

THE ECOSYSTEM OF EVIDENCE

Navigating the future
of the ecosystem of evidence

Artificial intelligence and digital transformation
in research and healthcare

11th EBHC International Conference
Taormina, 21st – 24th October 2026

#EBHC2026

30th GIMBE 1996-2026 EVIDENCE FOR HEALTH

Developing a Genomic Evidence Synthesis Hub at Cochrane South Africa to Strengthen Genomic Review Capacity

Mark E Engel, MPH, PhD

(*Together with: Dr Kimona Rampersadh*)

Personal Declaration

No conflict of interest to declare

I have no actual or potential conflict of interest in relation to this presentation.

I have no financial interest, arrangement, or affiliation with any organisation(s) that could be perceived as a direct or indirect conflict of interest in the context or content of this presentation.

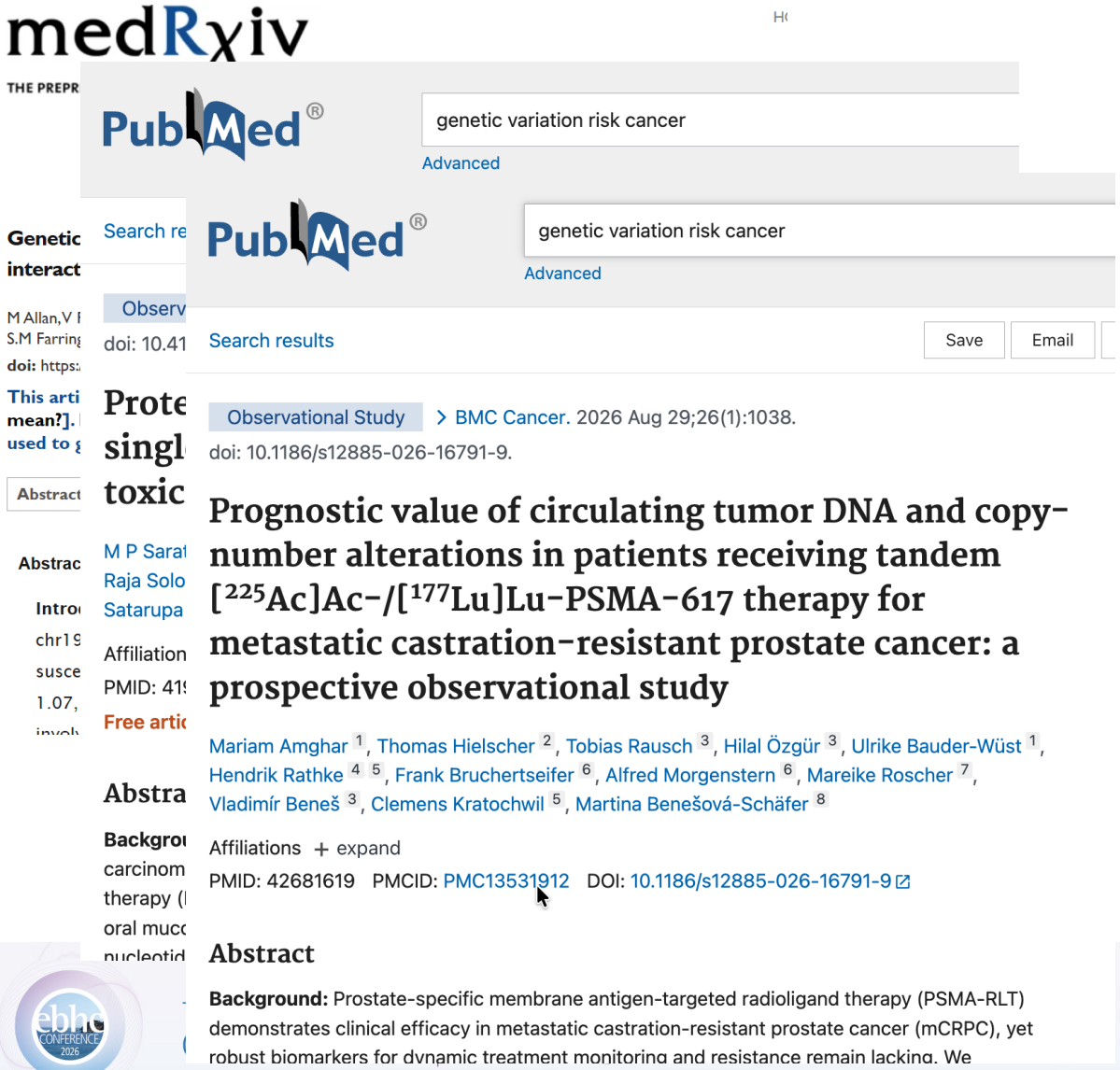
However, the SAMRC provided seed funding to help start the project, with no perceived conflict of interest.

