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## COMMENT

## Is precision medicine relevant in the age of COVID-19?

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The COVID-19 pandemic underscores the importance of public health initiatives in protecting population health. Large-scale testing, contact tracing, physical distancing, and mask wearing have been effective at slowing the spread of SARS-CoV-2 infections. But given the resurgence of the pandemic in many parts of the world, finding ways to support public health efforts remains an urgent goal. As we learn more about COVID-19, it may be possible to consider more targeted ways of preventing and treating infections. Precision medicine (PM) and precision public health (PPH), which aim to tailor treatment and interventions to unique individual or population-level traits, could complement conventional public health approaches. In this commentary, we argue that PM and PPH are relevant for addressing COVID-19 but caution against too great an emphasis on this approach. “Precise” interventions need to complement efforts to strengthen public health infrastructure and address fundamental social, economic, and environmental causes of illness.

**POTENTIAL ROLE OF PM AND PPH IN ADDRESSING THE PANDEMIC**

Precision medicine approaches emphasize more precise diagnosis and treatment based on a range of biomarkers, including genetic variants, and data about patients’ environment, lifestyle, and behaviors. PM approaches may be useful in understanding variations in individuals’ susceptibility and responses to COVID-19. For instance, recent studies have found that severe COVID-19 infections are associated with gene variants on chromosome 3 (3p21.31) and chromosome 9 (9q34.2),<sup>1</sup> ApoE e4 genotype,<sup>2</sup> and loss-of-function variants on X-chromosomal *TLR7*.<sup>3</sup> While there is debate over the clinical significance of these variants, findings such as these may provide initial insights into why patients who appear similar in terms of demographics and comorbidities can have vastly different responses.

A better understanding of biological vulnerabilities could offer leads for targeted therapies. In light of the recent findings on genetic vulnerabilities to COVID-19, PM approaches to developing future treatments could be analogous to initiatives in oncology where the genetic predisposition of the patient and the genetics of the tumor both come into play. Additionally, PM approaches may be valuable for identifying risks of adverse treatment effects for patients with certain genetic variants, as they have been for patients using drugs like abacavir and carbamazepine, which can help health-care providers make decisions on whether to alter dosages or avoid certain treatments for some patients.<sup>4</sup>

Precision public health—using more accurate measures of disease spread, susceptibility, and behavior to assess population health and develop targeted programs—can also support broader COVID-19-related public health efforts. The value of precise genetic information applies to the virus as well as the host. Pathogen genomics has been used to trace genetic variation of

the SARS-CoV-2 virus and its spread, which can help local officials make public health decisions about shelter-in-place orders and travel restrictions.<sup>5</sup> Expanded genetic characterization may provide more complete information on the SARS-CoV-2 virus that can then inform vaccine strain selection and improve vaccines’ effectiveness. Additionally, once a vaccine is developed, PM approaches hold promise for identifying biological, genetic, and environmental variables that could reduce vaccine response and may suggest that certain populations need alternative dosing.

In addition, PPH approaches using community-level data on infections from robust testing, Geographic Information Systems (GIS), spatial mapping, and digital data could be used to locate COVID-19 “hot spots” with higher risks of transmission or severe responses. For instance, the National Institute of Environmental Health Sciences (NIEHS) COVID-19 Pandemic Vulnerability Index (PVI) uses indicators of current infection rates, population concentration, intervention measures, and health and environmental vulnerabilities to show real-time county-level trends and vulnerabilities. This kind of data could help local officials make public health decisions, such as targeting high-risk communities for surveillance and messaging on the spread of COVID-19 and when and how to seek medical attention.<sup>6</sup> Additionally, prevention messages could be tailored to communities in culturally appropriate ways.

The “precision” approaches discussed above, though by no means an exhaustive review of current efforts, point to a wealth of data sources that are being leveraged to better understand the pandemic. Biobanks across the world, including the National Institutes of Health (NIH) All of Us Research Program, are collecting COVID-19 samples. Global research initiatives, like the COVID-19 Host Genetics Initiative, provide opportunities for scientists to collaborate as well as share and analyze data to better understand potential genetic determinants of COVID-19 susceptibility, severity, and outcomes. Bioinformatic tools are also being used to mine data in electronic health records to compare retrospective patient data with COVID-19 outcomes. As more COVID-19 data are collected, computational tools like machine learning could be used to predict risk of infection, transmission pathways, and clinical outcomes, as they have for conditions like *Clostridium difficile* infection and septic shock.<sup>7</sup>

**CAUTIONS ABOUT PM AND PPH IN THE AGE OF COVID-19**

Although PM and PPH approaches are relevant in several ways for addressing the pandemic, their application also raises concerns. If enthusiasm for PM diverts attention from less glamorous, but more effective, public health measures, the overall response will suffer.

