a composite endpoint, defined as the proportions of patients attaining ≥3 of five predefined treatment targets: blood pressure <130/80 mm Hg; haemoglobin $A_{1c}$ <7%; low density lipoprotein cholesterol <2.6 mmol/L; fasting triglyceride concentration <2.0 mmol/L; and use of renin-angiotensin system inhibitors for renoprotection. Livingstone et al[37] found a small improvement for the primary outcome, change in MedDiet score (mean difference 0.24, 95% CI 0.08 to 0.39), defined as adherence to a Mediterranean diet.

Among the 61 secondary outcomes analysed, only three results were significant.[53 60] Smit et al[60] reported an increased confidence in identifying melanoma, measured with the question "How confident are you in your ability to identify melanoma? (from 1=not at all to 5=very)," with a mean difference of 0.40 (95% CI 0.10 to 0.69). Wu Y et al[53] found a decrease in reported sunburn occurrence in the past month, assessed with an item from the Sun Habits Survey (from 0 times to five or more times) over the past month (mean difference −0.81, 95% CI −1.57 to −0.05). Also, Horne et al[68] found an improvement in saturated fat consumption, with a target of <10% of calories (relative risk 2.03, 95% CI 1.05 to 3.92). No significant results were reported for any of the other outcomes.

### Consistency between conclusions in articles and reported results

Among the 27 randomised controlled trials, 15 concluded in favour of the genetic intervention, five

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**Table 2 | Intervention and outcome characteristics of the 27 randomised controlled trials included in the systematic review**

| First author and publication year | No of arms | Intervention arm | Control arm | Primary outcomes |
|---|---|---|---|---|
| Halmesvaara 2025[54] Halmesvaara 2022[35] | 2 | Polygenic risk score communication, risk of developing type 2 diabetes or coronary heart disease (next 10 years) and traditional risk factors | Risk of developing type 2 diabetes or coronary heart disease (next 10 years) and traditional risk factors | Physical activity (MET minutes), alcohol consumption, vegetable and fruit consumption, seeking medical treatment or examination |
| Owaki 2024[56] | 2 | Polygenic risk score communication with conventional educational materials | Conventional educational materials | Change in daily alcohol consumption |
| Wu 2023[53] | 4 | Education with polygenic risk score | 1. Education only<br>2. Education+ultraviolet photo;<br>3. Education+ultraviolet photo+polygenic risk score | Self-reported sun protection and tanning behaviours |
| Lee 2023[57] | 2* | Polygenic risk score communication | No information or intervention | Change in dietary intake, including nutrients (carbohydrates, protein and fat (% energy/day), and energy (kcal/day), and their servings |
| Wolever 2022[52] | 4 | Polygenic risk score communication and standard risk assessment | 1. Standardised risk assessment<br>2. Standard risk assessment and health coaching<br>3. Standard risk assessment and health coaching and polygenic risk score | Self-reported behavioural measures: dietary intake and physical activity |
| Viigimaa 2022[58] | 2 | Polygenic risk score communication with provision of standard of care advice | Standard of care advice | Change in total 10 year risk of cardiovascular disease measured with KardioKompassi method |
| Ma 2022[59] | 2 | Polygenic risk score communication and genetic counselling, with traditional risk according to the JADE Programme | Traditional risk according to the JADE Programme | Proportion of patients reaching ≥3 of 5 predefined treatment targets† |
| Lacson 2022[51] | 2* | Polygenic risk score communication and information about skin cancer; genetic contribution to skin cancer development; guidelines for skin cancer prevention based on their genetics; and a guide to self or partner skin examinations | Information about skin cancer; generic skin cancer prevention behaviours; skin examination guidelines adapted from recommendations by the American Academy of Dermatology | Seven prevention outcome activities related to sun exposure |
| Watanabe 2021[50] | 2 | Polygenic risk score communication and health education | Health education | Difference in participation rate in breast and cervical cancer screening |
| Smit 2021[62] | 2 | Polygenic risk score communication, with a personalised booklet with own specific risk of developing melanoma, with a telephone call from genetic counsellor | Traditional risk information with a general educational booklet on melanoma | Objective total daily standard erythemal doses |
| Lacson 2021[49] | 2* | A. Polygenic risk score communication and information on melanoma and skin cancer;<br>B. genetic contribution to skin cancer development; and prevention behaviours according to genetic risk | Information on melanoma and skin cancer; and melanoma prevention behaviours recommended by the American Academy of Dermatology | Seven prevention outcome activities related to sun exposure |
| Horne 2020[48] Horne 2020[68] Horne 2020[69] | 2 | Polygenic risk score communication and lifestyle programme | Lifestyle programme with population based recommendations | Body composition changes (body fat) |
| Silarova 2019[61] | 4 | Polygenic risk score communication with web based lifestyle advice and phenotypic 10 year cardiovascular risk communication | 1. No information or intervention<br>2. Web based lifestyle advice only.<br>3. With phenotypic 10 year coronary heart disease risk | Change in objective physical activity assessed by accelerometer |
| Wu 2017[47] | 2 | Polygenic risk score communication and standard risk assessment | Standard risk assessment | Change in weight, body mass index, fasting blood glucose, and physical activity level |
| Knowles 2017[55] | 2 | Polygenic risk score communication with provision of standard of care advice | Standard of care advice | Change in low density lipoprotein cholesterol |