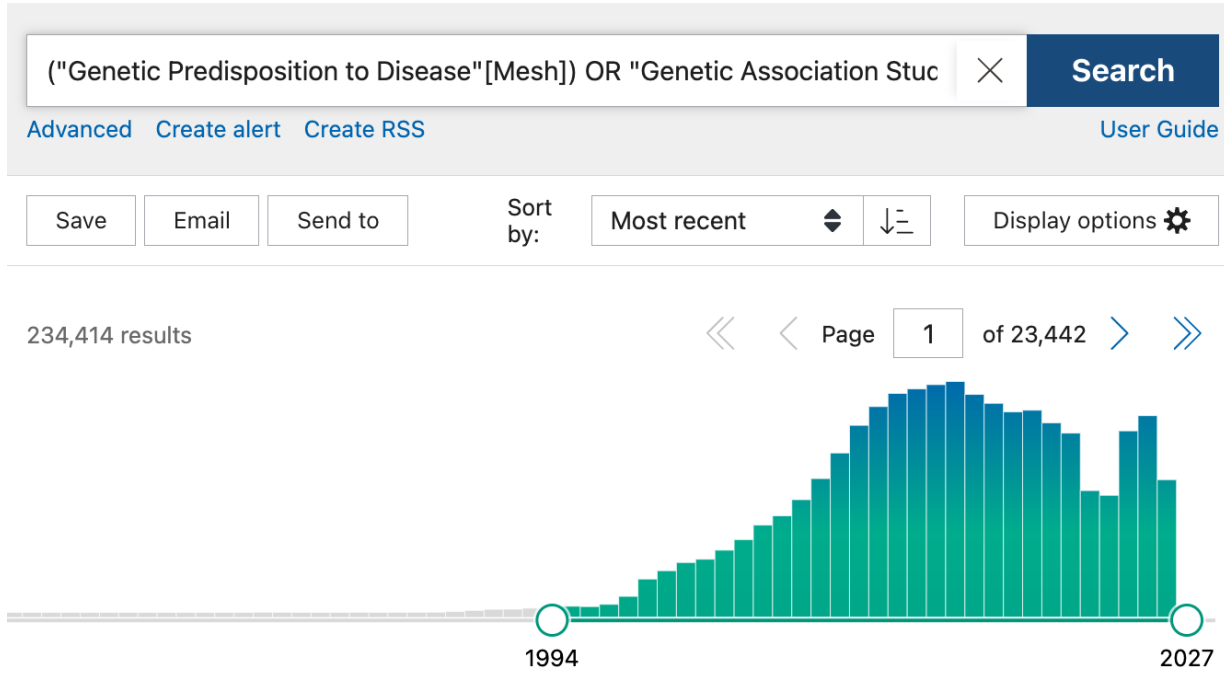
Acknowledgement

The South African Medical Research Council recognises the catastrophic and persisting consequences of colonialism and apartheid, including land dispossession and the intentional imposition of educational and health inequities.

Acknowledging the SAMRC's historical role and silence during apartheid, we commit our capacities and resources to the continued promotion of justice and dignity in health research in South Africa.

