Overcoming health disparities in precision medicine: Intersectional approaches in precision medicine

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1. Overview

The "Overcoming Health Disparities: Intersectional Approaches in Precision Medicine" session at the Pacific Symposium on BioComputing 2025 was aimed to advance computational methods and data science approaches to address racial, ethnic, and gender disparities in biomedical research and healthcare. Emphasizing the role of big data and electronic health records, the session focused on how social identities and categories like race, gender, and ethnicity interact to shape individual healthcare experiences and systemic inequalities. By tackling challenges in capturing and analyzing social determinants of health and environmental risk factors, this year session's papers highlight strategies such as multi-ancestry genetic studies, enhanced data collection from large population-based cohorts, and advanced geocoding clustering techniques. These efforts are crucial for integrating complex social and biological factors to reduce health disparities and improve precision medicine.

2. Advancing multi-ancestry genetic research

Historically, genetic studies have focused predominantly on individuals of European descent, leading to disparities in risk prediction and personalized medicine. While embracing genetic diversity aims to reduce these disparities, methodological challenges persist.

Jones and Cardone *et al.* (2025) examined how different methods of combining genetic data from diverse ancestry groups affect genome wide association study (GWAS) results, finding that multi-ancestry methods can identify shared signals but may diminish ancestry-specific associations, potentially masking important genetic insights for underrepresented populations. This highlights the need for methods that consider both shared and ancestry-specific variants to ensure equitable benefits.

Addressing this, Winters *et al.* (2025) developed a multi-ancestry polygenic risk score (PRS) for uterine fibroids using GWAS data from FinnGen and Biobank Japan, which outperformed single-ancestry PRSs across diverse cohorts, demonstrating improved model transferability. The findings

demonstrate that a multi-ancestry approach captures broader genetic variation and enhances model transferability across different racial groups.

Further exploring uterine fibroids, Akerele *et al.* (2025) investigated their genetic relationship with blood pressure traits using multi-ancestry GWAS datasets, finding that higher blood pressure increases fibroid risk and vice versa, suggesting shared genetic architecture. These findings enhance understanding of the mechanisms linking these conditions, potentially leading to better diagnosis and treatment strategies.

3. Integrating social determinants of health to enhance genetic risk models

While genetic studies have traditionally focused on the influence of genetic variants on phenotypes, they have largely overlooked the role of social determinants of health (SDoH) in disease incidence and health disparities. However, genetic associations alone cannot establish causation; additionally, SDoH may have an even stronger effect than genetic variation, and thus these factors are important to consider.

Guare *et al.* (2025) investigated how SDoH and lifestyle risk factors modulate genetic susceptibility in women's health outcomes by focusing on seven disorders within the All of Us Research Program. They computed PRSs and found that nine out of twelve PRSs were significantly associated with their respective conditions. Notably, higher environmental risk groups, such as individuals with elevated body mass index (BMI), were diagnosed earlier and exhibited increased genetic susceptibility, emphasizing the importance of integrating genetic and environmental data for more precise risk models.

Similarly, Mazzotti *et al.* (2025) analyzed electronic health record data from over 1.4 million individuals to identify social risk factor clusters and their association with obstructive sleep apnea (OSA) and cardiovascular outcomes. Using latent class analysis, they defined three social burden clusters and discovered that those with the highest social burden were less likely to be diagnosed with OSA compared to those with the lowest burden. Among OSA patients, clinical predictors of cardiovascular events varied across social risk clusters, indicating that social factors differently influence cardiovascular risk. These findings highlight significant health disparities in both the diagnosis of OSA and the prediction of cardiovascular diseases, underscoring the need for tailored interventions.

4. Methods to detect and mitigate disparities

New computational methods that consider various data modalities are essential to uncover biases and disparities in healthcare data, disease incidence, and outcomes. Liu *et al.* (2025) introduce a causal inference approach using proximal mediation analysis to detect clinician implicit biases in diagnosis decisions within large-scale medical data like the UK Biobank, quantifying how biases formed by racism, ableism, and sexism impact patient outcomes.