Continued

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**Table 2 Continued**

| First author and publication year | No of arms | Intervention arm | Control arm | Primary outcomes |
|---|---|---|---|---|
| Smit 2017[60] | 2 | Polygenic risk score communication, with a personalised booklet on genomic risk and a non-personalised booklet on melanoma with a genetic counselling telephone call | Traditional risk information with a non-personalised booklet on melanoma | Objective total daily standard erythemal doses |
| Nichols 2018[63] | 2 | Polygenic risk score communication with smoking cessation sessions | No risk communication with smoking cessation sessions | Smoking cessation |
| Kullo 2016[64]<br>Naderian 2025[41] | 2 | Polygenic risk score communication, with provision of traditional risk information | Traditional risk information | Change in low density lipoprotein cholesterol |
| Doménech 2016[46] | 2 | Traditional risk and polygenic risk score | Traditional risk factors | Change in 24 hour ambulatory blood pressure measurements |
| Livingstone 2016[37]<br>Celis-Morales 2017[38] | 4 | Polygenic risk score communication, with personalised dietary advice based on polygenic risk score, participants' diets and phenotypic data | 1. General population based dietary recommendations<br>2. Dietary advice based on participants' diets<br>3. Dietary advice based on participants' diets and phenotypic data | Dietary intake |
| Turner 2016[65] | 4 | Polygenic risk score communication only | 1. Family history risk<br>2. Polygenic risk score communication with pictograph<br>3. Family history risk with pictograph | Self-reported prostate specific antigen screening |
| Godino 2016[66] | 3 | Polygenic risk score communication with standard lifestyle advice | 1. Standard lifestyle advice<br>2. Phenotypic risk communication with standard advice | Objectively measured physical activity (kJ/kg/day) |
| Voils 2015[45]<br>McVay 2015[36]<br>Raghavan 2020[40] | 2 | Genetic counselling and test results | Control eye disease counselling | Weight at 3 months post-enrollment |
| Hietaranta-Luoma 2015[44] | 2* | Genotype based health information (high *v* low) | General health information only | Change in dietary fat quality |
| Weinberg 2014[43] | 2 | Gene environmental risk assessment | Usual care | Receipt of colorectal cancer screening at 6 months |
| Nielsen 2014[42] | 2* | Personalised DNA based dietary advice | General population based dietary advice | Change in dietary intake |
| Grant 2013[67]<br>Vassy 2018[39] | 2* | Polygenic risk score communication with genetic counselling, with a 12 week diabetes prevention programme | No information with 12 week diabetes prevention programme | Stage of change for achieving diabetes-related lifestyle changes |

*Intervention arm was subclassified into intervention low risk and high risk groups.

†Haemoglobin $A_{1c}$ <7%, blood pressure <130/80 mm Hg, low density lipoprotein cholesterol <2.6 mmol/L, triglyceride concentration <2.0 mmol/L, and use of renin-angiotensin system inhibitors.