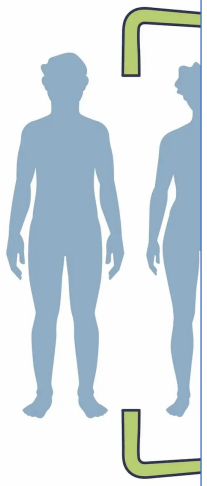
Background

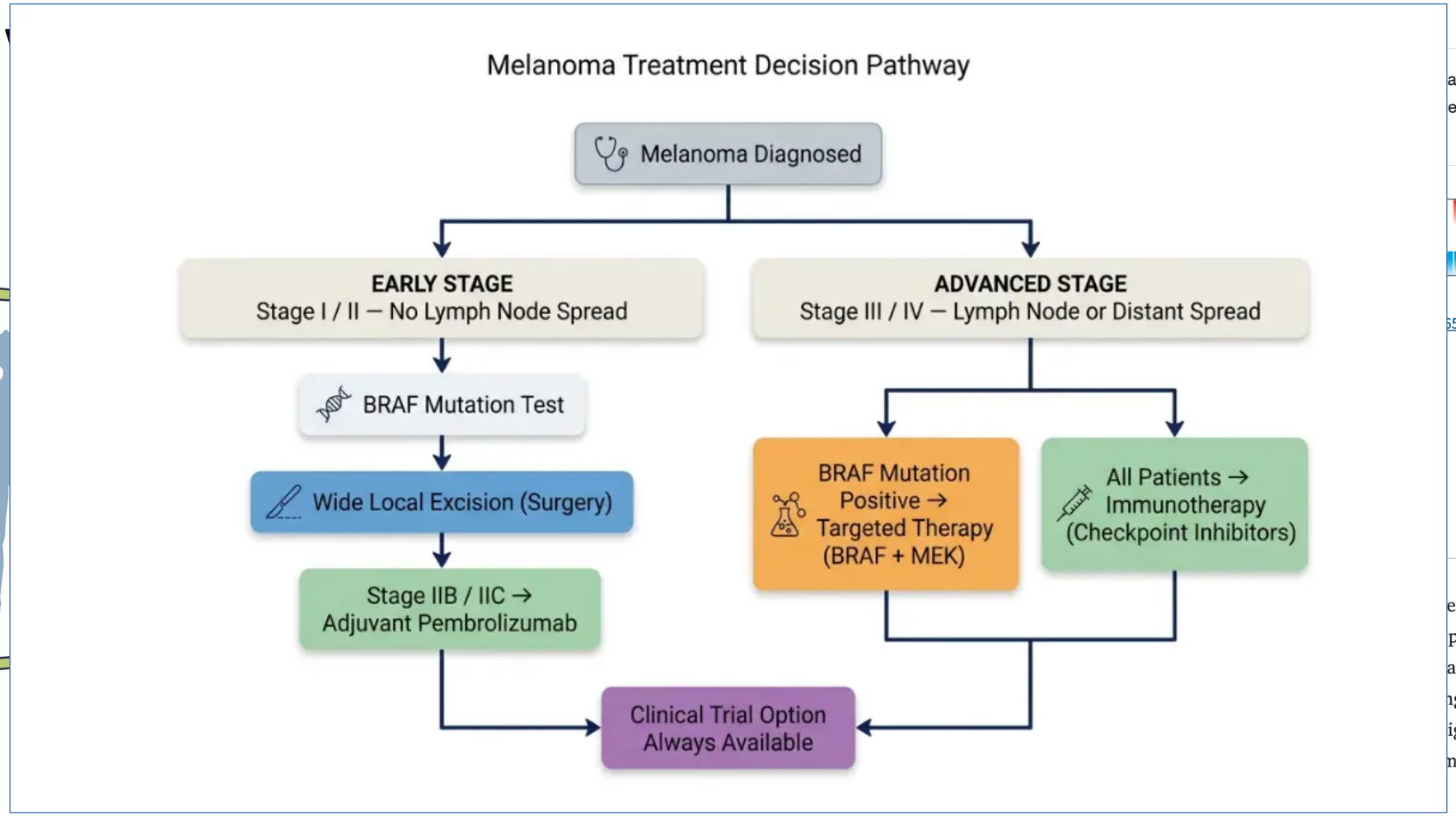

medRxiv
PubMed
genetic variation risk cancer
Advanced
PubMed
genetic variation risk cancer
Advanced
Search results
Save
Email
Observational Study
BMC Cancer. 2026 Aug 29;26(1):1038.
doi: 10.1186/s12885-026-16791-9.
Prognostic value of circulating tumor DNA and copy-number alterations in patients receiving tandem [225Ac]Ac-/[177Lu]Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer: a prospective observational study
Mariam Amghar, Thomas Hielscher, Tobias Rausch, Hilal Özgür, Ulrike Bauder-Wüst, Hendrik Rathke, Frank Bruchertseifer, Alfred Morgenstern, Mareike Roscher, Vladimír Beneš, Clemens Kratochwil, Martina Benešová-Schäfer
Affiliations + expand
PMID: 42681619 PMCID: PMC13531912 DOI: 10.1186/s12885-026-16791-9
Abstract
Background: Prostate-specific membrane antigen-targeted radioligand therapy (PSMA-RLT) demonstrates clinical efficacy in metastatic castration-resistant prostate cancer (mCRPC), yet robust biomarkers for dynamic treatment monitoring and resistance remain lacking. We


