**Annotated Bibliography**

Abbaoui, W., Retal, S., El Bhiri, B., Kharmoum, N., & Ziti, S. (2024). Towards revolutionizing precision healthcare: A systematic literature review of artificial intelligence methods in precision medicine. *Informatics in Medicine Unlocked*, *46*, 101475. <https://doi.org/10.1016/j.imu.2024.101475>

This research is a comprehensive, systemic literature review of all precision medicine literature relevant to artificial intelligence, machine learning, and deep learning methods from 2015 to early 2024. The article delves into various computational methods utilized by precision medicine publications and provides summaries of papers that use those methods under their respective sub-section. Additionally, it provides five publicly available datasets for use with precision medicine computational models, which I can potentially evaluate in my research for fairness and bias with regards to health equity amongst different demographics. This paper is also relevant to my research in that I can utilize its analysis of various methods used and research in precision medicine to contextualize the area of research and provide key examples of where analyzing health equity is important. The authors are all researchers in the area of artificial intelligence or related technical fields, with some conducting other research in the area of precision medicine as well, making the research credible.

*Achieving the Principles through a Precision Medicine Initiative Data Security Policy Framework*. (2020, September 13). All of Us Research Program | NIH. <https://allofus.nih.gov/protecting-data-and-privacy/precision-medicine-initiative-data-security-policy-principles-and-framework-overview/achieving-principles-through-precision-medicine-initiative-data-security-policy-framework>

In this webpage, the data security and protection aspect of the All of Us Research Program by the NIH is explained comprehensively, with methods to adhere to strict data protection highlighted. The authors outline many different levels of policy protections and safeguards that Precision Medicine Initiatives (PMIs) should take to ensure proper risk evaluations for patient health data. This resource is relevant and valuable to my research as it is part of an exploration of current policy surrounding precision medicine. This source is highly credible since it is from the NIH itself, and since the All of Us program is spearheaded by the NIH, there is no entity better qualified to make claims on aspects of the program.

Bellamy, R. K. E., Dey, K., Hind, M., Hoffman, S. C., Houde, S., Kannan, K., Lohia, P., Martino, J., Mehta, S., Mojsilović, A., Nagar, S., Ramamurthy, K. N., Richards, J., Saha, D., Sattigeri, P., Singh, M., Varshney, K. R., & Zhang, Y. (2019). AI Fairness 360: An extensible toolkit for detecting and mitigating algorithmic bias. *IBM Journal of Research and Development*, *63*(4/5), 4:1-4:15. IBM Journal of Research and Development. <https://doi.org/10.1147/JRD.2019.2942287>

This paper is written to accompany the development of the AI Fairness 360 toolkit by IBM. It details why such a toolkit is needed to evaluate fairness metrics and also offers bias-reduction algorithms that can be used by researcher to create more “fair” AI models. The article largely explains the various parts of the toolkit and how it can be leveraged to improve fairness and reduce bias in AI models. The research and more importantly, the toolkit, can be highly useful in my own research, as I can utilize the AI Fairness 360 toolkit to evaluate datasets (pre-processing aspect of toolkit), model itself (in-processing aspect of toolkit), and results of the model (post-processing aspect of the toolkit). The research is very credible, as all authors were directly involved in the creation of the AI Fairness 360 toolkit as part of IBM Research.

Ferryman, K., & Pitcan, M. (2018, February 26). *Fairness in Precision Medicine*. Data & Society; Data & Society Research Institute. <https://datasociety.net/library/fairness-in-precision-medicine/>

This article describes qualitative research done on understanding the biases in precision medicine. Identifies that there are biases in the data that precision medicine models are created on, as well as how precision medicine is delivered to patients, and which patients have access. The article delves into various considerations of bias that must be made, including biases in how medical records are created, how health data is created, etc. This is a very useful overview of bias in precision medicine, and is extremely relevant to my project, as it outlines possible avenues for investigation in the topic. The authors are Dr. Kadija Ferryman, an anthropologist who studies race, ethics, and policy in health technology at Johns Hopkins, and Mikaela Pitcan, a social scientist is currently a postdoctoral candidate at Fordham University.

