



A pragmatic clinical trial assessing the effect of a targeted notification and clinical support pathway on the diagnostic evaluation and treatment of individuals with left ventricular hypertrophy (NOTIFY-LVH)

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Background Electronic health records contain vast amounts of cardiovascular data, including potential clues suggesting unrecognized conditions. One important example is the identification of left ventricular hypertrophy (LVH) on echocardiography. If the underlying causes are untreated, individuals are at increased risk of developing clinically significant pathology. As the most common cause of LVH, hypertension accounts for more cardiovascular deaths than any other modifiable risk factor. Contemporary healthcare systems have suboptimal mechanisms for detecting and effectively implementing hypertension treatment before downstream consequences develop. Thus, there is an urgent need to validate alternative intervention strategies for individuals with preexisting—but potentially unrecognized—LVH.

Methods Through a randomized pragmatic trial within a large integrated healthcare system, we will study the impact of a centralized clinical support pathway on the diagnosis and treatment of hypertension and other LVH-associated diseases in individuals with echocardiographic evidence of concentric LVH. Approximately 600 individuals who are not treated for hypertension and who do not have a known cardiomyopathy will be randomized. The intervention will be directed by population health coordinators who will notify longitudinal clinicians and offer to assist with the diagnostic evaluation of LVH. Our hypothesis is that an intervention that alerts clinicians to the presence of LVH will increase the detection and treatment of hypertension and the diagnosis of alternative causes of thickened myocardium. The primary outcome is the initiation of an antihypertensive medication. Secondary outcomes include new hypertension diagnoses and new cardiomyopathy diagnoses. The trial began in March 2023 and outcomes will be assessed 12 months from the start of follow-up.

Conclusion The NOTIFY-LVH trial will assess the efficacy of a centralized intervention to improve the detection and treatment of hypertension and LVH-associated diseases. Additionally, it will serve as a proof-of-concept for how to effectively utilize previously collected electronic health data to improve the recognition and management of a broad range of chronic cardiovascular conditions.

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Keywords: Left ventricular hypertrophy; LVH; Pragmatic clinical trial; Cardiovascular population health; Undiagnosed hypertension; Cardiomyopathies

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Introduction

Despite impressive innovations in medical technology and therapeutics, cardiovascular disease remains the leading cause of mortality in the United States and worldwide.¹⁻⁴ While much focus and innovation has been devoted to disease management, there is a growing recognition that upstream preventive strategies that leverage easily measurable or previously collected data may yield significant improvements in overall population-health in a cost effective and scalable manner.⁵⁻⁹

With its vast amount of aggregated clinical data, the electronic health record (EHR) provides an opportunity to identify at-risk individuals who may benefit from targeted upstream interventions. Within the realm of cardiovascular disease, the EHR contains potential clues that an individual may have unrecognized cardiac conditions. One important example is the identification of left ventricular hypertrophy (LVH) on echocardiography.¹⁰⁻¹⁴ Even when LVH is reported, the finding may be underappreciated and not prompt further evaluation.

Determining the etiology of LVH and initiating targeted therapies can provide significant long-term benefits for patients. Specifically, since the most common cause of LVH is undiagnosed or untreated hypertension,¹⁵⁻¹⁸ the finding of LVH should—at a minimum—prompt a thorough evaluation for underlying hypertension. In the United States, hypertension and its downstream consequences account for more cardiovascular deaths than any other modifiable cardiovascular risk factor.^{19,20} Among US adults with uncontrolled blood pressure, more than 50% of individuals are either unaware of their diagnosis or are aware of their hypertension but are nonetheless untreated.²¹ Critically, many patients have evidence of subclinical end-organ damage from hypertension even before it is formally diagnosed and treated. Without sufficient treatment, the increased ventricular loading conditions from hypertension lead to structural changes within the myocardium and vasculature, predisposing individuals to heart failure and coronary artery disease.^{22,23} Additionally, when an individual is found to have LVH but does not have hypertension, a comprehensive workup is necessary to evaluate for alternate underlying causes.