("Genetic Predisposition to Disease"[Mesh]) OR "Genetic Association Stuc
Search
Advanced
Create alert
Create RSS
User Guide
Save
Email
Send to
Sort by:
Most recent
Display options
234,414 results
Page 1 of 23,442
1994
2027

Background

Why do





PMC PubMed Central®
Search PMC Full-Text Archive
Journal List | User Guide
an NLM database does not
e National Institutes of Health.
CROATIAN MEDICAL JOURNAL
55.169
e – aims to optimize
profiling. In modern medicine,
anisms of diseases at the
nges the "one size fits all"
ignificant shift from the old
ne Project and a considerable

The challenge

A Randomized Trial of Genotype-Guided Dosing of Warfarin

Authors: Munir Pirmohamed, Ph.D., F.R.C.P., Girvan Burnside, Ph.D., Niclas Eriksson, Ph.D., Andrea L. Jorgensen, Ph.D., Cheng Hock Toh, M.D., Toby Nicholson, F.R.C.Path., Patrick Kesteven, M.D., +12 , for the EU-PACT Group* Author Info & Affiliations

Published December 12, 2013 | N Engl J Med 2013;369:2294-2303 | DOI: 10.1056/NEJMoa1311386
VOL. 369 NO. 24 | Copyright © 2013

Genotype-guided dosing:

Table 2. Percentage of Time in the Therapeutic Range for International Normalized Ratio (INR).*

Analysis	Genotype-Guided Group		Control Group		Least-Squares Mean Difference†	
	No. of Patients	% Time in Therapeutic Range‡	No. of Patients	% Time in Therapeutic Range‡	Percentage Points (95% CI)§	P Value
Patients with ≥13 days of INR data	211	67.4±18.1	216	60.3±21.7	7.0 (3.3–10.6)	<0.001

CONCLUSIONS

Pharmacogenetic-based dosing was associated with a higher percentage of time in the therapeutic INR range than was standard dosing during the initiation of warfarin therapy.

Genomics improves warfarin dosing

A Pharmacogenetic versus a Clinical Algorithm for Warfarin Dosing

Authors: Stephen E. Kimmel, M.D., Benjamin French, Ph.D., Scott E. Kasner, M.D., Julie A. Johnson, Pharm.D., Jeffrey L. Anderson, M.D., Brian F. Gage, M.D., Yves D. Rosenberg, M.D., +24 , for the COAG Investigators* Author Info & Affiliations

Published December 12, 2013 | N Engl J Med 2013;369:2283-2293 | DOI: 10.1056/NEJMoa1310669
VOL. 369 NO. 24 | Copyright © 2013

Genotype + clinical factors:

Table 2. Percentage of Time in the Therapeutic INR Range through Week 4 of Therapy, According to Subgroup.*

Variable	No. of Patients	Genotype-Guided Group	Clinically Guided Group	Mean Difference (95% CI) †	P Value
		percent		*percentage point*	
Primary analyses	955				
All patients		45.2±26.6	45.4±25.8	−0.2 (−3.4 to 3.1)	0.91‡
Patients stratified by absolute difference between algorithms in predicted dose					0.63 ¶
≥1.0 mg/day§	392	45.1±25.5	46.5±27.1	−1.1 (−6.2 to 4.0)	0.67‖
<1.0 mg/day	563	45.2±27.4	44.7±24.8	0.5 (−3.7 to 4.8)	0.81

CONCLUSIONS

Genotype-guided dosing of warfarin did not improve anticoagulation control during the first 4 weeks of therapy.

Genomics does not improve Warfarin dosing

Lee MT, Klein TE. Pharmacogenetics of warfarin: challenges and opportunities. J Hum Genet. 2013;58(6):334-8. doi: 10.1038/jhg.2013.40.

Core activities of the GES Hub

1. Conduct and facilitate systematic reviews of evidence-based genomic research

2. Produce GES Plain Language Summaries

3. Develop and refine methods for synthesizing human genetic association studies

    1. Provide mentorship and support
    2. through in-person and on-line platforms
    3. Statistical analysis support

Components of GES Reviews

A structured approach to synthesising genetic evidence

COMPONENTS	DEFINITION
01 Clearly formulated objective / question	Defines the genetic association being investigated and its relevance to public health, a disease of interest or, pharmacological phenomenon.
02 Inclusion criteria	Specifies which population-based genetic studies are eligible (e.g., case-control, cohort).
03 Search strategy	Describes systematic methods for identifying relevant genetic epidemiology literature. Use multiple databases.
04 Screening	Screen for articles meeting with inclusion criteria / PICO elements.
05 Data extraction	• Key variables such as allele frequencies, effect sizes, and study characteristics • Methodological approach (study design, sampling, etc) • Methodological quality of included studies (e.g., risk of bias- NOS, study design) • Effects of intervention, with results presented by outcome (e.g., allele frequencies, odds ratios)