Geneviève, L. D., Martani, A., Shaw, D., Elger, B. S., & Wangmo, T. (2020). Structural racism in precision medicine: Leaving no one behind. *BMC Medical Ethics*, *21*(1), 17. <https://doi.org/10.1186/s12910-020-0457-8>

This article focuses on racial disparities in medicine, and how they can be exacerbated in precision medicine as well. The research highlights that the inclusion of genetic and other forms of data from minorities is lower in studies, but the main driver of this issue is not enrollment decision of minorities, but rather poor research design. Three areas where structural racism can play a role in precision medicine are identified: “the quality of health data collected; the integration of these data in PM initiatives; and the development of new therapeutics, diagnostics or disease prevention strategies”. This paper will be instrumental in outlining areas of possible racial bias in precision medicine in my own research and provides areas that I can target in my methodology to examine racial biases. The first author of this paper, Lester Darryl Geneviève, is a biomedical ethicist and postdoctoral researcher at the Institute for Biomedical Ethics of the University of Basel in Switzerland, so her analysis on racial biases in the medical field is credible.

Hicks, S. A., Strümke, I., Thambawita, V., Hammou, M., Riegler, M. A., Halvorsen, P., & Parasa, S. (2022). On evaluation metrics for medical applications of artificial intelligence. *Scientific Reports*, *12*(1), 5979. <https://doi.org/10.1038/s41598-022-09954-8>

The research aims to first outline and explain the various current metrics used to evaluate machine learning model performance. The article then recalculates the discussed metrics for various papers utilizing ML models in gastroenterology, and comments on the pitfalls made in each paper with regard to the original calculation of the metrics. Finally, they discuss the tool that they have created, MediMetrics to calculate the discussing ML metrics in an easy manner for both researchers and doctors to use when evaluating ML models. This research is relevant to my proposed study because I can look at how ML models are currently evaluated and utilize/modify these calculation mechanisms to fit my research on health equity in AI precision medicine. If I develop a ML model in my research as a way to evaluate health equity, I can use the discussed metrics myself to evaluate model performance. The authors of this research are largely researchers at the Oslo Metropolitan University in Norway, and the paper was published in Nature Scientific Reports, establishing sufficient credibility.

Jansen, J. P., Trikalinos, T. A., & Phillips, K. A. (2022). Assessments of the Value of New Interventions Should Include Health Equity Impact. *Pharmacoeconomics*, *40*(5), 489–495. <https://doi.org/10.1007/s40273-022-01131-z>

This article speaks to the importance of including quantitative measures of how a new intervention or treatment affects overall health equity. The research surrounds using a distributional cost-effectiveness analysis (DCEA) model to evaluate treatment effects on overall health and health equity in a quantitative manner using available data on treatment effects and demographic data. It touches on limitations of this approach, such as insufficient data on certain social subgroups of interest, which results in high uncertainty, but also provides example analyses on aducanumab, a treatment for AD, to outline possible benefits of using such a model. This research is very useful to me as it also provides code to perform DCEA on various treatments. I can possibly look at the methodology used in this research to understand some of the elements I can incorporate into analyzing health equity impact in precision medicine. The authors of this paper are very credible, as they are researchers from the UCSF Center for Translational and Policy Research on Precision Medicine. This research institution has multiple publications in the field of policy research surrounding precision medicine and is well-reputed.

Johnson, K. B., Wei, W., Weeraratne, D., Frisse, M. E., Misulis, K., Rhee, K., Zhao, J., & Snowdon, J. L. (2021). Precision Medicine, AI, and the Future of Personalized Health Care. *Clinical and Translational Science*, *14*(1), 86–93. <https://doi.org/10.1111/cts.12884>

This research article is a review of the potential impacts AI and precision medicine can make on the field of health care. The authors discuss the scope of how AI and precision medicine can leverage advancements in technology and data collection to provide much more individualized medical and treatment approaches to patients. The research highlights several distinct examples of applications of AI precision medicine, including integration with EHR data, clinical decision support systems, and more. The article is useful to my research as background information to contextualize the importance of my research. If AI is going to be so impactful in the future of medicine, then it is important to build robust tools that can analyze the health equity of these approaches, as researchers should not exacerbate already existing disparities in medicine. The authors of this paper are researchers at either the Vanderbilt University Medical Center or IBM Watson Health, and possess expertise in both the fields of AI and medicine, making this article very credible.