JADE, Joint Asia Diabetes Evaluation; MET, metabolic equivalent of task.

reported mixed conclusions and called for further research, and seven were not in favour of the intervention (online supplemental table 8). Among the 15 studies that concluded in favour of the intervention, however, only five reported results that were both favourable and significant: Kullo et al[64] reported a significant reduction in levels of low density lipoprotein cholesterol in the intervention group compared with baseline; Viigimaa et al[58] found significant changes in most of the analysed outcomes (ie, low density lipoprotein cholesterol and total cholesterol, and hypertensive drug treatment) in the intervention versus the control group; Horne et al[48] reported a significant increase in physical activity; and Doménech et al[46] reported significant changes in blood pressure. Livingstone et al[37] also reported an improvement in dietary score.

In contrast, the remaining 10 randomised controlled trials that concluded in favour of the genetic intervention did not show any significant effects in their main outcomes. In these cases, effects were limited to specific subgroup analyses or to short term improvements: three studies reported effects only among participants classified as having a high genetic risk[42 47 63]; two studies found differences exclusively within groups[53 56]; two studies found effects both in high risk individuals and within group comparisons[49 51]; two studies reported effects restricted to other subgroups (eg, men)[57 62]; and one study found a significant effect at 10 weeks that was not sustained at follow-up.[44]

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## Discussion

### Principal findings

In this comprehensive systematic review and meta-analysis of 27 randomised controlled trials, we assessed the effects of polygenic risk score communication on health related outcomes. Across 22 outcomes meta-analysed, no significant effects emerged for behavioural changes (ie, diet, physical activity, smoking, or screening attendance), psychological measures (ie, anxiety, depression, or risk perception), or clinical endpoints (ie, lipid levels, blood pressure, body mass index, or weight). A small number of individual trials reported favourable results, often restricted to short term or subgroup analyses, but these findings were not consistent across studies and did not translate into significant summary effects when combined with other studies. Overall, the results of our study did not support meaningful changes in patient behaviour or clinical outcomes after disclosure of polygenic risk scores. Also, our results suggest that disclosure of polygenic risk scores was not associated with detectable psychological harm, including increases in anxiety, distress, or depressive symptoms.

### Strengths and limitations of this study

Our review used a standard protocol and followed standard methods and reporting guidelines, allowing us to conduct a meta-analysis of a wide range of outcomes. Also, the artificial intelligence platform, otto-SR, was used to validate both the retrieval of eligible studies and data extraction values, ensuring that no potentially relevant trials or information were overlooked. We found high concordance for data extraction, resulting in retrieval of an additional trial missed during the screening phase by the reviewers.

Our study had several limitations. We found considerable heterogeneity in the way polygenic risk scores were constructed and communicated. Only a small number of studies used modern genome-wide polygenic risk scores that include millions of variants, whereas most relied on a limited number of single nucleotide polymorphisms. Nearly a third of trials were assessed as being at high risk of bias, often because of missing outcome data. Sample sizes were generally modest, and follow-up periods were short (median six months), limiting the ability to detect any long term effects and imposing limits on the assessment of important clinical outcomes. Outcomes were frequently self-reported, particularly for diet and physical activity, which reduces reliability. Moreover, different questionnaires and scales were used across studies, further limiting comparability. In several trials, baseline and final values were not consistently reported, with some studies presenting only differences or final measurements, thereby restricting the number of studies that could be meaningfully compared. The methodological challenges of these randomised controlled trials may have a substantial effect on the evaluation of the efficacy of disclosure of polygenic risk scores, as already indicated in the literature.[70]




**Figure 2 | Risk of bias for the 27 trials[37 42–67] included in the systematic review, assessed with the revised Cochrane risk-of-bias tool for randomised trials (RoB 2)**

