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Algorithmic identification of persons with dementia for research recruitment: ethical considerations

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ABSTRACT

Underdiagnosis, misdiagnosis, and patterns of social inequality that translate into unequal access to health systems all pose barriers to identifying and recruiting diverse and representative populations into research on Alzheimer's disease and Alzheimer's disease related dementias. In response, some have turned to algorithms to identify patients living with dementia using information that is associated with this condition but that is not as specific as a diagnosis. This paper explains six ethical issues associated with the use of such algorithms including the generation of new, sensitive, identifiable medical information for research purposes without participant consent, issues of justice and equity, risk, and ethical communication. It concludes with a discussion of strategies for addressing these issues and prompting valuable research.

KEYWORDS

Artificial intelligence; algorithmic identification; dementia; ethics; research ethics

Introduction

As a result of the aging of the US population, Alzheimer's disease and Alzheimer's disease related dementias – commonly called AD/ADRD – are notably prevalent; it is estimated that more than 6.5 million Americans are living with AD/ADRD.[1] People living with dementia (PLWD) experience distressing symptoms while care partners and families experience significant physical, emotional, social and financial burdens.[1] Remarkably, dementia is often underdiagnosed or misdiagnosed.[2] For PLWD and their care partners, delayed and missed diagnoses prevent timely access to treatment, as well as timely linkage to services and supports.

Underdiagnosis is also a barrier to conducting research to test promising pharmacologic and nonpharmacologic interventions to improve care for PLWD or their care partners. Known racial and ethnic disparities in diagnosis – missed or delayed diagnoses are more common among Black and Hispanic older adults than White older adults – are a contributing factor to study populations that are often not representative of the larger community of PLWD.[3] To overcome these recruitment barriers, researchers have turned to computer algorithms or digital phenotyping that might identify PLWD by using routinely collected health care data or findings that are *consistent with* or *associated* with dementia but are not as specific as a diagnosis. These data might include dementia-related symptoms or common comorbidities such as delirium, frailty or functional dependence.

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Despite their promise, algorithms to identify PLWD raise a cluster of ethical issues. These issues stem, in part, from the moral importance, recognized in bioethics in general and research ethics in particular, of ensuring that medical and research practices safeguard the wellbeing of patients, respect their autonomy, and promote conditions of justice and fairness.[4–6] They also derive from difficulties diagnosing and addressing dementia within the US health system, the residual uncertainty associated with algorithmic identification, logistical challenges associated with approaching individuals who have been identified by an algorithm, and issues of justice and fairness that arise at the intersection of these dynamics. In what follows, we discuss these ethical issues, their implications for the use of algorithms to identify PLWD and offer recommendations for how these issues might be addressed.

Why is "case finding" difficult?

Identifying PLWD for recruitment into dementia-related research would be relatively simple in an ideal health system in which every person had access to routine medical care across their life span. In such a system, every individual would have a primary care provider to help them monitor and address their health needs, allowing for prompt detection of cognitive impairment. Patients experiencing signs of impairment could see their primary care physician with the goal of diagnosing the nature and source of their symptoms. Clear standards for clinical evaluation and cognitive testing using well-validated instruments would allow providers to: characterize the degree of cognitive impairment and its likely cause or causes; communicate the diagnosis and prognosis to patients and their care partners; and facilitate timely provision of care as well as linkage to services and supports. This information would be reflected clearly in the patient's electronic health record (EHR) – for example, through inclusion of clinically accurate and comprehensive diagnostic codes; documentation of care plans, goals of care, and patient preferences; and billing codes that accurately reflect clinical conditions. Researchers implementing dementia-related studies could then use this information to readily identify a list of potential research participants; moreover, these researchers could be confident in the patient's clinical diagnosis and certain that patients and care partners were aware of the patient's AD/ADRD diagnosis if approached for recruitment into a study.

Of course, the US does not have an ideal health system, and many of these elements of care are underdeveloped or entirely absent. Indeed, large segments of the population lack an ongoing relationship with a primary care provider.[7] Structural gaps in access to health services are also patterned – that is, they are not randomly distributed in the community but are more prevalent among individuals of lower economic status, from rural areas, and from socially marginalized groups, including populations that have been excluded from health care systems based on race or ethnicity.[8,9] These individuals may confront a limited supply of health care providers, lack of quality care, or limited access to transportation.[10] Despite near-universal insurance coverage for older adults through Medicare, many older adults report delaying or forgoing needed care because of cost.[11] For these reasons, many individuals lack access to care or face substantial barriers when seeking care.

Even when individuals have an ongoing relationship with a care provider, diagnoses of AD/ADRD are often missed or delayed. Clinician-level barriers to diagnosis include the complex nature of a workup, stigma associated with dementia, and perceived diagnostic futility.[7] Despite efforts to improve testing and detection, approximately 40% of people in the US with probable dementia are undiagnosed. Additionally, it has been estimated that about 20% of patients with a diagnosis of dementia are unaware of their diagnosis.[2] Unfortunately, these issues are not unique to the US. Countries with national health care systems including Canada and the United Kingdom have high rates of undiagnosed dementia.[12] For example, the prevalence of undiagnosed dementia in the United Kingdom is approximately 33% even though, relative to the US, general practitioners play a greater role in diagnosing dementia, the electronic patient records are more integrated, and the health care system is less fragmented.[13]

Finally, many PLWD are lost to follow up after diagnosis and are not linked to services and supports.[14] Again, such gaps in care are most pronounced among poor, rural, minority and other

marginalized populations.[15] For instance, the population of patients diagnosed with dementia earlier in the disease course tends to be wealthier and whiter, while less affluent patients and patients of color tend to be diagnosed later in the disease course.[15,16] As a result, the former group are also more likely to have greater engagement with the health care system and thus have more extensive data on follow-up care than the latter.

