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FRONTIERS IN CARDIOVASCULAR QUALITY AND OUTCOMES

Frontiers of Upstream Stroke Prevention and Reduced Stroke Inequity Through Predicting, Preventing, and Managing Hypertension and Atrial Fibrillation

A Call to Action From the Value in Healthcare Initiative's Predict & Prevent Learning Collaborative

ABSTRACT: Stroke is one of the leading causes of morbidity and mortality in the United States. While age-adjusted stroke mortality was falling, it has leveled off in recent years due in part to advances in medical technology, health care options, and population health interventions. In addition to adverse trends in stroke-related morbidity and mortality across the broader population, there are sociodemographic inequities in stroke risk. These challenges can be addressed by focusing on predicting and preventing modifiable upstream risk factors associated with stroke, but there is a need to develop a practical framework that health care organizations can use to accomplish this task across diverse settings. Accordingly, this article describes the efforts and vision of the multi-stakeholder Predict & Prevent Learning Collaborative of the Value in Healthcare Initiative, a collaboration of the American Heart Association and the Robert J. Margolis, MD, Center for Health Policy at Duke University. This article presents a framework of a potential upstream stroke prevention program with evidence-based implementation strategies for predicting, preventing, and managing stroke risk factors. It is meant to complement existing primary stroke prevention guidelines by identifying frontier strategies that can address gaps in knowledge or implementation. After considering a variety of upstream medical or behavioral risk factors, the group identified 2 risk factors with substantial direct links to stroke for focusing the framework: hypertension and atrial fibrillation. This article also highlights barriers to implementing program components into clinical practice and presents implementation strategies to overcome those barriers. A particular focus was identifying those strategies that could be implemented across many settings, especially lower-resource practices and community-based enterprises representing broad social, economic, and geographic diversity. The practical framework is designed to provide clinicians and health systems with effective upstream stroke prevention strategies that encourage scalability while allowing customization for their local context.

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Heart disease, stroke, and other cardiovascular diseases cause one-third of all deaths in the United States,[1] with stroke alone as the fifth overall cause of death.[2] Due in part to advances in medical technology, health care options, and population health interventions, the population is living longer with cardiovascular conditions. However, age-adjusted stroke mortality has stopped declining in recent years,[3] despite having dropped the previous decade.[4]

Rising stroke-related morbidity and mortality is compounded by sociodemographic inequities in stroke risk. Men have a higher stroke risk yet women are more likely to die[5] and have poorer post-stroke outcomes.[6,7] Many racial and ethnic minority groups have worse stroke morbidity and mortality, emergency department wait times, and care quality, as well as face potential biases in care delivery.[8] They also experience inequitable stroke prevention due to cultural and communication barriers, and other forms of structural inequity.[9,10]

These challenges are addressable by focusing on predicting and preventing modifiable upstream stroke risk factors. This article describes a framework for the implementation of a program on stroke prediction and prevention, identifying frontier recommendations meant to complement existing primary stroke prevention guidelines.[11] It was designed from a literature review paired with the unique stroke leadership and expertise from the Predict & Prevent Learning Collaborative, comprised of diverse stakeholders representing patients, clinicians (cardiologists, vascular neurologists, family medicine), health systems, disease-specific advocacy groups, academia, government, professional associations, payers, pharmacy, industry, and others. The collaborative is part of The Value in Healthcare Initiative,[12] a collaboration of the American Heart Association and the Robert J. Margolis, MD, Center for Health Policy at Duke University.

LEARNING COLLABORATIVE BACKGROUND, PROCESS, AND DELIVERABLE

Studies show that perhaps 80% of strokes are preventable, but investment is rarely concentrated on upstream interventions.[13] Further, clinically apparent strokes only affect ≈3% of the population, but 10% to 30% experience silent or whispering asymptomatic strokes,[14] which contribute to dementia and other conditions of declining function. Any improvement in early identification of stroke risk factors can have a wider impact on not just symptomatic strokes, but also asymptomatic strokes and brain health at-large.

Accordingly, The Value in Healthcare Initiative[12] created the Predict & Prevent Learning Collaborative to identify the frontier of thought leadership for shifting the health system focus on stroke from acute, episodic care to upstream prevention. They met throughout 2019 to scope, refine, deliberate on, and develop this work.

Narrowing the Collaborative Scope

After considering the many medical and lifestyle upstream causes of stroke,[5,15] the learning collaborative chose hypertension and atrial fibrillation prediction, prevention, and management for the focus of the practical framework for stroke prevention.