Despite the recognition that poorly-controlled hypertension leads to adverse cardiovascular events and that delayed cardiomyopathy diagnosis leads to significantly worse outcomes, there are often barriers in care delivery systems that contribute to substandard treatment. Such obstacles include suboptimal patient identification and diagnosis, therapeutic inertia, significant delays in medication initiation, and potential lack of patient engagement.⁶ Notably, prior work built upon EHR-based registries focused on cardiovascular disease management has yielded impressive results using remote, centralized interventions.²⁴⁻²⁹ Whether such an approach can leverage previously collected and potentially actionable car-

diovascular imaging findings to impact patient care is unknown.

Accordingly, through a pragmatic randomized clinical trial, we plan to implement and study the impact of a centralized clinical support pathway on the diagnosis and treatment of LVH-associated disorders. Our preliminary data demonstrate that there is a large population of individuals with LVH who are neither treated for hypertension nor have a diagnosis of a known cardiomyopathy who may benefit from targeted evaluation prior to the onset of clinically significant pathology. In addition to advancing the early recognition and treatment of LVH-associated diseases, we believe that our work will serve as proof-of-concept for how to utilize routinely collected but underutilized electronic health data to improve the detection and management of a broad range of chronic cardiovascular conditions.

Study aims

The NOTIFYLVH trial has 2 aims. The primary aim is to determine whether a targeted notification regarding a clinical marker suggestive of abnormal ventricular loading conditions—namely, the presence of concentric LVH on echocardiography—can increase the rates of detection and treatment of hypertension through a centralized population-health based clinical support intervention. The secondary aim is to determine whether offering a thorough screening for hypertension in individuals with LVH can lead to an increase in the diagnosis of other causes of thickened myocardium such as infiltrative and genetic cardiomyopathies.

To achieve these aims, we will use echocardiogram data previously collected through routine medical care within the Mass General Brigham (MGB) system to identify individuals with concentric LVH. For individuals with concentric LVH who have not been treated with antihypertensive medications and who do not have a known cardiomyopathy, we will notify their longitudinal health-care clinicians about the presence of LVH and offer to facilitate further diagnostic evaluation. If the patient is ultimately recognized to have hypertension, we hypothesize that patients and their clinicians will be likely to pursue blood pressure control measures since they have been alerted to objective evidence of the end-organ impact of untreated hypertension.³⁰ Additionally, by prompting the further evaluation of LVH, we hypothesize that individuals with LVH—but who do not have hypertension—will be more likely to receive thorough evaluations and potential diagnoses of alternate causes of abnormal myocardial structure.

Materials and methods

Overall study design and pragmatic intervention

We plan to conduct a randomized, pragmatic clinical trial to achieve our aims. Once the cohort has been es-

tablished (see “Entry Criteria” below), we will randomize individuals 1:1 to an intervention arm that is directed by trained population health coordinators and overseen by trial physicians. For subjects randomized to the intervention arm, population health coordinators will notify the identified clinician that their patient has a prior echocardiogram demonstrating concentric LVH. If the subject has an established longitudinal specialty clinician, that clinician will be the primary contact. A “longitudinal specialty clinician” will be defined as a cardiologist or nephrologist with whom the subject had one or more visits in the prior 12 months or two or more visits in the prior 24 months. If the subject does not have an established longitudinal specialty clinician, the population health coordinator will communicate with the primary care provider (PCP). The identified outpatient clinician will be notified via the EHR messaging system that the finding of LVH—in the absence of significant valvular heart disease or a previously diagnosed cardiomyopathy—may reflect undiagnosed or untreated hypertension.