These various factors create notable disparities in health care utilization and health outcomes for AD/ADRD,[14] which have ripple effects into research. When researchers seek to identify PLWD for recruitment into dementia-related research using a list generated by searching on diagnostic or billing codes, the lists generated will be shorter than they should be due to the overall lack of diagnosis. Further, the individuals populating the list are generally not representative of the larger population of PLWD because of inherent biases related to who is diagnosed and when in the course of disease, they receive a diagnosis. An important ambition of algorithmic identification is to address these problems.

Algorithmic identification

Health care systems and researchers are increasingly using algorithms and digital phenotyping to identify PLWD [Supplemental Table].[17–28] Algorithmic identification often involves digital phenotyping, understood as the use of multiple sources of electronic data to construct a model that can be used to identify patients with a particular pathology or impairment.[29] Assembling the data used in this process also often involves a process of data-linkage in which information about a single patient is extracted from multiple data sources such as electronic health records, administrative and billing records, and potentially other data sources as well.[30] As a result, efforts at algorithmic identification will inherit uncertainties related to the validity of features used to construct a digital phenotype as well as uncertainties related to data linkages, such as recording error or probabilistic uncertainties related to data that cannot be deterministically linked to a particular patient. We focus on the use of algorithms in this process because they are the computational tool used to construct a model from data and, as such, they embody a range of choices regarding appropriate operating characteristics (such as thresholds on sensitivity, specificity, positive predictive value, negative predictive value), the way an assessment or output is represented (e.g., as a binary classification or as a probability density), and because algorithms can sometimes be adjusted to account for biases or other deficiencies in underlying datasets when those problems are known and their magnitude can be reliably estimated.

With the growth of available datasets, increases in computing power, and the sophistication of statistical and computational techniques that can be used to generate models to predict or identify patients with a particular health issue, algorithmic identification is appealing because of the prospect that it might facilitate rapid, real-time identification of cognitively impaired individuals for purposes of population management or, our focus here, research.

Today's commonly used algorithms rely on data generated through health care delivery, utilizing a combination of information documented in EHRs and/or billing claims. Such algorithms use routinely collected health care data; this might include a documented diagnosis of a neurodegenerative disease or of cognitive impairment – such as the ICD-9/10 diagnosis codes for Alzheimer's disease or related dementias – or relevant billing codes – such as a CPT Code for assessment of, and care planning for, cognitive impairment. They might also include prescriptions the individual has received (e.g., cholinesterase inhibitors, NMDA antagonists). Yet algorithms that generate a dementia phenotype based on documented health care data, such as diagnosis and procedure codes, have their own inherent limitations related to accuracy and completeness.[26,28]

The true power and promise of these algorithms, however, lies in the prospect that they might identify PLWD – or even those at heightened risk for cognitive impairment – using data or findings that are *consistent* or *associated* with dementia but not as specific as diagnosis. Such algorithms can assign a risk score to patients based on dementia-related symptoms, health care utilization patterns, or other factors identified from medical records.

For example, the EHR Risk of Alzheimer's and Dementia Assessment Rule (eRADAR) tool uses existing EHR data – dementia risk factors, dementia-related symptoms, and health care utilization patterns – to detect individuals with *unrecognized* dementia.[18] This recently developed tool addresses the reality that a large proportion of PLWD don't have a dementia diagnosis in their EHR. They may, however, have other documentation related to a cluster of dementia-related symptoms (e.g., psychosis, underweight, nontricyclic antidepressant fills). Claims-based algorithms, such as the Bynum algorithm, rely on diagnostic codes on Medicare reimbursement claims to indicate whether a person has diagnosed dementia.[22,26,28] Other algorithms, such as the PheKB dementia phenotype,[20,23] use natural language processing and machine learning approaches to scan clinical notes for words and concepts related to cognitive impairment.

It is worth noting that dementia-detection algorithms rarely include data from neuropsychological tests. This is because only a small fraction of patients undergo such testing; thus, relying on these data would systematically exclude people without access to these services, particularly those in non-academic or rural health care settings.[31]

Ethical considerations

The use of dementia-detection algorithms is motivated by important ethical goals. Research is essential to reduce or close evidentiary gaps regarding the merits of interventions or services that health systems might use to address the social, psychological and economic burden AD/ADRD places on patients, families and health systems. However, if these goals are to be realized in practice, these algorithms must be used in ways that respect the autonomy of individuals, safeguard and promote their wellbeing, and comply with or advance requirements of justice and fairness. We elaborate six categories of concerns, grounded in these ethical values, before considering how they might be addressed in the following section.

Generating sensitive information

To begin with, algorithmic identification often involves the creation of new, sensitive, private, identifiable information about a patient. This information is *new* in cases where a patient does not already have a diagnosis of dementia in their medical record and an algorithm uses likely relationships or complex statistical relations between features that are associated with such a diagnosis to identify or assign a risk score for dementia to a patient. This information is *sensitive* and *private* because dementia is a medical condition that has profound effects on a person's ability to function across the full range of life activities including relationships that they value. There is also substantial stigma associated with AD/ADRD.[32] It is *identifiable* because information from different sources must be linked to the same individual for an identification to be made.

Identification for research purposes

It is important that in the scenarios we are considering, the motivating rationale for identifying PLWD is *not* the goal of fulfilling a direct medical duty to the individual patient. This would be the case if the dementia-detection algorithm was used for a clinical purpose such as identifying PLWD for population management, evaluating their quality of care, and linking those lacking adequate services and supports to appropriate providers or resources. Here, however, we are considering cases in which algorithmic identification is used to facilitate recruitment into research intended to generate generalizable knowledge, for instance, by evaluating interventions or models of care.