A summary of the rationale for this decision is 3-fold. First, these risk factors are most directly linked to upstream stroke compared to other medical or behavioral risk factors that may have more diffuse or indirect ties to stroke. Hypertension is the single strongest predictor of all known risk factors for stroke,[16–18] affects the broadest segment of the population (diagnosed[19] and undiagnosed[20]) and very small incremental improvements in blood pressure are associated with significant reduction in stroke. For instance, reducing blood pressure by only 10 mm Hg is associated with a 10% reduction in stroke, suggesting that prevention interventions are tenable at the population level.[21] Atrial fibrillation is one of the most common causes of stroke, particularly among the elderly, among whom it is responsible for ≈24% of ischemic strokes.[22] Incident stroke-related to atrial fibrillation, however, has nearly tripled in the past three decades.[23] Further, ≈2.7 million people remain undiagnosed, resulting in limitations on the ability of health systems and clinicians to adequately support patients with effective interventions.[24,25] Identifying these patients earlier[11] is essential to downstream stroke prevention.

Second, strong evidence-based guidelines are in place to modify these upstream risk factors that can be feasibly implemented across diverse settings. Hypertension is noted as a condition most amenable to broad, scalable, low-cost, community-facing interventions.[26–28] Atrial fibrillation is also amenable to broad intervention. Up to 84% of strokes in atrial fibrillation patients could be effectively prevented with oral anticoagulation treatments,[24,25,29] and there are many new and effective such drugs[11,30–32] or devices,[33] but about half of patients do not receive proper therapy.[34,35]

Third, there are inequities in these risk factors by important demographic and socioeconomic statuses.[36–42] Reducing upstream risk inequities can have multiplicative effects in reducing downstream stroke. As just one example tying hypertension and atrial fibrillation together, atrial fibrillation risk factors are more prevalent among Black patients, and controlling hypertension is noted as crucial for preventing atrial fibrillation in Black patients.[41] This adds another multiplicative layer: reducing hypertension inequities can reduce atrial fibrillation inequities, which in turn can reduce inequi-

ties in downstream stroke. Even when there are potential clinical interventions, an unmet need is to identify those interventions that can be implemented in low-resource settings so that inequities are not worsened.

Goal of Framework and Its Implementation

The collaborative focused on developing a practical framework that leveraged evidence and implemented tools targeting patients most likely to benefit from early intervention. By including both prediction and prevention, the collaborative sought to identify the impact of interventions to prevent stroke and to target those interventions most effectively in the design of a practical framework.

The goal of this work is to complement existing primary stroke prevention guidelines[11] by identifying frontier strategies that address gaps in knowledge or implementation. Recognizing that some areas crucial to upstream stroke prevention do not yet have interventions with a strong evidence base, in some cases we used our expert learning collaborative members to make frontier recommendations. These recommendations are based off of promising early evidence and, while they require further research, they are creative strategies to improve upstream stroke prevention. This article accordingly makes recommendations for such an upstream stroke prevention program.

After identifying conceptual models for stroke intervention,[43] we then identified implementation strategies for addressing multiple barriers, including those related to regulatory and policy barriers, implementation in low-resource settings, technological limitations, and patient engagement challenges (especially medication adherence). This decision aligns with discussion in the stroke literature that successful, sustainable stroke prevention requires a framework to be a universal bulldozer: essentially, a cheap, scalable, and tailorable intervention that can bulldoze a universe of barriers at the same time.

Framework Summary and Limitations

Figure 1 presents a conceptual model illustrating how clinicians, health systems, and payers can use the framework in conjunction with official guidelines to build a tailored stroke prevention program with an emphasis on upstream medical risk factor prediction, prevention, and management. A more comprehensive summary of the process of the collaborative to create this framework as well as more context on the background of the collaborative and broader issue, including a decision-tree to identify risk factors, can be found in Appendix 1 in the Data Supplement and elsewhere in this journal issue.

There are 2 limitations to this approach, although we worked to minimize them. First, this article is not, and was not intended to function as, a systematic literature review. While this means it is possible that some studies related to program and implementation could have been missed, we took multiple approaches to identify extant information that complements existing primary stroke prevention guidelines. We evaluated both peer-reviewed and gray literature (such as reports, fact sheets, and other government documents) based on related literature searches on strategies for predicting, preventing, and managing stroke risk factors. We also worked with the large, multi-stakeholder learning collaborative to make sure we identified key topics, including numerous top-level experts: former American Heart Association (AHA) Stroke Council leadership, AHA senior leadership, a former Food and Drug Administration Commissioner and Centers for Medicare & Medicaid Services Administrator, among others. As a positive, in addition to what we found in the literature, this approach allows us to identify crucial unwritten gaps in practice or implementation of stroke prevention and a new frontier of ideas for practice and research. Second, like any such multi-stakeholder group, we cannot guarantee that all viewpoints are represented, and not all members could attend every meeting. However, the collaborative contained many different stakeholder groups and leaders in the field from a diverse spectrum of views, and versions of this work were circulated to all members at different stages of development so that constant feedback could be provided by all.