Public health measures require social solidarity. Overemphasizing personal risk factors—whether age, underlying conditions, or more “precise” factors such as blood type—could decrease the

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willingness of those who see themselves at lower risk to engage in preventive measures. For instance, increased COVID-19 rates in the United States during May–August 2020 were, in part, due to increased spread among young people.<sup>8</sup> Even as PM researchers discover genetic and other biological vulnerabilities to COVID-19, it is important for messaging aimed at the public—from political leaders, public health officials, and researchers themselves—to continue emphasizing actions, such as wearing masks, that support the collective good. Incorporating PPH approaches could be useful for identifying high-risk populations and tailoring messages to encourage preventive actions, but do not replace more broadly targeted efforts.

Additionally, acceptance of a COVID-19 vaccine will require public confidence and engagement. Vaccine hesitancy is a national and global concern. A Gallup poll in late September 2020 showed that Americans' willingness to be vaccinated against COVID-19 dropped to about 50%, with variation across age, gender, and political affiliation.<sup>9</sup> While genetic information about the virus and host can support vaccine development, this by itself will not be enough. Understanding and addressing public perceptions of vaccines will be important for their future use. In this case, PPH approaches could complement public health efforts. Standard messages that vaccines are safe and effective do not always resonate. Public health officials will likely need to address community-specific concerns, such as distrust in medical institutions, religious or philosophical beliefs, and potential sources of misinformation to improve vaccine acceptance.

As PM and PPH researchers identify more precise biological or geographic patterns, it is important not to lose sight of the broader social determinants that shape differential risk and responses to COVID-19. PM's focus on framing risk in terms of individual characteristics may detract attention from social conditions that shape people's ability to change behaviors or avoid risk of COVID-19. For instance, being an essential worker or living in a multigenerational home in a poor neighborhood makes it difficult to protect oneself and one's family from infection. Additionally, the racial inequalities in COVID-19 infections and deaths in the United States are in part due to social factors like increased exposure to risks, limitations in access to care, and understandable distrust of health-care institutions. Focusing on individual characteristics may exacerbate false perceptions of deviance among certain populations rather than contextualizing health behaviors.

Similarly, structural factors may also contribute to community-level risks of COVID-19 transmission. Research on residential segregation, for instance, shows how neighborhood concentrations of poverty, exposure to environmental hazards, and less access to nutritious foods and primary health care impact health on a community level.<sup>10</sup> The granularity in geographic data on COVID-19 is indeed useful, but also needs to be contextualized. Presented by itself, these data in certain cases may inadvertently reinforce historical place-based stigma, especially of low-income minority neighborhoods, which may lead to blame and further neglect of these communities. As PM and PPH researchers use more "precise" tools, they should bear in mind these fundamental causes in their interpretation and presentation of findings. Future interventions may consider both targeted prevention and treatment strategies as well as "fundamental solutions" that address social and economic concerns, like financial support during shelter-in-place, and advocate for policies that increase health equity.

Finally, while biobanks are a rich source of data, they do not adequately reflect underrepresented groups. Biobanks, and

medical research in general, tend to involve people who are whiter, better educated, and wealthier than the general population. Though there are efforts to create more diverse databases, there is a risk that a focus on "precision" solutions to COVID-19, including machine learning algorithms trained on data sets that contain systematic biases, could advantage already privileged groups. PM researchers could not only support efforts to create more diverse databases, but also incorporate a multidisciplinary approach that includes social scientists and ethicists to investigate how a commitment to diversity is defined, operationalized, and implemented.

## CONCLUSION

Though it is too early to know the full impact of PM and PPH approaches in addressing COVID-19, we have argued that "precision" is relevant to public health efforts in several ways, such as identifying individual risks, supporting public health surveillance, and improving vaccine efficacy. As PM and PPH approaches are taken, we must consider the possible unintended consequences and ensure that interventions do not exacerbate existing disparities. Precision approaches are promising, but should complement, rather than replace, efforts to strengthen public health infrastructure and address fundamental causes of illness.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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