Noting this difference in motivating rationales is not to imply that research participation is necessarily incongruous with the interests of patients. It is to say, rather, that the primary motivation for generating new, sensitive, private, identifiable information about patients in these cases is to produce knowledge for the benefit of others. Whether this goal can be reconciled with patients' best

interests depends on the attention given to multiple issues in the design and recruitment practices employed in these studies.[6] (p. 249–297) One of these issues involves the practices and procedures used to secure informed consent.

Consent to identification

Although generating new, sensitive, private, identifiable information about patients is common in medical practice and in many research contexts, algorithmic identification often occurs without direct interaction with the patient or their proxy and, thus, without a prior process of informed consent.

One of the roles of the informed consent process is to provide patients or their proxies with the information they require to understand the nature of a proposed test or procedure, the burdens and risks associated with it, and the benefits it is expected to produce.[33] Patients or their proxies can then assess this balance of risks and potential benefits to determine whether they are acceptable. One advantage of medical testing that involves direct interaction with patients is that patients or their proxies are present to engage in this process of informed consent.

But algorithms that use existing data to identify PLWD need not involve any direct interaction with patients, their proxies or care partners and so can operate in a context in which informed consent has not been – and cannot be – obtained. In cases where models draw directly on data relating to clinical evaluations of patients' cognition, it is possible that patients or their care partners provided consent to medical care with the intent of better understanding the nature and degree of the patient's cognitive impairment. But there may be instances where patients are identified using information that *was not* produced under a process that involved consent to possible identification of a cognitive impairment. For example, a natural language processing algorithm might identify language in clinical notes that is associated with a diagnosis of dementia – but without any indication that the possibility of cognitive impairment was disclosed to the patient or that the patient was referred for appropriate testing. For example, the clinician might have noted that, during a visit to address a respiratory concern, the patient asked the same question many times. When this is the case, algorithmic identification would involve the creation of new, private, identifiable medical information – and also the exposure of patients to any attending risks associated with this information – absent the patient's prior authorization or the proxy's authorization, where appropriate. This does not necessarily entail that generating such information is unethical. It does, however, require care and attention to ensure that the goals that are advanced by this information are of sufficient merit that they can justify the study and that strong protections for patient interests are in place to mitigate attending risks to their interests.

To address these concerns, some health systems might ask patients for "blanket consent" or general permission to use clinical data for future research purposes. However, the moral force of such blanket consent is severely attenuated given that, by definition, there are no clear specific purposes for which this information might be used. This concern is exacerbated by the fact that consent to use clinical data for research purposes is usually granted to advance the goal of research, namely, producing generalizable knowledge. But algorithmic identification involves using different types of data about a patient, (clinical and billing data, for example) to generate new private, identifiable information about that patient. As a result, it is unlikely that policies that solicit blanket consent for future data use are sufficient to respect the autonomy and the wellbeing of individual patient participants.

The ethics of generating new, sensitive, private, identifiable information about patients without their explicit, prior consent, hinges, in part, on the social value of the research and the extent to which study risks can be reduced and participation aligned with participant interests.

Social value, justice and equity

Because the goal of research is to generate generalizable knowledge, a necessary condition for the ethical conduct of research is that proposed studies must have sufficient social value to justify their conduct.[5,34,35] Efforts to use algorithms to promote recruitment of PLWD in research are often seen as

promoting social value because they are motivated by concerns of justice and equity, particularly improving care for this vulnerable population. As a general principle, fairness requires equals to be treated equally. When issues of fairness arise concerning the operation of social institutions that influence the ability of persons to function in ways that are critical to their personal and public life, those fairness issues constitute concerns of justice. As a criterion of justice, important social institutions should be capable of protecting, securing, or advancing the needs of the diverse individuals who rely on those institutions. When gaps exist in the ability of such institutions to function in this way, equity requires efforts to develop the means necessary to close those gaps and to advance the interests of those who are underserved.[6] (p. 148–172)

The social, psychological, and economic burdens dementia places on patients and families are life changing. Interventions to ameliorate these burdens are available, but the evidence to support their widespread dissemination in the health care system is incomplete. Existing research on dementia care interventions is limited by the number of short-term studies with small sample sizes, and a focus on individual-level (rather than community-, policy-, or society-level) interventions.[36] Moreover, the experiences of diverse populations are not reflected in the data.[36] Research is essential to better support PLWD and their care partners by informing decision-making about which interventions should be broadly implemented. When studies are designed to generate the knowledge necessary to address the needs of this population, identifying PLWD for recruitment into research is supported by a strong *prima facie* claim to advance the ends of justice.

As discussed above, disparities in access to established effective care for PLWD exist across demographic groups and within those groups as well. Addressing the needs of PLWD from marginalized and underserved populations advances the goals of equity as well.[9] However, these background disparities further pose a fundamental problem for the use of algorithms to identify PLWD: algorithmic identification relies on sources of data that reflect prior access to, or engagement with, health systems. Broadening the array of data used to identify PLWD may not be sufficient to avoid creating algorithms that recapitulate prior patterns of unequal access to established effective care or that deprioritize marginalized or underrepresented groups. The reason is that the same structural dynamics that influence the likelihood that members of a marginalized group receive a dementia diagnosis frequently influence other aspects of their medical care. This includes disparities in the extent to which members of these populations access health systems more generally, disparities in the probability that their conditions are diagnosed, whether their symptoms are recorded accurately in non-pejorative terms,[37] and how likely they are to access care after diagnosis. Unless care is taken to address the underlying dynamics that create this problem, these systems could exacerbate, rather than rectify, existing patterns of exclusion and injustice.[38]

For example, patients in less contact with health systems are likely to have a smaller data footprint than patients with more regular care, across clinical, administrative, and financial databases. As a result, a critical weakness of algorithms is the systematic under-ascertainment of cases in marginalized populations, such as people who identify as Black. The inherent reliance on clinical and diagnostic information to identify PLWD is hampered by systematic differences in health care access and utilization. These systemic issues extend to other historically excluded and marginalized groups including other racial and ethnic minorities, those who are socioeconomically disadvantaged, and those residing in rural communities. Thus, there is real potential to exacerbate current health disparities, or introduce new health inequities, if caution is not exercised when using algorithms that rely on data generated from engagement with health systems (such as EHR and claims-based data) to identify PLWD for clinical research or care initiatives.