Through a structured EHR-based correspondence with the identified clinician, the population health coordinator will offer to schedule a dedicated visit for the clinician and their patient to discuss the echocardiographic finding of LVH. Additionally, the population health coordinator will offer to coordinate free-of-charge 24-hour ambulatory blood pressure monitoring before or after the patient visit as part of the evaluation of LVH. Many individuals with clinical manifestations of hypertension but without a known diagnosis may have “masked hypertension,” whereby blood pressure measurements outside of a clinical setting are, in fact, elevated to the hypertensive range. Such individuals are likely to benefit from further workup with extended home blood pressure monitoring, for which 24-hour ambulatory blood pressure monitoring is considered the gold standard methodology.^{19,31} Finally, for subjects without established cardiology care and whose etiology of LVH remains undetermined after clinical evaluation, the population health coordinator will offer to coordinate a visit with a cardiologist to discuss the finding of LVH. See [Figure 1](#) for an overall schematic of the trial design and intervention.

Consistent with existing operational approaches for other disease conditions, the population health coordinator will communicate directly with clinicians and study subjects to facilitate the requested intervention(s).²⁶ Specifically, the population health coordinator will interface with clinicians via the MGB internal EHR communication system (“Epic In-Basket”) using templated messages. The population health coordinator will communicate with subjects preferentially via the EHR patient portal (“Epic Patient Gateway”) using standardized messages. For subjects without access to the EHR patient portal or for those who prefer to communicate by telephone, the population health coordinator will interface

with the subject by telephone. See the *Supplement* for the detailed population health coordinator protocol and the associated standardized clinician and subject messages.

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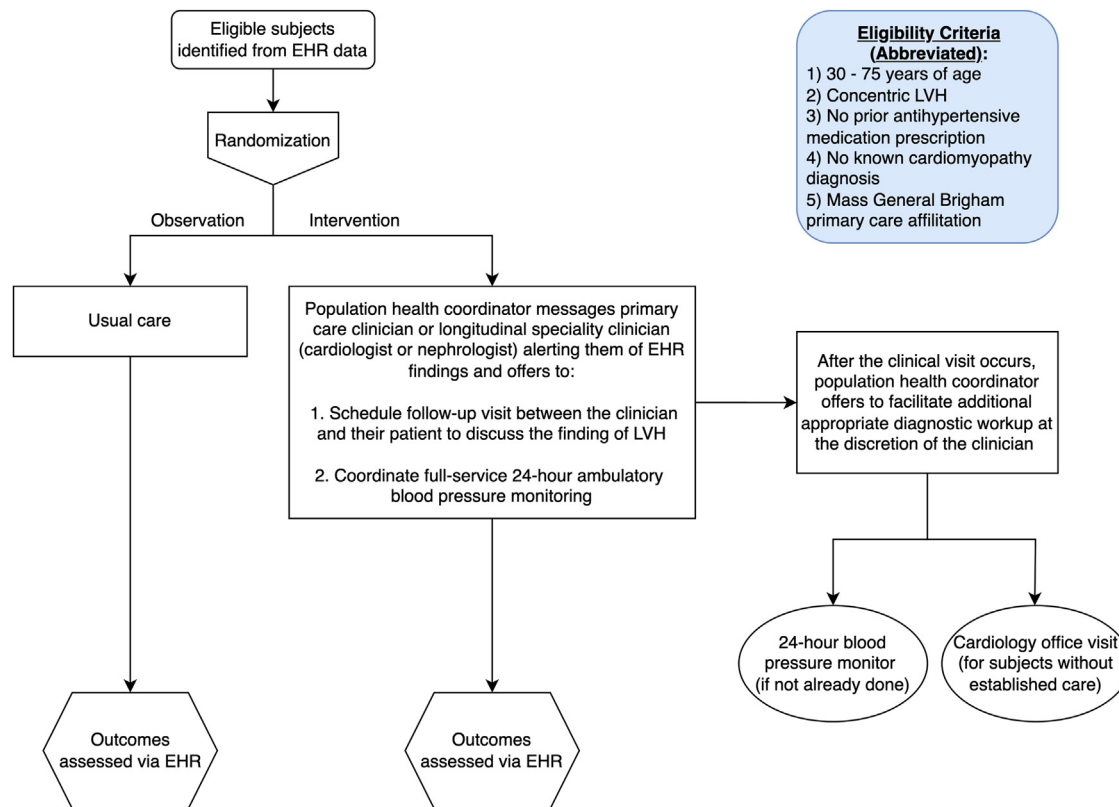
Data sources and baseline covariate assessment

