Is large-scale population screening coming to psychiatry?

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See Articles page e229

Large-scale population screening has long been proposed in oncology, though it still remains controversial.[1] Psychiatry has mostly been insulated from the screening fever, perhaps because of the scarcity of reliable biomarkers of psychiatric illness[2] or the fact that questionnaire-based screening is simultaneously time-consuming and not empirically supported (eg, for depression).[3] Can machine learning approaches be a game changer?

Using a 1:1 case-control design on one of the largest real-world databases of electronic health records (EHRs), covering approximately 15% of the US population in both primary and secondary care, Lars Lau Raket and colleagues[4] developed a risk prediction model to detect individuals at risk for developing a first episode of psychosis. The Dynamic ElecTronic hEalth reCord deTection (DETECT) model was able to identify individuals with first episode of psychosis who later developed schizophrenia with a prognostic accuracy of 0·774 and an area under the receiver operating characteristics (AUROC) of 0·856 in the validation dataset, and with a prognostic accuracy of 0·724 and AUROC of 0·799 in the external validation subset. Although replication in a population-based sample is explicitly advocated, DETECT's main appeal rests with its possible usefulness for large-scale screening of EHRs, by potentially identifying individuals not actively seeking help at secondary care units, such as clinical high risk for psychosis (CHR-P) specialised clinics.

Important questions arise about both the opportunity and ethics of large-scale population screening. Regarding opportunity, identifying individuals at high risk for psychosis would presumably be followed by interventions to prevent a first episode of psychosis. For young individuals classified as CHR-P, preventive interventions might add benefits versus usual care on transition to first episode of psychosis at 12 months.[5] Various proposed preventive interventions include simple and safe interventions like ω-3 fatty acids, complex interventions like cognitive behavioral therapy, and of course, antipsychotics. Yet a recent network meta-analysis found limited long-term benefits for all these interventions on attenuated psychotic symptoms, a primary assessment target for young individuals (mean age 19·6 years [SD 2·98]) classified as CHR-P.[6] These findings reinforce doubts that available interventions might just delay and not prevent the onset of psychosis.[7]

Early identification of the risk of first episode of psychosis, particularly in asymptomatic individuals, should also consider prognosis. Only a minority of CHR-P cases (20% [95% CI 17–25])[7] ultimately transition to first episode of psychosis. Moreover, long-term prognosis of first episode of psychosis is more heterogeneous than previously considered. The AESOP study[8] found that at 10-year follow-up, 213 (65%) of 326 participants with a first episode of psychosis were symptom free and, in 303 participants with complete data, 140 (46%) had been so for the previous 2 years. In a recent meta-analysis, remission rates of first episode of psychosis by the Remission in Schizophrenia Working Group criteria (which consider both symptomatic improvement and duration for persistence of mild or absent symptoms) were around 57% (95% CI 48·9–64·5).[9] Recovery rates, operationalised with clinical and functional components, along with a duration of sustained improvement for 2 years or more, were around 38% (95% CI 30·0–46·4).

The CHR-P approach is not recommended for large-scale screening, because of its very low positive predictive value (5·74%)[10] in the general population. Despite the impressive sample size and sophisticated statistical approach, DETECT does not overcome this problem. For a screening tool, AUROCs ranging from 0·799 to 0·856 are not ideal. Moreover, because of their dependence on disease prevalence, the negative and positive predictive values cannot reliably be computed from 1:1 case-control designs like DETECT. Assuming a first episode of psychosis incidence of 26·6 per 100 000 person-years[4], large-scale testing could produce a conspicuous number of false positives, to an extent difficult to estimate, hence fuelling overdiagnosis and its corollary, over-treatment. Moreover, owing to reliance on retrospective data, we do not know how DETECT compares with clinician evaluations. The authors recommend using DETECT in a sequential approach, but costs might have been underestimated. Individuals identified as at risk of first episode of psychosis would most likely have to receive further clinical evaluation to confirm their status, with costs

rising with the number of false positives. Moreover, the appropriate course of action for individuals identified as high risk but asymptomatic is unclear. Should they be included in specialised preventive intervention or just followed up? Some of the preventive interventions sought or recommended, such as antipsychotics, can come with persistent and considerable adverse effects. Overdiagnosis might lead to fragmentation and divestment of already limited resources from individuals classified as CHR-P who are actively seeking treatment, or from those who could benefit most from specialised interventions.

The looming ethical implications are even more complex. Finding out you carry a risk for developing psychosis, based on a non-intuitive combination of risk factors, could bring confusion and huge personal upheaval, with perhaps considerable associated distress. These problems are compounded by the uncertainty regarding which treatment to follow (if any), particularly in asymptomatic individual who screened positive, who can also be non-adherent to interventions that are complex or might carry adverse effects. Moreover, screening must be the result of shared decision-making, weighing benefits and harms. To enable shared decision-making, a screening tool must meet high evidence-based standards. For proof-of-concept studies like DETECT, the digital age involved moving from small to big data, but unfortunately it did not also move towards ensuring evidence is adequate for clinical use.

We declare no competing interests.

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