Finally, the limitations of drawing on health system data to rectify patterns of unequal access to health systems is an indicator of additional issues of justice and equity that are likely to arise when patients from underserved populations are recruited into research. In particular, one goal of some approaches to research, such as pragmatic trials, is to allocate participants to study interventions under conditions that directly reflect the circumstances under which those interventions are likely to be administered in practice.[39–41] Such studies thus seek to evaluate interventions against a baseline that

reflects the status quo in health systems. When patients are underserved, however, the care and services they currently receive may fall below a level that experts would regard as medically appropriate. In this case, the status quo for such patients is ethically problematic because it reflects deficits in the ability of health systems to equitably, effectively or efficiently provide care or services that are already established as effective. In such cases, study pragmatism may directly conflict with equity and the rights and interests of study participants.[9]

Reasonable risk

Another necessary condition for ethically permissible research is that the risks of research participation must be reasonable in relationship to anticipated benefits. The risks of research procedures and interactions are typically divided into two categories: (1) risks that are part of activities that have the prospect of providing direct benefits to participants and (2) risks that are part of activities that hold no prospect of direct benefit to participants. Risks in the first category can be justified by the prospect of direct benefit. Risks in the second must be justified by the social value of the information to be generated in the research.

One source of risks associated with the algorithmic identification of PLWD derives from the degree of uncertainty surrounding the identification procedure and the relative probability that some results represent false positives. In recent years, efforts have been made to validate models developed to identify PLWD, but their operating characteristics in actual practice and across settings of care are subject to considerable uncertainty [Supplemental Table].

Typically, when identifying PLWD in practice, researchers prioritize models with higher positive predictive value (PPV) and specificity. PPV of these models range from 50.0–80.4 for diagnosed dementia and 73.0–89.7 for cognitive impairment and dementia phenotype. Specificity of these models range from 88.0–99.1 for diagnosed dementia, 92.0–97.0 for cognitive impairment and dementia phenotype. When identifying people with undiagnosed dementia, researchers typically seek models that optimize sensitivity and specificity. Sensitivity of these models range from 22.5–82.5 and specificity ranges from 83.2–96.4 for diagnosed dementia [Supplemental Table].

Algorithms may be over-inclusive in that they may capture patients who do not have dementia (i.e., false positives) or detect early abnormalities in cognitive function that may not be clinically significant or have little to no impact on activities of daily living (ADL) during the individual's lifetime (i.e., overdiagnosis).[26,42,43] Some might have mild cognitive impairment (MCI) or might be experiencing normal, age-related cognitive changes. In false positive cases, patients may not have age-related cognitive impairments at all but may be experiencing symptoms that are caused by non-neurodegenerative medical conditions, such as depression, sleep disorders, or medication side-effects. However, one validation study found that older adults with a false positive flag on an algorithm were likely to have self-reported memory concerns (51%) and many had ADL (11%) and IADL (34%) limitations.[26] Approximately 30% of these false positives received a dementia diagnosis within the next 2 years. Finally, natural language processing models often lack sufficient context to identify speech patterns that are an indication of dementia from speech patterns produced by a wide range of non-dementia related pathologies or natural variations among speakers. This creates another possible source of inaccurate findings.

Algorithmic identification creates risk for patients incorrectly identified as having dementia. If patients are contacted for study participation in a way that indicates they have dementia, those individuals might experience psychological harm associated with their (false) beliefs about their medical condition,[44] encounter risks from any medical or non-medical actions they take on the basis of this information,[45] or experience stigma[46] (e.g., from others who learn this information). Similarly, if this misinformation is recorded in the patient's medical record, the individual may be subjected to unnecessary testing or experience stigma associated with a dementia diagnosis.

As a result, the risks associated with algorithmic identification are a function of several factors. First is the novelty of the information. Algorithms that create new, private, identifiable

information about which patients or their care providers are unlikely to be aware imposes more risks than approaches that utilize clinical information that is likely associated with clinical testing that indicated an awareness on the part of patients or their care providers of some form of cognitive decline. Second is how this information is recorded and stored. If the results of algorithmic identification are recorded in a patient's medical record, then the patient is exposed to harms from false positives and to the risks associated with disclosure. If these results are stored in a database that is used solely for research purposes, then the harms of false positives might be reduced; storing this information in a way that is not identifiable further mitigates these risks. Third is how this information is communicated to patients, which we turn to next.

Ethical communication

Even in contexts in which patients give consent to medical testing, providers must follow a process that takes care when communicating results that present sensitive medical information. This includes consideration of who communicates the results of algorithmic identification, who receives this information, and what is said to the PLWD or their caregivers; we consider these in turn.

First, dementia can be highly stigmatizing and the revelation of the diagnosis can be an emotionally charged event.[47] As a result, disclosure of this information is best handled by clinicians with experience necessary to meet the emotional and informational needs of patients. Research coordinators or other study team members regularly tasked with routine recruitment tasks might not have the background necessary to meet these needs.

Second, it is critical to determine who ought to receive this information. When algorithms are used to identify PLWD, patients are not present. Although cognition is not the same as capacity, the presence of dementia increases the likelihood that a patient has marginal capacity or lacks capacity. As a result, efforts to contact patients based on algorithmic identification may be directed at patients who cannot comprehend and respond to this information in light of their considered values or are unaware of their potential dementia diagnosis. In particular, if a patient has either marginal or no ability to process this information and to make decisions in light of it, their provider ought to include someone else, such as a caregiver or a proxy, in the disclosure process. The need to identify a caregiver or proxy may arise frequently in algorithmic identification of PLWD, as cognitive deficits may contribute to difficulty comprehending and appreciating information. Complicating this, caregivers' contact information is often not easily found in EHRs.