Lim, S. S., Semnani-Azad, Z., Morieri, M. L., Ng, A. H., Ahmad, A., Fitipaldi, H., Boyle, J., Collin, C., Dennis, J. M., Langenberg, C., Loos, R. J. F., Morrison, M., Ramsay, M., Sanyal, A. J., Sattar, N., Hivert, M.-F., Gomez, M. F., Merino, J., Tobias, D. K., … Franks, P. W. (2024). Reporting guidelines for precision medicine research of clinical relevance: The BePRECISE checklist. *Nature Medicine*, *30*(7), 1874–1881. <https://doi.org/10.1038/s41591-024-03033-3>

The literature outlines a checklist for precision medicine research to support scientific best practices and address “health equity or PPIE considerations in their design”. The checklist is very comprehensive and well-made, and sparks the question of how many studies are actually following the guidelines proposed by this checklist. The article is very useful to my research, as I can examine the standards that research in this area is being held to, and use that to inspire policy recommendations in current gaps. The article is a consensus statement from Nature Medicine, a journal with very high recognition and impact, so we can confidently assume credibility. Additionally, it is a recently published article (July 2024) which suggests that it provides unexplored avenues for research.

MacEachern, S. J., & Forkert, N. D. (2021). Machine learning for precision medicine. *Genome*, *64*(4), 416–425. <https://doi.org/10.1139/gen-2020-0131>

This research delves into a brief history of the development of precision medicine, touching on how the incorporation of multi-omics data greatly advanced the field. The source also provides an overview of various machine learning methods, and this can be useful to use in my background section to contextualize my specific research. Finally, the research delves into multiple instances of how machine learning is currently being used in precision medicine, and touches on the implicit limitations of ML methods, mentioning biases that form from the data that ML models are trained on. I can use this research to provide background information and contextualize my findings, as it contains several useful examples on AI in precision medicine. Additionally, I can delve further into the examples mentioned in the paper to examine possible datasets I can evaluate in my research. The authors of this research are from the Department of Pediatrics at the Cumming School of Medicine and specifically they are leading members in the Precision Neurodevelopment Lab at that institution, verifying their credibility in areas of precision medicine research.

Marshall, D. A., Grazziotin, L. R., Regier, D. A., Wordsworth, S., Buchanan, J., Phillips, K., & Ijzerman, M. (2020). Addressing Challenges of Economic Evaluation in Precision Medicine Using Dynamic Simulation Modeling. *Value in Health : The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, *23*(5), 566–573. <https://doi.org/10.1016/j.jval.2020.01.016>

This research article focuses on defining a need for more dynamic simulation techniques to model the economic value of precision medicine, as precision medicine is different from traditional medical technologies in that its impact varies case-by-case and can have both upstream and downstream effects on care. The article describes two common approaches, Discrete Event Simulation and Agent Based Simulation, and provides various contexts in which these and other simulation models have been implemented in healthcare. This research is useful to my project because of its overview and introduction to dynamic simulation methods in healthcare, as it provides a starting point to understand how these quantitative methods apply to precision medicine. Additionally, the limitations and further considerations offered in the paper provide opportunities for possible avenues of research. The authors of the paper are highly credible, as they are either precision medicine research scientists or health economics researchers.

Mehrabi, N., Morstatter, F., Saxena, N., Lerman, K., & Galstyan, A. (2022). *A Survey on Bias and Fairness in Machine Learning* (No. arXiv:1908.09635). arXiv. <https://doi.org/10.48550/arXiv.1908.09635>

In this research, the authors examine the different possible biases possible at each step in creating a machine learning algorithm or artificial intelligence system. The article outlines biases in data collection, dataset design, and algorithm creation itself, describing extensively how each type of bias may affect the application of AI with examples. This paper is useful in identifying which biases I may see in precision medicine datasets, and I can reference the various types of biases in my discussion section. Additionally, this article mentions various AI bias evaluation tools which I can explore in my research and possibly utilize in my methodology. Mehrabi, the first author of this paper, is an Applied Scientist at Amazon AGI, working specifically on developing ethical and responsible AI systems. The paper itself has been cited multiple thousands of times, a testament to its credibility and widely-accepted nature in the scientific community.

Phillips, K. A., Douglas, M. P., Trosman, J. R., & Marshall, D. A. (2017). “What Goes Around Comes Around”: Lessons Learned from Economic Evaluations of Personalized Medicine Applied to Digital Medicine. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, *20*(1), 47–53. <https://doi.org/10.1016/j.jval.2016.08.736>

This article discusses the economic evaluation and comparison of personalized medicine with digital medicine. The findings of the review largely focus on the need for cost-effectiveness analysis on areas of digital medicine, as there are many challenges to quantifying these values. The research is useful for me to understand since it highlights an area for potential novel research. The authors of this paper are very credible, as they are researchers from the UCSF Center for Translational and Policy Research on Precision Medicine. This research institution has multiple publications in the field of policy research surrounding precision medicine and is well-reputed.