There will be two primary and interrelated data sources for this trial: (1) the MGB Research Patient Data Registry (RPDR)³² and (2) the MGB Enterprise Data Warehouse (EDW). Both systems represent centralized data warehouses that consolidate clinical information from sites of care within the MGB network. MGB is a large, multi-institutional and integrated healthcare delivery network serving the greater Boston, MA area and includes 5 academic and 6 community hospitals along with affiliated outpatient clinics. MGB has approximately 2.5 million unique clinical encounters per year and has more than 800,000 patients within its primary care network. The MGB data repositories consolidate sociodemographic details, diagnosis and procedural codes, encounter details, medication prescription data, clinical documentation, and imaging reports.

For the NOTIFYLVH trial, we have developed and validated a custom natural language processing (NLP) module^{33,34} using the open-source Canary platform. This platform allows for the development of highly accurate language models that can be implemented at scale.³⁴⁻³⁷ Through a rigorous physician-led validation process, the NLP module demonstrated excellent performance characteristics across 10 subtypes of LVH, with sensitivity and specificity exceeding 96%, a positive predictive value of 99.5%, and a negative predictive value of 96.3%.³³ After identifying subjects with concentric LVH on prior echocardiogram reports using these NLP methods, baseline characteristics for eligible trial subjects will be obtained from the above-mentioned MGB data repositories. Variables will include age, sex, self-reported race/ethnicity, medical insurance type, and relevant comorbidity data gathered from the subject’s current EHR problem lists. Key comorbidities will include diagnoses of diabetes, hypertension, history of myocardial infarction or stroke, and chronic kidney disease. Additionally, from transthoracic echocardiogram reports, we will extract echocardiogram parameters including ejection fraction, left ventricular wall and cavity dimensions, and the narrative clinical descriptors of LVH.

Markers of socioeconomic status will be incorporated into our work using the Area Deprivation Index (ADI). The ADI is a validated marker of neighborhood level socioeconomic disadvantage, a surrogate for individual so-

Figure 1



Schematic of the overall pragmatic trial design and intervention.

cioeconomic status. The ADI combines 17 measures of employment, income, housing, and education from the American Community Survey to create a score for each geographic unit in the United States.³⁸⁻⁴⁵ Each subject's home address will be indexed to its associated ADI score and incorporated into baseline characteristics.

Entry criteria

Subject selection will occur in the following manner and a complete list of study eligibility criteria is detailed in Figure 2. First, we will query the MGB data repositories for individuals aged 30 to 75 years who underwent a transthoracic echocardiogram as of January 01, 2019 at an MGB institution.

Next, using the validated NLP module, we will extract which of the queried individuals have documented concentric LVH on their most recent echocardiogram reports. The natural language model was designed to extract both narrative clinical descriptions of LVH as well as technical echocardiographic measurements to allow for specific calculations such as relative wall thickness⁴⁶ to improve the specificity of our algorithms. Relative wall thickness will be defined as $(2 \times \text{posterior wall thickness}) / (\text{left ventricular internal dimension at end diastole})$ in accordance with the American Society of Echocardiography guidelines.⁴⁷ Only subjects with echocardiograms with relative wall thickness ≥ 0.42 - indicative of "concentric remodeling" or "concentric hypertrophy" - will be eligible for study inclusion.

Subjects with NLP-derived (1) nonspecific references to LVH, (2) mild LVH, or (3) moderate LVH will be selected for cohort entry. Subjects with NLP-derived moderate or severe aortic stenosis, severe concentric LVH, or any subtype of asymmetric LVH will be excluded from the cohort as the cause of LVH in these individuals is unlikely to be primarily due to untreated hypertension or an unknown cardiomyopathy. Additional details regarding the NLP-derived LVH definition for trial eligibility and LVH subtypes are available in the *Supplement*.