Third, it is important to carefully evaluate what is said to PLWD or their caregivers. When dementia algorithms are generated for the purpose of facilitating recruitment into research studies, cold-calling patients[48] and providing a truthful explanation of the reason for contacting them risks disclosing medical information that might come as a shock, that might be stigmatizing for patients or their families, and that might also be false. To the extent that researchers want to be sure that the patients they recruit into a study are actually PLWD, it is likely that they would want potential participants to receive additional screening or testing. Trying to avert the risks of shocking, stigmatizing, or sharing false information by withholding the reason for contacting the patient until they can complete additional screening or testing prior to study recruitment may avoid some of these problems but also raises the prospect of actively deceiving patients or of asking patients or their care givers to undergo research-related procedures without having an explicit understanding of their goals and rationale.

Further, if a patient was not previously aware of their dementia diagnosis, disclosing a diagnosis through research recruitment might undermine trust in their healthcare providers and possibly lead some patients or their families to sue providers for malpractice.[49]) Whether such claims would succeed is a fact-specific determination. Even if unsuccessful, however, the legal process can be a source of distress for clinicians and patients alike.

Discussion

We have elaborated six sources of ethical concern about using algorithms to identify PLWD to improve study recruitment. Our exposition is intended to explain the nature and source of distinct ethical issues that are likely to be intimately related in practice. For example, although informed consent is a cornerstone of ethical research with humans, there are accepted criteria and conditions under which institutional review boards (IRBs) can grant waivers of some or all the requirements for prospective, written informed consent. Two of these conditions are relevant to algorithmic identification of PLWD.

The first possibility is focused directly on screening and recruitment. In the US, recently revised federal regulations, known as the "Common Rule," now include provisions for waiving informed consent for research proposals in which "an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative" (45CFR46.116(g)).[50] This waiver can be granted if either: "(1) The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or (2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens."

Interestingly, it is not clear whether these provisions are an appropriate ground to waive consent for algorithmic identification. This uncertainty stems from the fact that this provision speaks of "obtaining" private identifiable information "by accessing records." The underlying ethical idea behind this provision is likely that there is little risk to the rights and interests of patients if researchers are allowed to use information already included in their medical record to identify them as potential candidates for inclusion in a clinical trial. The paradigm case for this kind of waiver would be identifying patients who use a particular medication as possible candidates for a deprescribing study or for taking a different medication instead. But as we have seen, some algorithms combine information from a range of sources to produce new, private, identifiable information, such as a probability for a diagnosis that might not be explicitly recorded in the patients EMR. In the latter cases, the identification process itself creates new information that is relevant to patient interests and that can entail potentially significant risks. In such cases, the determination of whether a waiver can be provided should be based on a substantive consideration of the nature of the information generated and its relationship to the rights and interests of the patient.

The second ground for justifying a waiver of some or all consent provisions is more general and requires researchers to make explicit how they are managing some of the ethical issues we identify in the previous section. In particular, a waiver can be granted if the research meets the following requirements:

(i) The research involves no more than minimal risk to the subjects;
(ii) The research could not practicably be carried out without the requested waiver or alteration;
(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation. (45CFR46.116(f))[51]

In cases where algorithms go beyond merely obtaining private information that is already explicitly stated in a patient's medical record, it is reasonable to require the provision of a waiver to meet these conditions. Doing so requires that researchers and IRBs consider how best to ensure that algorithmic identification both respects the rights and interests of study participants and promotes social value.

As a general strategy, taking careful steps to align the algorithmic identification process with access to established effective clinical care and services can address three ethical concerns. It can reduce the risks associated with algorithmic identification, create a context for securing informed consent and ethically communicating clinical results and mitigate concerns about the lack of access of patients to dementia-related care. An example of how this might be done is Medicare's yearly "wellness" visit that includes the detection of the presence of "any cognitive impairment."[52] Health systems have significant latitude in how they determine priority for such visits. If a risk ranking of the kind contemplated here were used to determine priority for such a visit, then the risk score could be used to place individuals believed to be at high risk of dementia earlier in the cue for an appropriate clinical evaluation.

The results of the algorithmic identification might be recorded only as a priority score for a wellness-visit to detect cognitive impairment. Treating the score as an administrative, rather than a diagnostic, tool might limit risks associated with falsely identifying an individual as having a high likelihood of living with dementia. During the wellness visit, care providers could seek informed consent for cognitive testing and clinical evaluation necessary to assess the extent, nature, and source of an individual's cognitive impairment. During this process, clinicians could also identify patients who have either marginal or no capacity to make their own decisions and determine the proper proxy for medical decisions. If the outcome of the assessment shows dementia, the patient and their care partner will receive appropriate care and be connected, as needed, with services and supports. Part of this conversation could involve the extent to which the patient is interested in participating in research studies or recruitment into a study.

A consequence of this approach is that patients with dementia who are not identified as high risk (i.e., false negatives) will receive lower priority for medical evaluation than other patients with higher risk scores. Whether these risks are permissible will depend on the operating characteristics of the algorithm in question and whether the use of the algorithm is likely to increase the overall number of PLWD who are identified.

Using algorithms to prioritize clinical assessments rather than to recruit patients directly into research studies allows for several ethical issues to be carefully managed. First, this approach recognizes the significant uncertainty surrounding the accuracy of these risk scores and mitigates the risks of false positives because scores are used only to give priority to clinical encounters. This approach strikes an appropriate balance between concern for the wellbeing of patients who might be at high risk of an undiagnosed medical condition and the avoidance of harm from disclosing findings to patients that turn out to be false positives. Second, by seeking patient or proxy consent to cognitive testing, patients or their proxies can be informed about the nature and purpose and implications of cognitive testing prior to its administration. This allows patients or their proxies to make informed decisions about whether they are willing to undergo cognitive testing. Third, this process seeks to link patients to care at the time of diagnosis and can help to situate study participation within a larger plan for advancing patient interests. Fourth, using algorithms to determine priority for more accurate clinical testing and screening helps to ensure that clinical characteristics of study populations are known prior to study initiation, facilitating techniques such as matching or stratification necessary to preserve or enhance the scientific and social value of research.

