

deaths (28.6%), with the main causes being premature delivery and low birthweight, followed by mothers' poor socioeconomic status and inadequate antenatal care.⁵ Furthermore, reported higher rates of female neonate death compared with male neonate death indicate emerging issues, because the survival of female newborns is directly linked to the population's ability to grow and sustain in numbers.⁵ Stillbirth and early neonatal death are two major risk factors responsible for poor perinatal health in India's Scheduled Tribes. These adverse outcomes of pregnancy are preventable by adequate antenatal care and childbirth in hospitals. However, in 2024, there is low coverage of maternal and child health services in India, as only 23% of women in Scheduled Tribes received antenatal care and only 82% of births are in hospitals.⁶ Not only do low income, low literacy rates, and inadequate antenatal care influence adverse pregnancy outcomes, but so do stillbirths, fetus loss, and early neonatal deaths. Moreover, in 2023, only 75% of newborns received all birthdose immunisations, which indicates insufficient age-appropriate vaccination among children in Scheduled Tribes.³ Birthdose immunisations are crucial for neonates.

India's Scheduled Tribes face substantial health-care challenges, with insufficient prenatal, natal, and child vaccinations contributing to poor perinatal health. Additionally, marriage at a young age, birth at a low gestational age, short birth spacing, low awareness of health issues, and mistrust in public health services are a few factors that affect perinatal health.^{5,6} Consequently, pregnancies with complications and high risks must be treated through essential emergency obstetric services to reduce the risk of stillbirth, and preterm babies with low birthweight require specialised nursing care to lower perinatal risk. Hence, there is a strong need to improve outreach health services and community-based interventions.

We declare no competing interests.

Taranand Singh, *Dinesh Kumar
kumar.dn@icmr.gov.in

Indian Council of Medical Research–National
Institute of Research in Tribal Health,
Jabalpur 482003, India (TS, DK)

- 1 WHO. Perinatal conditions. World Health Organization, 2024. <https://platform.who.int/mortality/themes/theme-details/topics/topic-details/MDb/perinatal-conditions> (accessed July 4, 2024).
- 2 Ministry of Tribal Affairs, Government of India. Statistical profile of Scheduled Tribes of India 2013. Government of India, 2013. <https://tribal.nic.in/ST/StatisticalProfileofSTs2013.pdf> (accessed July 3, 2024).
- 3 Kusuma YS, Kumari A, Rajbangshi P, et al. Vaccination and associated factors among tribal children of 1 year age in nine Indian districts: a cross-sectional study. *Trop Med Int Health* 2023; **28**: 530–40.
- 4 Shah S, Desai S, Desai T, Szkwardo D, Desai G. Trends and risk factors in tribal vs nontribal preterm deliveries in Gujarat, India. *AJOG Glob Rep* 2021; **1**: 100026.
- 5 Kumar D, Srivastava S. Neonatal mortality and associated factors in tribal community. *Indian J Public Health* 2024; **68**: 336–37.
- 6 Kusuma YS, Kumari A, Rajbangshi P, et al. Maternal healthcare seeking and determinants of adequate antenatal care and institutional childbirth among Indian tribes: a cross-sectional study from nine districts. *Eur J Obstet Gynecol Reprod Biol* 2024; **292**: 163–74.

Violating independence assumption in medical statistics

In a Correspondence by Mohammad Ali Mansournia and Maryam Nazemipour,¹ the authors provide an essential overview of common statistical shortcomings in medical research and offer valuable guidelines for improving statistical reporting. I commend the authors for their comprehensive review and insightful recommendations, which underscore the crucial role of robust statistical practices in enhancing research validity and transparency.

Although I fully support the outlined recommendations, I would like to highlight an essential, yet frequently overlooked issue in the statistical analysis of medical research data—specifically, the violation of the assumption of the independence of observations. This issue is prevalent

in medical specialties, such as ophthalmology, otorhinolaryngology, and internal medicine, in which both eyes or sides of the same patient are often included in analyses, and in in vitro cell studies characterised by pseudoreplication.^{2,3}

As emphasised in the literature, including both eyes or sides of the same patient in a study and treating them as independent observations violates fundamental statistical principles.^{2,4} This practice can lead to erroneous conclusions due to the inflated sample size and underestimated variance (inflated type 1 error). Similarly, in cell studies, running one sample multiple times without acknowledging that they are not independent observations (pseudoreplication) compromises the integrity of the research findings.^{3,4}

To address these challenges, it is imperative that researchers adopt statistical methodologies that account for the inherent within-subject or within-participant correlation in such data. Advanced statistical models, such as mixed-effects models and generalised estimating equations, provide robust frameworks for analysing data with nested structures or repeated measurements, thereby accommodating the correlation between observations from the same subject or participant.^{4,5}

The guidelines provided by the Partnership for Assessment and Accreditation of Scientific Practice offer valuable resources for researchers to avoid common pitfalls associated with pseudoreplication.⁶ Emphasising the importance of these guidelines in research publications will not only enhance the quality of submitted manuscripts, but also ensure that research findings are reliable and reproducible.⁶ Therefore, I propose that scientific journals consider incorporating explicit guidelines regarding the treatment of correlated observations and pseudoreplication into their submission criteria. Such a move would set a precedent for

rigorous statistical analysis and reinforce the journals' commitment to publishing methodologically sound research.