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**Table 3 | Meta-analysis of differences from baseline to final follow-up in the 27 randomised controlled trials included in the systematic review**

| Outcome | Measure | No of studies (intervention; control participants) | Value (95% CI) | $I^2$ (%) | References |
|---|---|---|---|---|---|
| Low density lipoprotein cholesterol | Mean difference | 4 (514; 537) | −3.64 (−7.88 to 0.60) | 0 | 55 59 61 64 |
| High density lipoprotein cholesterol* | Mean difference | 3 (411; 437) | −0.21 (−2.65 to 2.23) | 1.7 | 55 59 61 |
| Total cholesterol* | Mean difference | 2 (391; 391) | −2.01 (−8.27 to 4.26) | 0 | 59 61 |
| Diastolic blood pressure | Mean difference | 3 (247; 276) | −1.88 (−4.17 to 0.42) | 0 | 46 55 59 |
| Systolic blood pressure | Mean difference | 3 (247; 276) | −1.26 (−4.44 to 1.92) | 10.1 | 46 55 59 |
| Weight | Mean difference | 5 (520; 480) | −0.33 (−0.87 to 0.20) | 0 | 55 61 66 67 69 |
| Body mass index | Mean difference | 4 (357; 308) | −0.12 (−0.63 to 0.39) | 0 | 57 59 67 69 |
| Physical activity | Standardised mean difference | 4 (508; 511) | −0.01 (−0.13 to 0.11) | 0 | 55 61 64 66 |
| Diet (energy/day) | Standardised mean difference | 4 (587; 547) | −0.11 (−0.22 to 0.01) | 0 | 38 57 66 68 |
| Diet (fat/day) | Standardised mean difference | 3 (186; 149) | 0.03 (−0.18 to 0.25) | 1.4 | 57 64 68 |
| Alcohol consumption | Standardised mean difference | 2 (277; 266) | −0.11 (−0.28 to 0.06) | 0 | 56 61 |
| Intentional tanning | Standardised mean difference | 4 (1109; 1120) | −0.03 (−0.11 to 0.06) | 0 | 49 53 60 62 |
| Peak sun exposure | Standardised mean difference | 2 (533; 548) | 0.02 (−0.10 to 0.14) | 0 | 60 62 |
| Sun protection | Standardised mean difference | 2 (533; 548) | 0.04 (−0.08 to 0.16) | 0 | 60 62 |
| Total sun exposure | Standardised mean difference | 3 (1091; 1101) | 0.00 (−0.09 to 0.08) | 0 | 49 60 62 |
| Incidence of disease | Relative risk | 3 (467; 418) | 0.95 (0.32 to 2.79) | 68.3 | 39–41 |
| Screening attendance | Relative risk | 3 (990; 748)† | 1.12 (0.77 to 1.61) | 25.5 | 43 50 65 |
| Use of statins* | Relative risk | 3 (760; 791) | 1.50 (0.98 to 2.29) | 88.7 | 58 59 64 |
| Depression* | Standardised mean difference | 2 (245; 237) | −0.05 (−0.23 to 0.13) | 0 | 57 59 |
| Perceived risk* | Standardised mean difference | 2 (379; 379) | −0.04 (−0.21 to 0.13) | 31.1 | 61 66 |
| Anxiety* | Standardised mean difference | 5 (702; 671) | −0.02 (−0.13 to 0.08) | 0 | 55 57 64–66 |
| Worry* | Standardised mean difference | 3 (718; 733) | −0.06 (−0.23 to 0.10) | 42.4 | 60 62 66 |

*Secondary outcomes in all studies

†In Watanabe et al,[50] screening attendance for both breast and cervical cancer was assessed.

CI, confidence interval.

### Comparison with other studies

Our findings align with previous systematic reviews of genetic risk communication, which also reported minimal impact on health behaviours or psychological outcomes.[18–20] Previous reviews frequently included single gene variants or even pathogenic mutations, however, whereas our review focused specifically on polygenic risk scores, and many more randomised controlled trials examined polygenic risk scores rather than single genetic variants. Despite the additional genetic information, the evidence was generally not supportive of substantive benefits, as also shown by a recent review on disclosure of polygenic risk scores for cardiometabolic diseases.[71] Our review emphasises the persistent gap between the theoretical promise of polygenic risk score guided prevention and the currently limited real world effectiveness.