Transparent | Systematic | Reproducible | Evidence-driven

saMRC advancinglife | Cochrane South Africa

Methods Foundation

1. Evidence-based healthcare commonalities
2. Systematic review methodology
3. PRISMA reporting standards
4. HuGENet approaches
5. Hardy Weinberg Evaluation

The HuGENet™ HuGE review handbook, version 1.0

Article · January 2006

CITATIONS
80

READS
527

8 authors, including:



Julian Little
University of Ottawa
570 PUBLICATIONS **26,083** CITATIONS
SEE PROFILE



Molly Bray
University of Texas at Austin
179 PUBLICATIONS **10,422** CITATIONS
SEE PROFILE

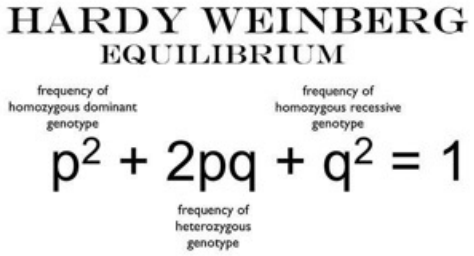


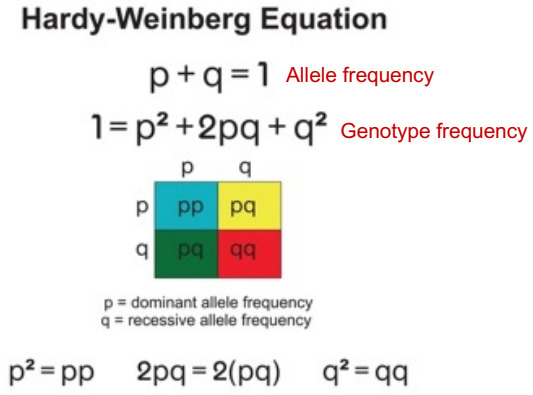
John Ioannidis
Stanford University
1,013 PUBLICATIONS **248,137** CITATIONS
SEE PROFILE



Muin J Khoury
Centers for Disease Control and Prever
736 PUBLICATIONS **46,478** CITATIONS
SEE PROFILE

Hardy-Weinberg Equilibrium Assessment





Assumptions of HWE:

- No Selection
- No mutation
- No migration
- Large population (small populations vulnerable to genetic drift)
- Random mating

- **Bias detection**: Deviations from HWE in control groups may indicate selection bias or population stratification.
- **Genotype checks**: Control group genotype distributions are assessed for HWE compliance.
- **Sensitivity analysis**: Studies violating or lacking HWE data are treated as deviating in sensitivity analyses to test robustness.

Discussion

How to conduct a GES review?

Meta-analysis: synthesising genetic evidence

1 SEARCH → 2 EXTRACT → 3 ASSESS BIAS → 4 Meta-Analysis

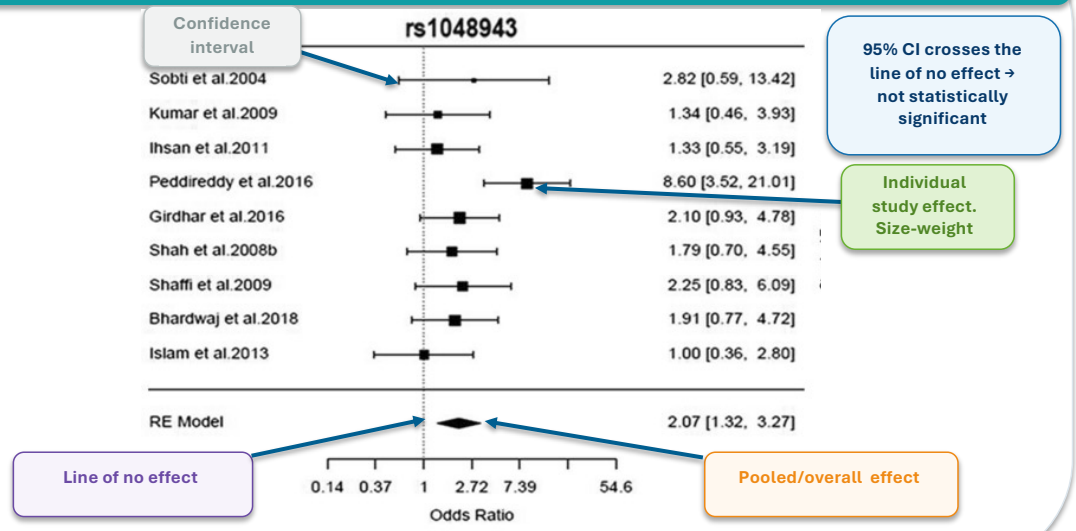
What does a meta-analysis show?