On the other hand, the paper of Niu *et al.* (2025) presents the Gaussian Process Spatial Clustering (GPSC) method, a novel algorithm that clusters census tracts based on spatial location and socioeconomic status. GPSC captures both geographic and other characteristic patterns simultaneously, enabling the identification of meaningful clusters of census tracts based on

socioeconomic and environmental indicators associated with health and cancer risk in the Carolina Breast Cancer Study.

5. Addressing Disparities in Adverse Drug Reactions

Finally, addressing disparities in adverse drug reactions, Muse *et al.* (2025) developed a statistical approach using multistate Cox models to detect and quantify potential adverse drug events (ADEs) resulting from polypharmacy, focusing on differences between patient subgroups such as males and females. Analyzing data from nearly 2 million patients in Denmark, they computed hazard ratios for changes in laboratory test results before and after drug exposure, linking these findings to a drug-drug interaction database. Their models have potential applications for medical safety agencies and could improve efficiency in drug approval pipelines. By revealing how ADEs differ among patient subgroups, this work contributes to enhancing patient safety through precision medicine. This study complements the other research by emphasizing the importance of considering demographic factors in healthcare data analysis to reduce disparities and improve health outcomes.

6. Conclusion

Collectively, these studies highlight the role of innovative computational methods and multi-ancestry approaches in addressing health disparities across various medical domains. By integrating genetic data with social determinants of health, researchers are developing more precise risk models that account for the complex interplay of factors influencing disease outcomes, which may ultimately lead to a better understanding of causation. Advances in detecting and mitigating biases—in clinical decision-making, spatial analysis, and machine learning—contribute to reducing systemic inequalities in healthcare. The papers in this session demonstrate how intersectional and data-driven strategies in precision medicine can potentially overcome existing limitations and promote health equity.

7. Acknowledgments

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References

Akerele A.T., Piekos J.A., Hellwege J.N., Khankari N.K., Edwards T.L., and Velez Edwards D.R. (2025) Uterine fibroids show evidence of shared genetic architecture with blood pressure traits. In *Pacific Symposium on Biocomputing*.

Guare L.A., Das J., Caruth L., and Setia-Verma S. (2025) Social Determinants of Health and Lifestyle Risk Factors Modulate Genetic Susceptibility for Women's Health Outcomes. In *Pacific Symposium on Biocomputing*.

Jones S.C., Cardone K.M., Bradford Y., Tishkoff S.A., and Ritchie M.D. (2025) The Impact of Ancestry on Genome-Wide Association Studies. In *Pacific Symposium on Biocomputing*.

Liu K., Altman R., and Syrgkanis V. (2025) Detecting clinician implicit biases in diagnoses using proximal causal inference. In *Pacific Symposium on Biocomputing*.

Mazzotti D.R., Urbanowicz R., and Jankowska M. (2025) Social risk factors and cardiovascular risk in obstructive sleep apnea: a systematic assessment of clinical predictors in community health centers. In *Pacific Symposium on Biocomputing*.

Muse V.P, Haue A.D, Rodríguez C.L., Orozco A.A., Biel J.H., and Brunak S.. Assessment of Drug Impact on Laboratory Test Results in Hospital Settings. In *Pacific Symposium on Biocomputing 2025*.

Niu H., Troester M., and Li D.. Spatial Clustering for Carolina Breast Cancer Study. In *Pacific Symposium on Biocomputing 2025*.

Winters J.L.G., Piekos J.A., Hellwege J.N., Dikilitas O., Kullo I.J., Schaid D.J., Edwards T.L., and Velez Edwards D.R. Constructing a multi-ancestry polygenic risk score for uterine fibroids using publicly available data highlights need for inclusive genetic research. In *Pacific Symposium on Biocomputing 2025*.