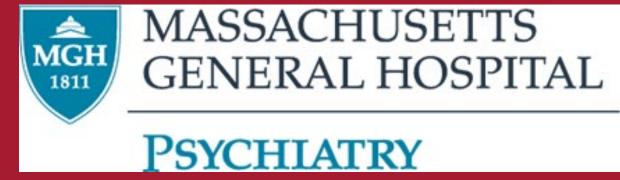
Clinical Implementation of Polygenic Risk Scores in Child and Adolescent Psychiatry: Clinicians' Views and Experiences

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BACKGROUND

- A recent survey of U.S.-based child and adolescent psychiatrists (CAP) revealed 54% felt polygenic risk scores (PRS) were at least slightly useful now, or will be in five years (87%).
- A subset of CAP (14%) reported having experience clinically ••• managing PRS in the past year (i.e., either generating PRS or patients bringing in PRS), and ~25% expressed they would help

"Would you help a patient generate scores if they requested them?"

Approximately half of CAP said they would help generate scores (10/23), with a few noting that they would only do so *if a patient was determined to do* so (3/23). One CAP also noted that although they may help a patient generate, they would do so 'off-the-

"I would do that because it's a concrete objective data. So even if we don't know how to interpret it, if somebody wants to get the data done...I don't see any harm in getting it done because we will hopefully become more advanced in interpreting it anyway."

generate a patient's psychiatric PRS upon patient request.

However, there are no guidelines on clinical management of PRS and ** no research on CAP psychiatric genetics experts' views on the opportunities, challenges, and responsible management of PRS in clinical care.

METHOD

- In-depth, semi-structured interviews where conducted with CAP who ••• reported experience managing psychiatric PRS in clinical care or with research expertise in psychiatric genetics as evidenced by relevant publications.
- Interviews underwent thematic content analysis and major themes identified in preliminary analyses are discussed.

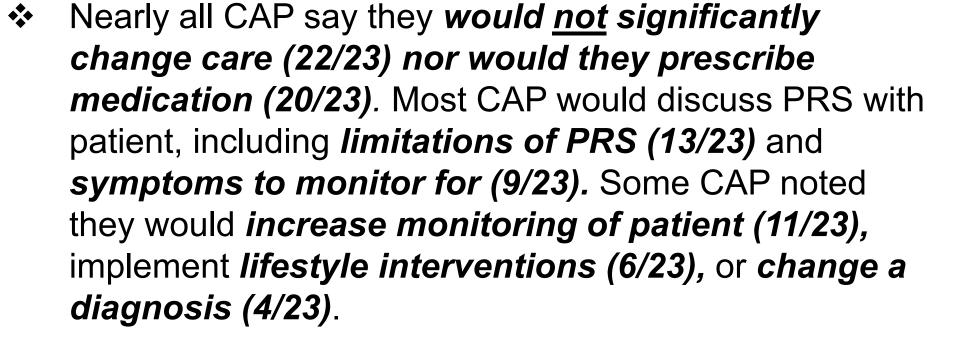
record' and would not enter the results into the EMR.

RESULTS



"What would you do if a patient brought PRS to you?"

"I would provide some education about what polygenic" risk scores can and can't do for us at this point."



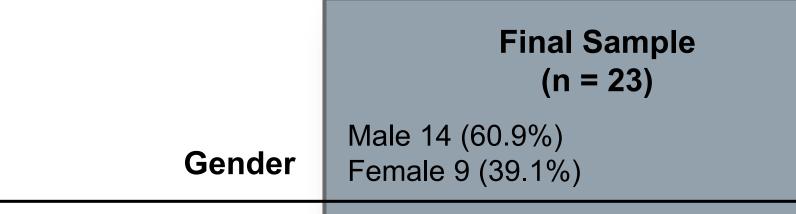
"What challenges have you encountered/might you anticipate with managing PRS?"