To maximize accurate data capture for both enrollment eligibility and eventual outcome assessment, individuals will be eligible for study inclusion if they have an MGB PCP and have had at least 1 PCP practice visit within the prior 24 months. Additionally, subjects must *not* have been previously prescribed an outpatient antihyperten-

Figure 2

<p>Inclusion Criteria:</p> <ol style="list-style-type: none"> 1) Age 30-75 years 2) Transthoracic echocardiogram as of 1/1/2019 3) Concentric LVH* 4) Mass General Brigham PCP affiliation with at least 1 PCP practice visit within the last 24 months <p>Exclusion Criteria:</p> <ol style="list-style-type: none"> 1) Current or previous outpatient blood pressure medication prescription (based on EHR records) 2) Known cardiomyopathy (or had an outpatient visit diagnosis for a cardiomyopathy) 3) Moderate or severe aortic stenosis* 4) Severe concentric LVH* 5) Asymmetric LVH* 6) Active cancer treatment plan 7) History of prosthetic heart valve 8) History of heart or lung transplantation 9) Bicuspid aortic valve 10) Autonomic dysfunction 11) Dementia 12) Residents of nursing homes or long-term care facilities 13) Current pregnancy <p>* Derived through natural language processing</p>
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Study eligibility criteria.

Table I. Outpatient antihypertensive agents considered for eligibility criteria and the primary study outcome

ACE inhibitors	Angiotensin receptor blockers	Calcium channel blockers	Diuretics	Beta blockers	Alpha blockers	Vasodilators
Benazepril	Azilsartan	Amlodipine	Amiloride	Acebutolol	Doxazosin	Clonidine
Captopril	Candesartan	Diltiazem	Bumetanide*	Atenolol	Terazosin	Hydralazine
Enalapril	Eprosartan	Felodipine	Chlorthalidone	Carvedilol		Isosorbide
Fosinopril	Irebesartan	Nifedipine	Eplerenone	Labetalol		
Lisinopril	Losartan	Verapamil	Furosemide*	Metoprolol		
Perindopril	Olmesartan		Hydrochlorothiazide	Nadolol		
Quinapril	Telmisartan		Indapamide	Nebivolol		
Ramipril	Valsartan		Spironolactone	Pindolol		
Trandolapril			Torsemide*	Propranolol		
			Triamterene			

* These agents will only be considered for the exclusion criteria but will not be considered antihypertensive agents for the primary study outcome measure

sive medication based on EHR records prior to randomization as detailed in Table I. Furthermore, individuals with a known cardiomyopathy coded on their medical problem list (or had an outpatient visit diagnosis for a cardiomyopathy) based on International Classification of Diseases-10 (ICD-10) codes (as detailed in the *Supplement*) will be excluded. Finally, individuals on active cancer therapy treatment plans, individuals with prosthetic heart valves, individuals with a history of heart or lung transplantation, individuals with bicuspid aortic valves, individuals with autonomic dysfunction, individuals with dementia, individuals whose primary address is in a nursing home or long-term care facility, and pregnant subjects will be excluded.

Enrollment and randomization

The NOTIFYLVH trial obtained approval from the MGB Institutional Review Board (protocol number

2022P002383; approved December 21, 2022). Given the pragmatic nature of the clinical trial and its integration into routine care, the MGB Institutional Review Board waived the requirement for informed consent. The trial has been registered at clinicaltrials.gov, identifier: NCT05713916.

After applying the entry criteria and randomizing the eligible study cohort, MGB clinicians (the PCP or longitudinal specialty clinician) will be contacted about their patients randomized to the intervention arm of the study. The population health coordinator will offer to assist the clinician in pursuing additional diagnostic evaluation for their patient with LVH as detailed in "Overall Study Design of the Pragmatic Intervention" above. The population health coordinator will work within their usual scope of care, providing clinician support by coordinating visits and arranging diagnostic testing at the discretion of the patient's longitudinal clinician.

