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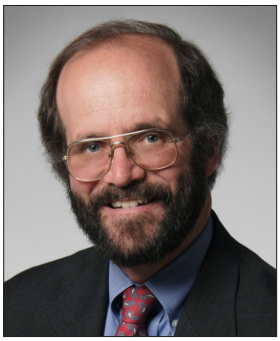

Robert N. Golden, MD

Mechanistic Health Disparities Research: Aligning Science With Solutions

Amy J.H. Kind, MD, PhD; Robert N. Golden, MD

Health is not distributed equally. According to the National Institutes of Health (NIH), health disparities are experienced disproportionately by American Indians/Alaska Natives, Asian Americans, Blacks/African Americans, Hispanics/Latinos, and Native Hawaiians and other Pacific Islanders; socioeconomically disadvantaged populations; underserved rural populations; and sexual/gender minorities. Wisconsin is particularly challenged by these disparities, with worse health outcomes observed across all health disparities groups as compared to the national averages.

Therapeutics and interventions that effectively ameliorate disparities are critically needed. In the past, health disparities research focused primarily on documenting and describing the problem. As the field has matured, it increasingly aligns with action by embracing a precision-medicine approach—unlocking how social factors interact with biology to produce disease, and then designing solutions that are precisely tailored for targeted conditions, systems, and populations. This area of "mechanistic" health disparities research illustrates the ways fundamental factors, such as race, ethnicity, and identity, interact with a complex array of geopolitical, socioeconomic, health care, cultural, social, psychological, physiological, genetic, and cellular factors to produce disparate population health outcomes. Many of these factors are adversely influenced by systemic inequities, such as structural racism. Recognizing the urgent need to move beyond description, the NIH has endorsed this action-oriented, mechanistic health disparities research approach.

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This emerging field brings together a diverse array of multidisciplinary research teams spanning cellular biology to sociology in order to better understand the role that structural processes and systems play in perpetuating disparities, as well as the biological pathways that these systems trigger to result in increased morbidity and mortality. By its nature, mechanistic health disparities research is broadly inclusive. Any effective intervention in this area requires the unified action of diverse individuals toward a common goal. This is a welcome philosophy as, ultimately, the mitigation of health disparities is a responsibility we all share.

Cutting-Edge Science

Nationally, leading academic institutions are rapidly tailoring their infrastructure to align with NIH-promoted approaches to mechanistic health disparities research. Infrastructure capable of supporting this next-generation research enables the linkage of cellular and molecular mechanisms to community- and health-system-level factors. Modern, social-biological phenotyping allows for advanced characterization of the "exposome"—individual environmental, social, and biological exposures from before birth across the life course—to execute translational research that mechanistically links

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these exposures to fundamental biological processes. Advanced analytic approaches capable of capturing the multiple levels, dimensions, interactions, and intersections for elucidating mechanisms of disparities from cell to community are made possible through the integration of emergent computational, statistical, "omic," and geoanalytic techniques, often applied across the life course. Through integrated, translational application of these approaches, new levels of rigor, validity, and generalizability can be attained for health disparities research.

Center for Health Disparities Research

To remain at the forefront of this revolution in health disparities research, we recently established the Center for Health Disparities Research (CHDR) at the University of Wisconsin-Madison. The center provides a next-generation, collaborative, research infrastructure and a means for delivering resources that address social-biological interactions, multilevel analytics, and mechanistic-focused system innovations. This, in turn, is expected to unlock opportunities for the development of new therapies, precision medicine approaches, and interventions capable of addressing the consequences of health disparities while also effectively targeting their complex, causal foundations.

CHDR's leadership team consists of Amy Kind, MD, PhD, director, CHDR, incoming director, Wisconsin Partnership Program, and professor, Department of Medicine, UW School of Medicine and Public Health (SMPH); Andrea Gilmore-Bykovskyi, PhD, RN, deputy director, CHDR, and assistant professor, UW School of Nursing; and Barbara Bendlin, PhD, deputy director, CHDR, and professor, Department of Medicine, SMPH. All are international leaders in mechanistic health disparities research with scientific backgrounds that span the translational research spectrum, resulting in diverse leadership that aligns with CHDR's mission, scope, and philosophy.

CHDR's mission is to catalyze research, clinical innovation, and educational activities in mechanistic-focused health disparities research; to accelerate the development of a robust, fully integrated health disparities research-and-practice community; and to bring the benefits of multilevel mechanistic health disparities research across campus and to all corners of this state in fulfillment of the Wisconsin Idea. Housed in the SMPH, CHDR strategically complements existing cross-campus strengths in research, clinical care, and education domains, functioning as an interactive nexus to amplify the impact and reach of mechanistic health disparities research across key stakeholders that have aligned vision and foci. CHDR will provide the latest educational programming and tools to promote incorporation of a mechanistic lens for a diverse array of learners. We expect CHDR's infrastructure to become a cornerstone of health disparities research operations, attracting philanthropy, research funding, faculty, and learners in a synergistic manner that advances solutions, innovations, and cures.

Research to Action

Since the center's establishment in fall 2021, the CHDR team has already made key strides. CHDR recently was awarded a $28.5 million NIH R01 grant to lead a 22-site national mechanistic-focused health disparities research study. This project, "The Neighborhoods Study," will establish a national consortium to assess how dosage and timing of exposure to neighborhood socioeconomic disadvantage across the life course impacts brain function, structure, neuropathology, and the risk for Alzheimer's disease. This new, national consortium spans leading academic institutions across the United States and involves some of the brightest minds in neuroscience, genetics, sociology, and clinical intervention. The goal is for this to be the first of many large interdisciplinary mechanistic health disparities NIH grants facilitated by CHDR.

Additionally, CHDR is now the home of the Neighborhood Atlas, a nationally recognized data-democratization tool that enables anyone to perform customized mapping or download data on precise geometrics of neighborhood socioeconomic contextual disadvantage for the full United States. Such metrics provide a key step in social exposome assessment, and the Atlas platform has been heralded by the NIH as a model for open science.

The Neighborhood Atlas has deep Wisconsin roots, as it has been developed, curated, disseminated, and updated by an SMPH team led by Dr Kind. The Neighborhood Atlas' data have been accessed nearly 500,000 times, and the data are being used for research, health, and policy applications throughout the nation. For example, Atlas metrics are being applied for active mitigation of disparities in COVID-19 therapy and vaccine prioritization across a number of US states; leveraged as a resource-targeting tool across many large health systems; and used as a cornerstone for health policy decision-making in Maryland. Simultaneously, these same Atlas metrics have been utilized by thousands of researchers to link neighborhood disadvantage exposure to epigenetic expression, premature aging, and a diverse array of morbidity and mortality outcomes spanning the fields of cardiovascular disease, cancer, brain health, diabetes, pediatric mental health, addictions, and more.

This next stage in the evolution of health disparities research offers new hope for real-world solutions. It is a research area that is expanding with purpose. We welcome CHDR as a key resource to facilitate cross-disciplinary advancement and to bring together as many brilliant minds as possible, with a shared vision of eliminating health disparities. It is a unifying cause that needs us all.

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