Finally, this approach might help to mitigate some concerns grounded in justice and equity. We noted that when patient populations are underserved, the baseline of care and services they receive might fall below the *de jure* standard of care. This describes a baseline of care and service that is attainable and sustainable in the health system infrastructure and that reflects the application of existing knowledge and resources to secure and advance the medical interests of the patients in question.[53] When the status quo for a population falls below the *de jure* standard of care then researchers have an obligation to ensure either that potential study participants will be linked to appropriate care and services outside of the study or that the baseline of care and services provided within the study eliminates gaps in access to established effective care that characterizes the current status quo.[6] (p. 407–418) This requirement does not preclude the

conduct of pragmatic clinical trials designed to test strategies for closing such care gaps so long as the strategies under investigation are not known to be less effective than the available alternatives.

Using algorithmic identification to advance equity by identifying PLWD and closing gaps in access to care is an ethically sound goal. However, algorithmic identification is no panacea. The dependence of these approaches on data generated through contact with health systems represents a structural barrier to identifying PLWD in the most underserved populations. Algorithmic approaches are thus no substitute for efforts to improve access to care among the most underserved or minoritized populations. Similarly, successfully identifying PLWD will only advance the cause of equity if health systems can overcome additional barriers that prevent patients from accessing care after they have been identified.

If algorithmic identification for research recruitment is undertaken in cases that do not follow the strategy of aligning the identification process with access to established effective clinical care, then steps will need to be taken to address each of the concerns in the network of ethical issues identified here. To the extent that algorithmic identification involves the production of new, private, identifiable information about a patient, waivers of consent to produce this information should be evaluated under the general requirements outlined earlier ((45CFR46.116(f)) that include an assessment of the associated risks to participants, the feasibility of alternative approaches, and provisions regarding what information will be provided to patients in subsequent meetings or follow-up.

The residual uncertainty associated with algorithmic identification should be considered when evaluating the relationship between patient identification and trial design. For example, using an algorithm to identify patients who might be experiencing some form of cognitive impairment might be more feasible than identifying patients experiencing symptoms of the dementia syndrome. Using an algorithm to identify patients in the latter category for direct recruitment into a study raises issues about the validity of the resulting study population and the reliability of inferences made from a population with uncertain disease etiology.

Because of the under-ascertainment of patients in this population, especially among groups that are already underserved by health systems, careful consideration must be given to the standard of care available to patients in the various arms of such a study. In particular, there are strong reasons to regard it as ethically inappropriate to identify patients who are at high risk for living with dementia but whose condition remains undiagnosed and then to randomize those patients to the status quo in cases where the status quo falls below the provision of treatment or services that would be recommended for such patients by conscientious and informed clinicians.

Finally, we echo calls from the larger literature on algorithms in medicine and urge developers of algorithms to go beyond internal validation (evaluating the performance of an algorithm on a portion of data that has been set aside for evaluation purposes) and external validation (evaluating the performance of a model on an independent data set) to carry out prospective studies that evaluate an algorithm's performance under real-world conditions using metrics that are directly relevant to the judgments of clinicians.[38,54,55]