Randomization will be performed at the individual subject-level (as opposed to clinician or practice-level cluster randomization). This approach is justified as the likelihood of contamination in the usual care arm is expected to be extremely low as the eligible population comes from numerous hospitals and clinics within MGB's large healthcare network. As part of feasibility testing, the median number of eligible subjects per clinician was 1 (IQR 1, 2). Additionally, clinicians who are contacted about a patient randomized to the intervention arm will be unaware as to whether they have additional patients who meet eligibility criteria for this intervention. Finally, given the relatively short trial period of 12 months, the risk of contamination is further minimized.

Subjects will be randomized in a 1:1 fashion to the intervention and observation arms of the study (see "Statistical Analysis Plan" below). Stratified randomization will be performed to help better achieve balance in key covariates.^{48,49} The categorical variables that will be employed for stratified randomization include: (1) **age:** 30 to 60 years versus 61 to 75 years and (2) **echocardiogram year:** January 01, 2019 to December 31, 2020 versus those performed after January 01, 2021. These stratification variables were chosen as they are likely to be important factors that influence a clinician's likelihood of pursuing further evaluation and potential management of LVH. A statistician who is not involved in the study design or the intervention procedures will perform the stratified randomization and assign individuals to the intervention and observation groups.

For the intervention arm, the start of follow-up for each subject will be defined as the date the first EHR message is sent to the subject's identified clinician. To ensure equal follow-up, corresponding intervention-observation subject dyads will be generated at randomization to establish the start of follow-up for subjects in the observation arm. Accordingly, for the observation cohort, the start of follow-up for each subject will be defined when the corresponding intervention subject's clinician is messaged.

Outcome measures

The *primary outcome* of the NOTIFY-LVH trial will be the initiation of an antihypertensive medication. The initiation of an antihypertensive medication will be confirmed by manual chart review blinded to treatment assignment to ensure that the medication was not started primarily for another diagnosis (e.g., propranolol for anxiety). *Secondary outcomes* will be (1) new hypertension diagnoses and (2) new cardiomyopathy diagnoses (e.g., infiltrative cardiomyopathy, hypertrophic cardiomyopathy, etc.) that were not previously identified. Outcomes will be assessed 12 months from the start of follow-up through review of the MGB data repositories (e.g., RPDR, EDW, and/ or EHR data). The detailed adjudication pro-

cess for the study's secondary outcomes is described in the *Supplement*.

Statistical analysis plan

For the primary analyses, we will perform logistic regression to assess the impact of the intervention on the outcomes of interest. Analyses will be adjusted for the 2 stratification variables (e.g., categorical age and echocardiogram year) used as part of the randomization schema to improve precision.^{48,49} Due to the randomized nature of the study design, no adjustment for additional covariates is planned in the primary analyses. However, if there are statistically significant imbalances in baseline covariates between groups despite randomization, we will adjust for those covariates in sensitivity analyses.

Within the study outcomes, the intervention's effect will be assessed in different subgroups using logistic regression. The variables that will be assessed for effect modification will include age (30-60 vs 61-75), sex, race/ethnicity, year of echocardiogram (January 01, 2019 to December 31, 2020 vs after January 01, 2021), Area Deprivation Index (as a marker of socioeconomic status), primary language, prior diagnosis of hypertension, diabetes status, history of myocardial infarction or stroke, degree of NLP-derived LVH, calculated left ventricular mass index, and the presence of a longitudinal cardiologist at baseline.

Key aspects of the trial's implementation—such as clinician response rate, dedicated visits scheduled, 24-hour ambulatory blood pressure monitors ordered, cardiology referrals, downstream cardiovascular testing, etc. – will be collected. Qualitative data describing clinician responses to the notifications will also be recorded. Additionally, to directly elicit clinician and patient perspectives of the trial intervention, we plan to solicit structured and unstructured information using validated qualitative survey techniques and focus-groups. These data will be used to assess the effect of this intervention as well as inform the development of future pragmatic clinical trials within cardiovascular population health.