I believe that addressing this issue is crucial for advancing the accuracy and reliability of medical research. I am hopeful that bringing attention to the importance of correctly handling correlated observations and avoiding pseudoreplication will foster a stronger foundation for statistical practices in medical research.

I declare no competing interests.

Georgios D Panos

georgios.panos@nottingham.ac.uk

Department of Ophthalmology, Eye & ENT Centre, Queen's Medical Centre, Nottingham University Hospitals NHS Trust, Nottingham NG7 2UH, UK; Division of Ophthalmology and Visual Sciences, School of Medicine, Faculty of Medicine and Health Sciences, University of Nottingham, Nottingham, UK

- 1 Mansournia MA, Nazemipour M. Recommendations for accurate reporting in medical research statistics. *Lancet* 2024; **403**: 611–12.
- 2 Murdoch I. People and eyes: statistics in ophthalmology. *Community Eye Health* 1998; **11**: 43.
- 3 Nikinmaa M, Celander M, Tjeerdema R. Replication in aquatic biology: the result is often pseudoreplication. *Aquat Toxicol* 2012; **116–17**: iii–iv.
- 4 Panos GD, Boeckler FM. Statistical analysis in clinical and experimental medical research: simplified guidance for authors and reviewers. *Drug Des Devel Ther* 2023; **17**: 1959–61.
- 5 Li M, Kong X. Comparing generalized estimating equation and linear mixed effects model for estimating marginal association with bivariate continuous outcomes. *Ophthalmic Epidemiol* 2023; **30**: 307–16.
- 6 Emmerich C. Accurate design of in vitro experiments – why does it matter? Partnership for Assessment and Accreditation of Scientific Practice. 2019. <https://paasp.net/accurate-design-of-in-vitro-experiments-why-does-it-matter/> (accessed Feb 17, 2024).

Low-value population screening

All screenings can harm (eg, by causing fear, false positive findings, stressful investigations, or overdiagnosis), some do good, and those that can be recommended must do “more good than harm at a reasonable cost”.¹ As raised by Clare Turnbull and colleagues, it is not clear if the genomic screening

part of the initiative Our Future Health will do more good than harm at a reasonable cost if implemented at a population level.² This screening could therefore increase the problem of low-value screening.

Low-value care is care that brings minimal or no benefit to the patient and it is a growing concern for health-care systems. The population, as well as policy makers and many health-care providers, expect a lot from screening, but the actual benefits—particularly for common chronic conditions, such as cancer—are generally low.¹ In addition, screening practice often does not follow recommendations regarding the frequency of testing or the ages at which to start and stop. Many screenings providing no benefit are also commonly done, such as thyroid cancer screening,³ which means that low-value screening is frequent.

The eagerness for screening, even if of low value, is built on the sincere belief that it is always useful to identify diseases at an early stage, enabling early treatment and better outcomes. However, for many conditions, earlier detection and treatment is not better than treatment initiated later and, due to improvements in treatment, the gains of treating screening-identified conditions over clinically detected conditions decrease.³ In addition, it is not sufficiently realised that many screenings are merely tools for estimating the probability of future disease, but do not enable early diagnosis; this is the case for screening for the genomic risk of common diseases. In the era of predictive and personalised medicine, the blurred boundaries between risk and disease are driving the endless expansion of the screen-and-treat strategy.⁴

Finally, the implementation of a preventive genomic risk screening strategy could increase socioeconomic inequalities in health, as the uptake of such screening will be more

frequent among people in a high socioeconomic position, as has been observed for screenings for cancer or cardiovascular disease risk factors.⁵ The opportunity cost of implementing such screening at a population level will have to be carefully considered.

I declare no competing interests.

Arnaud Chiolero

arnaud.chiolero@unifr.ch

Population Health Laboratory (#PopHealthLab), University of Fribourg, Fribourg 1700, Switzerland; School of Population and Global Health, McGill University, Montreal, QC, Canada

- 1 Gray JAM, Patnick J, Blanks RG. Maximising benefit and minimising harm of screening. *BMJ* 2008; **336**: 480–83.
- 2 Turnbull C, Firth HV, Wilkie AOM, et al. Population screening requires robust evidence—genomics is no exception. *Lancet* 2024; **403**: 583–86.
- 3 Welch HG. Cancer screening—the good, the bad, and the ugly. *JAMA Surg* 2022; **157**: 467–68.
- 4 Aronowitz RA. The converged experience of risk and disease. *Milbank Q* 2009; **87**: 417–42.
- 5 Capewell S, Graham H. Will cardiovascular disease prevention widen health inequalities? *PLoS Med* 2010; **7**: e1000320.

Polygenic risk scores for genomics and population screening

In their Viewpoint, Clare Turnbull and colleagues¹ focus on polygenic risk scores (PRS) and assert that PRS are genomic tests that are being hastily ushered in for population screening without robust evidence to support them. We agree with the importance of generating robust evidence before incorporating PRS in screening programmes. However, we believe that there are common misconceptions around the potential use of PRS in screening and it is paramount that these are first clarified for the benefit of health-care policy makers, clinicians, and patients, to empower them to undertake a truly robust and balanced evaluation of the evidence on PRS in screening.

PRS, which are the aggregate predictions from multiple inherited disease-risk variants, are not