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| **About the Measure** | |
| **Domain** | Smoking Cessation, Harm Reduction and Biomarkers |
| **Measure** | Polygenic Risk Score (PRS) |
| **Definition** | A single scored value that quantifies an individual’s genetic disposition to a trait, used to estimate the risk of disease or other clinically relevant outcomes including cardiovascular disease and breast cancer. Typically, PRSs are calculated by summing the number of trait-associated alleles in an individual weighted by per-allele effect sizes from genome-wide association study (GWAS) data and normalized using a relevant population distribution. |

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| **About the Protocol** | |
| **Description of Protocol** | The National Human Genome Research Institute (NHGRI) Clinical Genome Resource’s (ClinGen) Complex Disease Working Group and the Polygenic Score Catalog (PGS) together define the Polygenic Risk Score Reporting Standards (PRS-RS). The PRS-RS are a suite of standard items outlining the minimal information needed to develop, implement, interpret and evaluate PRSs regarding reproducibility and transparency throughout the PRS development process, especially for downstream clinical applications. Reporting standards include the background of risk scores, study populations, development of risk models, interpretation, and model parameters. The PGS is an open database of polygenic risk scores and consistently curated metadata needed for transparency and reproducibility of PRSs. Many, but not all, traits and diseases are listed in the PGS. If a trait is not listed, the investigative team will need to develop the PRS for that trait. |
| **Protocol Text** | NHGRI ClinGen Complex Disease Working Group and the PGS Catalog’s PRS-RS are published in Wand et. al., 2021. The PGS Catalog is available at <https://www.pgscatalog.org/>. The PGS Catalog contains links to summary statistics used to derive PGSs in the NHGRI-EBI GWAS Catalog, available at <https://www.ebi.ac.uk/gwas/downloads/summary-statistics>. |
| **Participant** | All ages |
| **Source** | Wand, H., Lambert, S. A., Tamburro, C., Iacocca, M. A., O'Sullivan, J. W., Sillari, C., Kullo, I. J., Rowley, R., Dron, J. S., Brockman, D., Venner, E., McCarthy, M. I., Antoniou, A. C., Easton, D. F., Hegele, R. A., Khera, A. V., Chatterjee, N., Kooperberg, C., Edwards, K., Vlessis, K., … Wojcik, G. L. (2021). Improving reporting standards for polygenic scores in risk prediction studies. *Nature*, *591*(7849), 211–219. |
| **Language of Source** | English |
| **Personnel and Training Required** | Training in the use of PRS analysis software. |
| **Equipment Needs** | This method requires the use of software to analyze and calculate the PRS. |
| **Protocol Type** | Secondary Data Analysis |
| **General References** | Buniello, A., MacArthur, J.A.L., Cerezo, M., Harris, L.W., Hayhurst, J., Malangone, C., McMahon, A., Morales, J., Mountjoy, E., Sollis, E., Suveges, D., Vrousgou, O., Whetzel, P.L., Amode, R., Guillen, J.A., Riat, H.S., Trevanion, S.J., Hall, P., Junkins, H., Flicek, P., Burdett, T., Hindorff, L.A., Cunningham, F. and Parkinson, H. (2019). The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics 2019. *Nucleic Acids Research*, 47 (Database issue), D1005-D1012.  Choi, S. W., Mak, T. S., & O'Reilly, P. F. (2020). Tutorial: a guide to performing polygenic risk score analyses. *Nature protocols*, *15*(9), 2759–2772.  Khera, A. V., Chaffin, M., Wade, K. H., Zahid, S., Brancale, J., Xia, R., Distefano, M., Senol-Cosar, O., Haas, M. E., Bick, A., Aragam, K. G., Lander, E. S., Smith, G. D., Mason-Suares, H., Fornage, M., Lebo, M., Timpson, N. J., Kaplan, L. M., & Kathiresan, S. (2019). Polygenic Prediction of Weight and Obesity Trajectories from Birth to Adulthood. *Cell*, *177*(3), 587–596.e9.  Lambert, S. A., Gil, L., Jupp, S., Ritchie, S. C., Xu, Y., Buniello, A., McMahon, A., Abraham, G., Chapman, M., Parkinson, H., Danesh, J., MacArthur, J., & Inouye, M. (2021). The Polygenic Score Catalog as an open database for reproducibility and systematic evaluation. *Nature genetics*, 10.1038/s41588-021-00783-5. Advance online publication.  Liu, M., Jiang, Y., Wedow, R., Li, Y., Brazel, D. M., Chen, F., Datta, G., Davila-Velderrain, J., McGuire, D., Tian, C., Zhan, X., 23andMe Research Team, HUNT All-In Psychiatry, Choquet, H., Docherty, A. R., Faul, J. D., Foerster, J. R., Fritsche, L. G., Gabrielsen, M. E., Gordon, S. D., … Vrieze, S. (2019). Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. *Nature genetics*, *51*(2), 237–244.  Martin, A. R., Daly, M. J., Robinson, E. B., Hyman, S. E., & Neale, B. M. (2019). Predicting Polygenic Risk of Psychiatric Disorders. *Biological psychiatry*, *86*(2), 97–109. |
| **Process and Review** | Not Applicable |