Previous work in population-health interventions to improve hypertension control increased rates of achieving target blood pressures by 5% to nearly 30%.^{28,29} Assuming that 5% of individuals in the observation group will be started on an antihypertensive medication over the study period without any intervention, we anticipate that the intervention will increase the prescription of an antihypertensive agent to 15%. Using a 2-sided alpha of 0.05 and accounting for 90% power, this would require 188 individuals per arm of the pragmatic trial. To further account for the possibility of missing data capture in our EHR screening algorithms (e.g., a patient is, in fact, already on an antihypertensive agent) as well as potentially significant clinician non-response in the intervention arm, at least an additional 112 individuals will be added to each arm of the trial to ensure sufficient

statistical power. Accordingly, the planned target enrollment will be 300 individuals in the intervention group and 300 in the observation group for a 1 to 1 randomization schema.

All analyses will be performed based on the intention-to-treat principle. Sensitivity analyses will be performed using an “as treated” approach. For those in the intervention arm, individuals will be characterized “as treated” if the population health coordinator receives a positive response from the identified clinician and the subject is seen in a follow up visit where the finding of LVH is planned to be discussed and/ or the patient undergoes 24-hour blood pressure monitoring.

Conclusion

There is an urgent need to develop cost effective and scalable approaches to improve overall cardiovascular population health. Patient data stored in EHR systems and collected during routine medical encounters has the potential to significantly improve patient care through upstream population-health based approaches.^{5,6} As the amount of electronic health information continues to grow, there is a tremendous opportunity to identify and leverage data that are “hiding in plain sight” for targeted interventions.

Moreover, with the proliferation of electronic health data, it is becoming increasingly difficult for clinicians to aggregate and synthesize patient information. While the transition to the EHR over the last decade has brought many benefits, there is increasing evidence that these systems—and the overwhelming amount of data they generate—are leading to clinician burnout.⁵⁰⁻⁵³ Accordingly, designing novel care delivery systems that train and employ skilled individuals who are not typically responsible for direct patient care (such as population health coordinators), has the potential to significantly improve outcomes while also offloading certain clinical and administrative tasks from patient-facing clinicians.^{24,25}

While the focus (from the design and primary outcome perspective) of the NOTIFYLVH trial is the recognition and management of hypertension, the importance of our secondary outcome must be emphasized. With advancing therapeutics, there is an important need to improve the early detection and management of infiltrative and genetic cardiomyopathies prior to the onset of clinical morbidity. While there may be varying degrees of cost effectiveness for such treatments on a population-level—an area that will undoubtedly evolve over time—there is significant patient-level benefit derived from prompt detection and potential tailored treatment. Such examples include directed therapies for cardiac amyloidosis, preventive strategies and risk prognostication for individuals with hypertrophic cardiomyopathy, and enzyme replacement therapies for individuals with Fabry’s disease.

While the NOTIFYLVH trial will likely be underpowered for this prespecified secondary outcome given the relative rarity of these diagnoses, we believe that the trial’s intervention and framework will yield important insights into the role that centralized interventions may play, even for rare cardiovascular disorders.

While there has been an improvement in overall cardiovascular mortality over the last 2 decades,⁵⁴ hypertension-related deaths have increased, with marked racial, socioeconomic, and geographic disparities.⁵⁵⁻⁵⁹ Similar trends and disparities have been described within heart failure epidemiology and treatment.⁶⁰⁻⁶² Given the importance of understanding how therapies and clinical innovations impact different populations, we plan to assess the differential association of key sociodemographics on the study’s outcomes. In particular, through the use of the ADI—a well-established surrogate for individual and community-level socioeconomic factors based on US census data—we will be positioned to better understand how a centralized cardiovascular population health intervention may yield different results for subsets of the target population. Finally, should this intervention be found effective and then implemented widely, the impact of a broad adoption strategy should be prospectively studied, with a key focus on which patient-level factors predict improved outcomes.