ASSESSING THE STATE OF UPSTREAM STROKE PREDICTION TOOLS AND PREVENTION INTERVENTIONS

We first took a broad look at how commonly used cardiovascular prediction tools apply to stroke and then at less common tools that aim to predict stroke or stroke risk. We then generally examined major initiatives to address cardiovascular risk upstream and how they apply to stroke. We identified 2 gaps in the current landscape.

Limited Applicability of Widespread Cardiovascular Prediction Models to Stroke, Limited Spread of Tools Identifying Highest Stroke Risk

While there are several commonly used and widespread heart disease related prediction tools, to date these have focused on coronary artery disease or broader cardiovascular disease as opposed to stroke specifically.[44–46] Further, these tools do not provide information on absolute risk of stroke[47] and tend to underestimate the risk

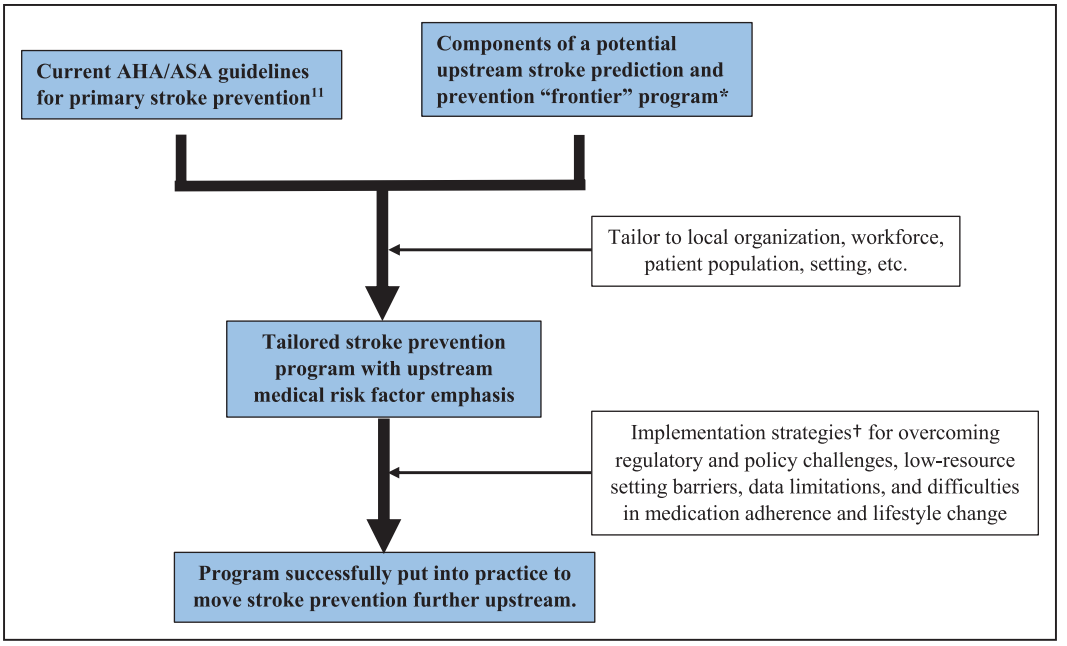

Figure. Conceptual model of how to use the proposed practical framework for moving stroke prevention upstream.
*First half of framework. Summarized in Table 1 of this article; see full text for more detail. †Second half of framework. Summarized in Table 2 of this article; see full text for more detail. AHA indicates American Heart Association; ASA, American Stroke Association.

of stroke, as compared with heart disease, in minority populations.[48] Some tools like $CHADS_2$ and CHA_2DS_2-VASc are designed to help clinicians recognize who is at risk for stroke among patients with atrial fibrillation and when to initiate anticoagulation. Though these tools do provide evidence for predicting the absolute risk of stroke for a given patient, they can be burdensome to calculate without knowing a complete patient history, and can yield inconsistent results across populations.[47] There are newer efforts to identify patients at the highest risk of stroke, such as the HAVOC scoring system (hypertension, age, valvular heart disease, peripheral vascular disease, obesity, congestive heart failure, and coronary artery disease) which identifies higher likelihood of detection of atrial fibrillation after transient ischemic attacks and strokes,[49] with the goal of reducing future stroke risk. These tools are not yet widely used and require validation in additional subpopulations but represent a frontier possibility for atrial fibrillation-related stroke prediction.