Several factors may explain the lack of meaningful benefit from disclosure of polygenic risk scores. Firstly, patients may find it difficult to understand or act on probabilistic genetic information,[72] especially when absolute risks are modest compared with classic lifestyle and environmental factors.[9] Furthermore, clinicians may face challenges in interpreting the results of polygenic risk scores, which can hinder effective risk communication to patients.[73] Secondly, polygenic risk scores still have limited predictive power compared with traditional clinical risk factors,[10 74] and this finding may have reduced their motivational effect. Thirdly, most interventions were simple disclosure of the results of the polygenic risk score, which may not produce sustained lifestyle change without accompanying substantive behavioural or counselling support.[75 76] Evidence from personalised nutrition similarly suggested that the integration of genetic feedback gives only small and inconsistent effects on dietary change.[16 17] For clinicians, these findings indicate that polygenic risk score information should not be expected to independently improve adherence or outcomes in preventive care. For policy makers, the results suggest that although polygenic risk scores may have some potential to categorise innate risk, these scores may not have translational impact on behavioural changes and health outcomes, limiting their clinical value in this setting. Alternatively, polygenic risk scores may be integrated into predictive algorithms and population risk classification strategies,[77 78] rather than providing simple information disclosure. Further research is needed, however, into the integrated use of polygenic risk scores to evaluate realworld clinical use in relation to the costs and ethical considerations associated with genomic testing.[79]

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The consistency of null or near null behavioural effects across a large number of randomised trials raises the possibility that these findings reflect more fundamental constraints inherent in polygenic risk score communication for common diseases, and that expectations about what genetic information can realistically accomplish in prevention remain unclear and require further investigation. Because polygenic risk scores describe shifts in population level risk distributions and typically confer modest absolute risk differences, communicating a probabilistic increase in risk alone, and not including a structured approach that involves lifestyle, environmental, and sociodemographic factors, may not be motivationally sufficient to induce preventive behaviours.[80 81] Evolving newer polygenic risk scores may achieve higher risk discrimination than the polygenic risk scores assessed in trials so far. The extent of risk discrimination, however, may not be the main limiting step in achieving preventive changes in behaviour. Most preventive behaviours can be difficult to change, even with the availability of strong information. Whether polygenic risk score disclosure that is better embedded within structured prevention pathways and supported by healthcare professionals can enhance risk understanding, personalisation of preventive strategies, and engagement in risk reducing behaviours needs to be assessed further.

### Study implications

Several questions remain. Communication of polygenic risk score information might be more effective in specific populations, such as individuals with a high baseline risk, those already motivated to change, or in younger cohorts who have a longer lifetime risk outlook.[13 82 83] The best method for presenting information on polygenic risk scores also needs to be investigated, including visual risk tools, tailored counselling, and integration with digital health platforms.[11] Long term effects are largely unexplored; most trials followed participants for less than one year. Long term effects are unlikely, however, given that no or few short term effects were detected. Furthermore, most trials were conducted in high income countries with limited numbers of under-represented groups.[84 85] The evidence suggests that disclosure of polygenic risk scores is not associated with meaningful psychological harm, a finding that may be reassuring given the ongoing concerns about the potential adverse effects of genetic risk communication. Finally, if clinical effectiveness is found, research on cost effectiveness[86] and ethical aspects, including equity and privacy,[79] will be critical to inform whether disclosure of polygenic risk scores should have a role in any routine preventive medicine programme.[73] Although newer genome-wide polygenic risk scores offer improved predictive performance, achieving these additional behavioural, ethical, and translational requirements may be challenging. The real world use of these personalised medicine tools requires further evaluation.

## Conclusions

In this systematic review and meta-analysis, we found no evidence from the randomised trials conducted so far that communication of polygenic risk scores alone leads to behavioural changes, psychological benefit, or improvement in clinical outcomes. In diverse populations, conditions, and outcome measures, disclosure of information on polygenic risk scores did not result in measurable improvements in preventive behaviours or risk factor control. These findings reflect the evidence currently available from a limited number of trials, many of which were characterised by small sample sizes, short follow-up durations, reliance on self-reported outcomes, and substantial heterogeneity in polygenic risk score definitions and communication approaches. Hence disclosure of polygenic risk scores alone did not measurably affect behaviour or clinical outcomes. To more robustly answer this question, future research should go beyond simple disclosure designs and test polygenic risk score informed interventions within comprehensive prevention pathways, in large scale trials with long term follow-up and clinically meaningful endpoints.


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