Limitations of this trial include its short follow-up period and its use of surrogate outcomes (i.e., the initiation of an antihypertensive medication and establishing new diagnoses). Additionally, while we expect to be more than adequately powered for our primary outcome, we anticipate that the study may be underpowered for the secondary outcomes and subgroup analyses. Despite this limitation, we believe that the secondary outcomes and subgroup analyses will yield valuable information and will help better assess the effect of the study’s intervention on important patient subpopulations. Finally, despite using highly accurate and validated NLP algorithms to characterize LVH on echocardiogram reports, we did not perform direct image adjudication as part of eligibility determination. Given the known inter-observer variability in LVH reporting, it is possible that the reported findings of LVH may have been imprecise, thereby leading to inaccurate study inclusion. While the potential misclassification of LVH could lead to some unnecessary primary care visits, 24-hour ambulatory blood pressure monitors, and/ or cardiology referrals, we believe that this constitutes minimal risk, especially in light of the potential beneficial outcomes being tested by our study. Since our trial’s goal is to demonstrate the effectiveness of this intervention in a real-world setting as part of a pragmatic intervention, we intentionally used the EHR data “as is.” While this may be a limitation, we believe that relying on the available EHR data significantly improves the generalizability of this specific intervention (and other related interventions) harnessing preexisting

cardiovascular EHR data aimed at improving cardiovascular population health.

Particular strengths of the NOTIFY-LVH trial include its rigorous pragmatic randomized trial design, its centralized implementation within a large and diverse healthcare system, and its foundation on open-source and reproducible algorithms to facilitate a future multicenter trial and / or dissemination to other healthcare systems. While the NOTIFY-LVH trial relies on surrogate outcomes (as highlighted in the above section on study limitations), we believe that our outcome measures are nevertheless clinically meaningful. Recognizing that an individual has untreated hypertension and initiating treatment or diagnosing a cardiomyopathy are critical foundational steps in patient care and cardiovascular population health. Should this intervention be studied in a future multicenter implementation trial with extended follow up, additional outcomes such as all-cause mortality and heart failure hospitalizations should be assessed.

We intentionally built the NLP algorithms on an open-source (and user-friendly) platform and designed the data architecture to rely exclusively on ICD-10 codes and electronic medication prescribing information to facilitate the intervention's portability and clinical adoption to other healthcare systems. Accordingly, if the NOTIFY-LVH trial intervention demonstrates clinical efficacy, its adoption by other health systems is anticipated to be quite feasible. Transthoracic echocardiograms with concentric LVH can be identified prospectively by either running our NLP at scheduled intervals or by extracting structured data from echocardiogram reports through the pre-built EHR "click boxes" that are now commonly used within reporting templates. Finally, while our intervention could have used automated EHR alerts with embedded order panels, we specifically opted to have trained and skilled population health coordinators lead the trial intervention. Our goal was to design the intervention in a way that would move care forward without adding significant burden to clinicians or contribute to EHR "alert fatigue." Future iterations of this intervention should consider testing other novel approaches to providing alerts and offering a diagnostic support pathway that is clinician-centered while working to minimize the associated programmatic costs and increasing the ability to implement this intervention widely.

To our knowledge, there have been no prior pragmatic clinical trials evaluating the impact of using previously collected cardiovascular imaging data to improve the detection and treatment of LVH-associated diseases through a centralized population-health based framework. If this intervention is ultimately proven to be effective, it will inform the development of automated pathways whereby individuals who are identified as having LVH (but are not on antihypertensive medications and have no prior diagnosis of a cardiomyopathy) are auto-

matically highlighted for further evaluation. Deploying such automated clinical pathways - especially in large healthcare systems - may enable the detection of a significant group of individuals who will benefit from either aggressive blood pressure control or further evaluation of LVH. Additionally, we hope that our work will serve as a proof-of-concept for how to better utilize routinely collected EHR data to improve the detection and control of a broad range of chronic cardiovascular conditions.

Disclosures

None reported.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.ahj.2023.06.014](https://doi.org/10.1016/j.ahj.2023.06.014).

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