Combine results from multiple studies to estimate an overall genetic association.

- **Individual studies** — Each study provides an effect estimate and confidence interval.
- **Pooled estimate** — The meta-analysis combines study estimates using a statistical model.
- **Uncertainty** — The confidence interval shows the precision of the pooled estimate.

Reading a forest plot : Association of rs1048943 with lung cancer

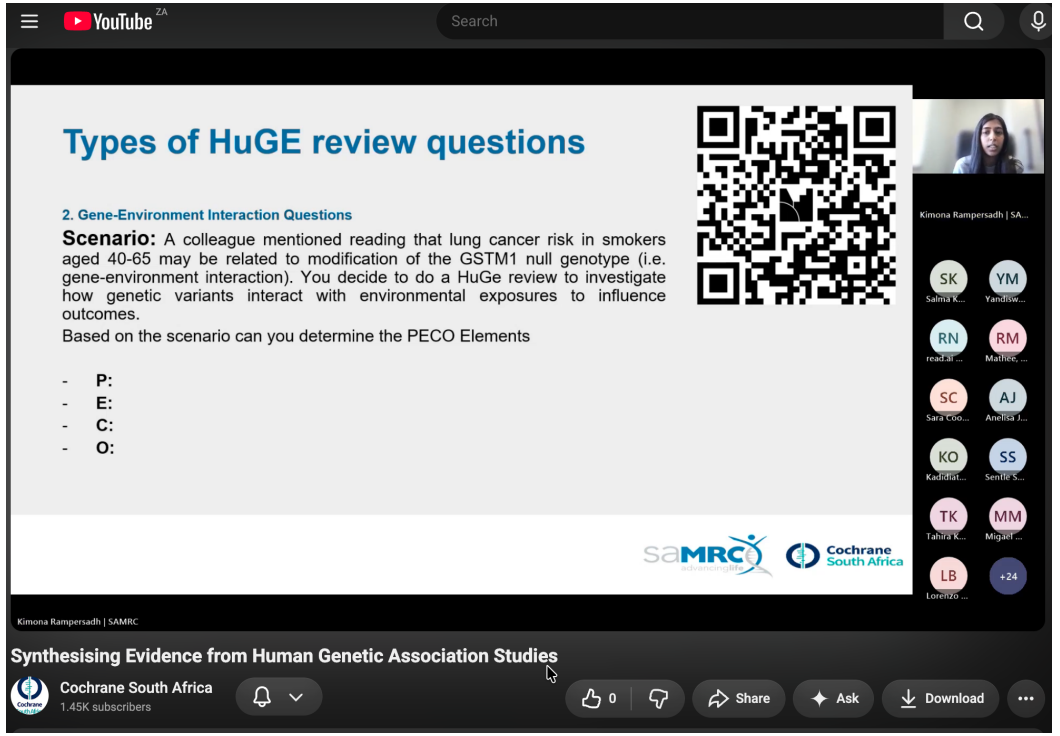


Meta-analysis quantifies the magnitude, consistency and uncertainty of genetic associations across studies.

Sengupta, D., Banerjee, S., Mukhopadhyay, P. *et al.* A comprehensive meta-analysis and a case–control study give insights into genetic susceptibility of lung cancer and subgroups. *Sci Rep* **11**, 14572 (2021). https://doi.org/10.1038/s41598-021-92275-z

Results

- GES Webinars
  - Genetic evidence synthesis techniques
  - Positive participant feedback



- Pilot project
  - Systematic review on genetic variation and drug bioavailability/pharmacokinetics in Malaria
  - Currently under peer review

- PLS
  - Systematic review on genetic variation and drug bioavailability/pharmacokinetics in Malaria

Conclusion

The Cochrane SA GES Hub

Lays the foundation for strengthening genomic evidence synthesis capacity, advancing methodological innovation, and supporting policy-relevant translation in South Africa and beyond.