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References

1. 2022 Alzheimer's disease facts and figures. 2022. Alzheimers Dement. 18(4):700–89. doi:10.1002/alz.12638
2. Amjad H, Roth DL, Sheehan OC, Lyketsos CG, Wolff JL, Samus QM. Underdiagnosis of dementia: an observational study of patterns in diagnosis and awareness in US older adults. J Gen Intern Med. 2018;33(7):1131–38. doi:10.1007/s11606-018-4377-y.
3. Gianattasio KZ, Prather C, Glymour MM, Ciarleglio A, Power MC. Racial disparities and temporal trends in dementia misdiagnosis risk in the United States. Alzheimers Dement (N Y). 2019;5(1):891–98. doi:10.1016/j.trci.2019.11.008.
4. Beauchamp TL, Childress JF. Principles of biomedical ethics. 7th ed. New York, NY: Oxford University Press; 2013.
5. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA. 2000;283(20):2701–11. doi:10.1001/jama.283.20.2701.
6. London AJ. For the common good: philosophical foundations of research ethics. New York, NY: Oxford University Press; 2022a.
7. O'Brien K, Burke R, Karlawish J. A roadmap for modifying clinician behavior to improve the detection of cognitive impairment. J Gen Intern Med. 2022;38(2):508–12. Online ahead of print. doi:10.1007/s11606-022-07824-7.
8. Goins RT, Williams KA, Carter MW, Spencer M, Solovieva T. Perceived barriers to health care access among rural older adults: a qualitative study. J Rural Health. 2005;21(3):206–13. doi:10.1111/j.1748-0361.2005.tb00084.x.
9. Quiñones AR, Mitchell SL, Jackson JD, Aranda MP, Dilworth-Anderson P, McCarthy EP, Hinton L. Achieving health equity in embedded pragmatic trials for PLWD and their family caregivers. J Am Geriatr Soc. 2020;68(Suppl 2):S8–S13. doi:10.1111/jgs.16614.
10. Bradford A, Kunik ME, Schulz P, Williams SP, Singh H. Missed and delayed diagnosis of dementia in primary care: prevalence and contributing factors. Alzheimer Dis Assoc Disord. 2009;23(4):306–14. doi:10.1097/WAD.0b013e3181a6bebc.
11. Osborn R, Doty MM, Moulds D, Sarnak DO, Shah A. Older Americans were sicker and faced more financial barriers to health care than counterparts in other countries. Health Aff (Millwood). 2017;36(12):2123–32. doi:10.1377/hlthaff.2017.1048.
12. Lang L, Clifford A, Wei L, Zhang D, Leung D, Augustine G, Danat IM, Zhou W, Copeland JR, Anstey KJ, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. BMJ Open. 2017;7(2):e011146. doi:10.1136/bmjopen-2016-011146.
13. Ford E, Rooney P, Oliver S, Hoile R, Hurley P, Banerjee S, van Marwijk H, Cassell J. Identifying undetected dementia in UK primary care patients: a retrospective case-control study comparing machine-learning and standard epidemiological approaches. BMC Med Inform Decis Mak. 2019;19(1):248. doi:10.1186/s12911-019-0991-9.
14. Aranda MP, Kremer IN, Hinton L, Zissimopoulos J, Whitmer RA, Hummel CH, Trejo L, Fabius C. Impact of dementia: health disparities, population trends, care interventions, and economic costs. J Am Geriatr Soc. 2021;69(7):1774–83. doi:10.1111/jgs.17345.
15. 2021 Alzheimer's disease facts and figures. Special report on race, ethnicity and Alzheimer's in America. Alzheimers Dement. 2021;17(3):327–406. doi:10.1002/alz.12328.
16. Lin PJ, Daly AT, Olchanski N, Cohen JT, Neumann PJ, Faul JD, Fillit HM, Freund KM. Dementia diagnosis disparities by race and ethnicity. Med Care. 2021;59(8):679–686. doi:10.1097/MLR.0000000000001577.
17. Amra S, O'Horo JC, Singh TD, Wilson GA, Kashyap R, Petersen R, Roberts RO, Fryer JD, Rabinstein AA, Gajic O. Derivation and validation of the automated search algorithms to identify cognitive impairment and dementia in electronic health records. J Crit Care. 2017;37:202–05. doi:10.1016/j.jcrc.2016.09.026.
18. Barnes DE, Zhou J, Walker RL, Larson EB, Lee SJ, Boscardin WJ, Marcum ZA, Dublin S. Development and validation of eRADAR: A tool using EHR data to detect unrecognized dementia. J Am Geriatr Soc. 2020;68(1):103–11. doi:10.1111/jgs.16182.
19. Coley RY, Smith JJ, Karliner L, Idu AE, Lee SJ, Fuller S, Lam R, Barnes DE, Dublin S. External validation of the eRADAR risk score for detecting undiagnosed dementia in two real-world healthcare systems. J Gen Intern Med. 2023;38(2):351–360. doi:10.1007/s11606-022-07736-6.
20. Group Health Cooperative. Dementia. PheKB. 2012. [accessed 2023 Jul 23]. https://phekb.org/phenotype/10
21. Jaakkimainen RL, Bronskill SE, Tierney MC, Herrmann N, Green D, Young J, Ivers N, Butt D, Widdifield J, Tu K. Identification of physician-diagnosed Alzheimer's disease and related dementias in population-based administrative data: a validation study using family physicians' electronic medical records. J Alzheimers Dis. 2016;54(1):337–49. doi:10.3233/JAD-160105.
22. Moura L, Festa N, Price M, Volya M, Benson N, Zafar S, Weiss M, Blacker D, Normand S-L, Newhouse J, et al. Identifying Medicare beneficiaries with dementia. J Am Geriatr Soc. 2021;69(8):2240–51. doi:10.1111/jgs.17183 .
23. Newton KM, Peissig PL, Kho AN, Bielinski SJ, Berg RL, Choudhary V, Basford M, Chute CG, Kullo IJ, Li R, et al. Validation of electronic medical record-based phenotyping algorithms: results and lessons learned from the eMERGE network. J Am Med Inform Assoc. 2013;20(e1):e147–e54. doi:10.1136/amiajnl-2012-000896.