Explaining PRS testing and the test results was the most commonly anticipated challenge (12/23), with some clinicians noting they did not feel their training was sufficient in this area. CAP were also concerned about establishing the reliability and validity of the specific PRS test being used (8/23).

"The nuances can be very complicated in that type of testing." Then patients always ask me questions that I don't anticipate. I could definitely foresee them asking me a question that I didn't feel qualified to answer."

RESULTS

 Table 1. Participant Demographic Information



Race/Ethnicity	White 17 (73.9%) Hispanic/Latinx 3 (13.1%) Middle Eastern 2 (8.7%) Asian or East Asian 1 (4.3%)
Years of CAP Practice	1-5 years 4 (17.4%) 6-10 years 5 (21.7%) 11-15 years 6 (26.1%) 16+ years 8 (34.8%)

"How useful are PRS from a clinical standpoint?"

The majority of CAP felt that psychiatric PRS have limited ** clinical utility in their current state, with many stating that the science isn't there yet (16/23).

"I certainly believe in science. And believe that science changes. And as new information comes in, we do need to change our position as new science comes in. But I have just not read anything yet that convinces me that the science is settled enough that I would myself decide to order it."

"In the future, how do you think PRS could be <u>beneficial</u> to the field of psychiatry?"

"I think there's more sort of potential there for research in terms of understanding like gene environment interactions and understanding sort of the genetic architecture of disorders. Like how do polygenic risk scores kind of map onto each other versus not, having a sort of more biological marker of a disorder."



Some CAP felt that PRS may benefit psychiatry as a ••• field by *contributing to research surrounding the* genetic architecture of psychiatric disorders (8/23), and several noted that once PRS testing is more accurate, PRS testing may be helpful with regard to guiding surveillance/treatment (12/23), diagnostic clarity (9/23), or to inform early intervention efforts (7/23).

"In the future, how do you think PRS could be <u>harmful</u> to the field of psychiatry?"

Two main concerns emerged: almost all CAP expressed concerns about the potential for PRS to be misinterpreted or misused by clinicians (13/23), patients and families (6/23), or insurance/corporate entities (6/23); many were also concerned about the potential for exacerbating existing stigma or worsening healthcare disparities (11/23).

"[S]ome psychiatrist is going to tell a family, "Yep. Your kid's in the second percentile for a schizophrenia polygenic risk score... Get ready. Your child's going to be schizophrenic in 10 years. This test shows it... And, they start to put them on all these meds and they get all side effects and all for nothing."

"How can we help ensure these issues are managed responsibly? Who should regulate?"

"I think educating our next generation of psychiatrists, being sure that they're aware of what the limitations are. The field changes so rapidly though, that it's really hard to stay current unless you're in the field."

CAP highlighted the need for *a formal testing* ** *infrastructure (13/23) including education for*

"What would motivate you to generate a psychiatric PRS?"

Some CAP indicated that *if PRS were accurate a complex* ** case may prompt them to order (5/23), or a case in which there is a strong neurological component (7/23) or suspected genetic involvement (7/23). Many CAP noted that nothing would currently prompt them (12/23) to order.

"I think, again, when there's complex situations that things are not straightforward...I think when there's other indications, strong family history or people have symptoms of a certain disorder, I think a polygenic risk score can be very helpful....I think that it'll become more and more important. And I think that'll probably become more and more mainstream."



clinicians and clear clinical guidelines for PRS *implementation.* Many CAP also noted that there is a need for more formal regulation surrounding PRS. CAP felt that the government (12/23), professional organizations (12/23), psychiatry experts (11/23) and genetics experts (8/23) should collaborate to create policy.



- Findings suggest CAP feel PRS are not ready for clinical use, citing a need for more research. •••
- Although PRS have potential to advance our understanding of genetic contributions to psychiatric conditions, CAP caution about harm due to PRS misinterpretation, genetic discrimination, and lack of guidelines.
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