24. Shao Y, Zeng QT, Chen KK, Shutes-David A, Thielke SM, Tsuang DW. Detection of probable dementia cases in undiagnosed patients using structured and unstructured electronic health records. BMC Med Inform Decis Mak. 2019;19(1):128. doi:10.1186/s12911-019-0846-4.
25. Tyagi T, Magdamo C, Noori A, Li Z, Liu X, Deodhar M, Hong Z, Ge W, Ye E, Sheu Y, et al. Using deep learning to identify patients with cognitive impairment in electronic health records. ArXiv. 2021. [accessed 2023 Jul 23] abs/2111.09115. doi:10.48550/arXiv.2111.09115.
26. Grodstein F, Chang C-H, Capuano AW, Power MC, Marquez DX, Barnes LL, Bennett DA, James BD, Bynum JPW. Identification of dementia in recent Medicare claims data, compared with rigorous clinical assessments. J Gerontol A Biol Sci Med Sci. 2022;77(6):1272–78. doi:10.1093/gerona/glab377.
27. Jaakkimainen L, Duchen R, Lix L, Al-Azazi S, Yu B, Butt D, Park S-B, Widdifield J. Identification of early onset dementia in population-based health administrative data: a validation study using primary care electronic medical records. J Alzheimers Dis. 2022;89(4):1463–72. doi:10.3233/JAD-220384.
28. McCarthy EP, Chang C-H, Tilton N, Kabeto MU, Langa KM, Bynum JPW. Validation of claims algorithms to identify Alzheimer's disease and related dementias. J Gerontol A Biol Sci Med Sci. 2022;77(6):1261–71. doi:10.1093/gerona/glab373.
29. Torous J, Kiang MV, Lorme J, Onnela JP. New tools for new research in psychiatry: a scalable and customizable platform to empower data driven smartphone research. JMIR Ment Health. 2016 May 5;3(2):e16. doi:10.2196/mental.5165. PMID: 27150677; PMCID: PMC4873624.
30. Harron K. Data linkage in medical research. BMJ Med. 2022;1(1):e000087. doi:10.1136/bmjmed-2021-000087.
31. Xu WY, Jung J, Retchin SM, Li Y, Roy S. Rural-urban disparities in diagnosis of early-onset dementia. JAMA Netw Open. 2022;5(8):e2225805. doi:10.1001/jamanetworkopen.2022.25805.
32. Rewerska-Juśko M, Rejdak K. Social stigma of people with dementia. J Alzheimers Dis. 2020;78(4):1339–43. doi:10.3233/JAD-201004.
33. Berg JW, Appelbaum PS, Lidz CW, Parker LS. Informed consent: legal theory and clinical practice. 2nd ed. New York, NY: Oxford University Press; 2001.
34. Wendler D, Rid A. In defense of a social value requirement for clinical research. Bioethics. 2017;31(2):77–86. doi:10.1111/bioe.12325.
35. Wenner DM. The social value of knowledge and the responsiveness requirement for international research. Bioethics. 2017;31(2):97–104. doi:10.1111/bioe.12316.
36. Larson EB, Stroud C, editors 2021. Meeting the Challenge of Caring for Persons Living with Dementia and Their Care Partners and Caregivers: A Way Forward. Washington, D.C.: National Academies Press; [accessed 2023 Jul 23]. doi: 10.17226/26026.
37. Sun M, Oliwa T, Peek ME, Tung EL. Negative patient descriptors: documenting racial bias in the electronic health record. Health Aff (Millwood). 2022;41(2):203–11. doi:10.1377/hlthaff.2021.01423.
38. London AJ. Artificial intelligence in medicine: Overcoming or recapitulating structural challenges to improving patient care? Cell Rep Med. 2022b;3(5):100622. doi:10.1016/j.xcrm.2022.100622.
39. Largent EA, Hey SP, Harkins K, Hoffman AK, Joffe S, Lima JC, London AJ, Karlawish J. Ethical and regulatory issues for embedded pragmatic trials involving people living with dementia. J Am Geriatr Soc. 2020;68(Suppl 2):S37–S42. doi:10.1111/jgs.16620.
40. Weinfurt KP, Hernandez AF, Coronado GD, DeBar LL, Dember LM, Green BB, Heagerty PJ, Huang SS, James KT, Jarvik JG, et al. Pragmatic clinical trials embedded in healthcare systems: generalizable lessons from the NIH Collaboratory. BMC Med Res Methodol. 2017;17(1):144. doi:10.1186/s12874-017-0420-7.
41. Welch MJ, Lally R, Miller JE, Pittman S, Brodsky L, Caplan AL, Uhlenbrauck G, Louzao DM, Fischer JH, Wilfond B. The ethics and regulatory landscape of including vulnerable populations in pragmatic clinical trials. Clin Trials. 2015;12(5):503–10. doi:10.1177/1740774515597701.
42. Capurro D, Coghlan S, Pires DEV. Preventing digital overdiagnosis. 2022. JAMA. 2022;327(6):525–26. doi:10.1001/jama.2021.22969.
43. Maki Y. Reconsidering the overdiagnosis of mild cognitive impairment for dementia prevention among adults aged ≥80 years. J Prim Health Care. 2021;13(2):112–115. doi:10.1071/HC20115.
44. Lingler JH, Sereika SM, Butters MA, Cohen AD, Klunk WE, Knox ML, McDade E, Nadkarni NK, Roberts JS, Tamres LK, et al. A randomized controlled trial (RCT) of amyloid positron emission tomography (PET) results disclosure in mild cognitive impairment (MCI). Alzheimers Dement. 2020;16(9):1330–37. doi:10.1002/alz.12129.
45. Hellmuth J, Rabinovici GD, Miller BL. The rise of pseudomedicine for dementia and brain health. JAMA. 2019;321(6):543–44. doi:10.1001/jama.2018.21560.
46. Milne A. The 'D' word: reflections on the relationship between stigma, discrimination and dementia. J Ment Health. 2010;19(3):227–33. doi:10.3109/09638231003728166.
47. Pinner G, Bouman WP. What should we tell people about dementia? Adv Psychiatr Treat. 2003;9(5):335–41. doi:10.1192/apt.9.5.335.
48. Clayton EW. Incidental findings in genetics research using archived DNA. J Law Med Ethics. 2008;36(2):286–91. doi:10.1111/j.1748-720X.2008.00271.x.

49. Morain S, Largent E. Think pragmatically: investigators' obligations to patient-subjects when research is embedded in care. Am J Bioeth. 2023;23(8):10–21. doi:10.1080/15265161.2022.2063435.
50. General requirements for informed consent: screening, recruiting, or determining eligibility. 45 C.F.R. § 46.116(f). [accessed 2023 Jul 23].
51. General requirements for informed consent: general waiver or alteration of consent. 45 C.F.R § 46.116(g). [accessed 2023 Jul 23]. https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.116.
52. Yearly "Wellness" Visits Coverage. Medicare.gov. [accessed 2023 Jul 23]. https://www.medicare.gov/coverage/yearly-wellness-visits.
53. London AJ. The ambiguity and the exigency: clarifying "standard of care" arguments in international research. J Med Philos. 2000;25(4):379–97. doi:10.1076/0360-5310(200008)25:4;1-A;FT379.
54. Adibi A, Sadatsafavi M, Ioannidis JPA. Validation and utility testing of clinical prediction models: time to change the approach. JAMA. 2020;324(3):235–36. doi:10.1001/jama.2020.1230.
55. McDermott MBA, Wang S, Marinsek N, Ranganath R, Foschini L, Ghassemi M. Reproducibility in machine learning for health research: still a ways to go. Sci Transl Med. 2021;13(586):eabb1655. doi:10.1126/scitranslmed.abb1655.