Limited Applicability of Upstream Cardiovascular Risk Prevention and Management Interventions to Stroke

There are some interventions working to address upstream risk factors, such as the Paul Coverdell National Acute Stroke Program[50] and the Million Hearts initiative.[51] While these programs aim to increase high-quality care for patients with stroke and those at high risk for stroke, they tend to focus either on stroke in the acute setting or broadly on an array of cardiovascular outcomes with stroke as a small piece of the initiative. Further, many upstream risk factors have been difficult to modify in practice, especially lifestyle factors (which introduces concerns about sustainable change and low specificity to directly prevent stroke). However, it is incredibly important that further research continues to identify better, and more sustainable ways to reduce behavioral and lifestyle risk factors for stroke, especially newer, innovative approaches such as healthy food prescriptions.[52]

The 2 sections below discuss the collaborative's upstream stroke prevention framework for hypertension and atrial fibrillation separately (summarized in Table 1). As noted earlier, many of these recommendations are frontier strategies drawn from the collaborative's front-line experience in stroke prevention.

IDENTIFYING FRONTIER EVIDENCE-BASED STROKE PREVENTION STRATEGIES FOR HYPERTENSION

This section summarizes key evidence regarding components of a frontier program to push stroke prevention further upstream through predicting, preventing, and managing hypertension. These strategies should be used to complement current guidelines for primary stroke prevention related to hypertension[11] (regular blood pressure screening, annual screening for high blood pressure among those with prehypertension, use of antihypertensives in those with hypertension, individualized antihypertensives based on patient

Table 1. Components of a Potential Upstream Stroke Prediction and Prevention Frontier Program*

	Hypertension	Atrial Fibrillation	Both
Screening for risk, follow-up	General population: Mass community screening for hypertension, potentially at places in low-resource communities people regularly visit (consider targeting high risk populations for initial screening and then expanding).	General population: supplement population hypertension screening with screening for pulse and left atrial disease (potentially via hand-held ultrasound screening, machine learning on normal sinus electrocardiograms).	Use of community health workers, other nonphysician clinicians to maximum credentialing: facilitate screenings and treatment, follow-up to ensure proper therapy.
		Patients with diagnosed A-Fib: screening for bleeding risk using HAS-BLED, screening for those with higher risk of stroke using CHA_2DS_2-VASc.	
		Widely available wearables (eg, Apple Watch) may be new options for screening patients for rate, rhythm.	
Medication or device therapy	Continue guideline-adherent hypertension medication therapy.	Continue guideline-adherent anticoagulant medication therapy for A-Fib.	Person-centered medication assessment (weigh patient preferences, side effects, ability to pay).
	Affordable generic polypill, with a rate-controlling antihypertensive and a lipid-lowering medication, may be a future option if made financially viable.	Potential use of Watchman™ device (work to make device more affordable).	
		Potential exploration of generic polypill including atrial fibrillation prevention compounds.	
Outcomes, data, technology	Leverage, link data sources (claims, pharmacy, clinical records) for tracking, managing hypertension at population level. Advanced sites may create physician performance metrics.	Integrate AHA Get With The Guidelines A-Fib with Get With The Guidelines-Stroke and claims data. Adapt from hospital to ambulatory and outpatient settings to create A-Fib registry that can follow individuals after hospitalization.	Use widely available smartphones for collecting patient-reported outcomes. Use integrated patient-generated data from wearables, other devices (eg, connected weight scales, BP cuffs), to facilitate adherence.
		Use EHR to automatically calculate CHA_2DS_2-VASc, HAVOC.	

AHA indicates American Heart Association; A-Fib, atrial fibrillation; HAVOC, hypertension, age, valvular heart disease, peripheral vascular disease, obesity, congestive heart failure, and coronary artery disease; HAS-BLED, Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage; and EHR, electronic health record.

*Program should complement primary stroke prevention strategies from official guidelines[11] to push stroke prevention further upstream.

characteristics and medication tolerance, self-measuring blood pressure, lifestyle modifications, and population screening for hypertension in the emergency department).

Strategies for Prediction, Screening, and Prevention

Because hypertension is a relatively common medical risk factor for cardiovascular disease that can be predicted and managed, population medical screenings (compared with sophisticated algorithms or screening tools) can catch active hypertension and target hypertension upstream by identifying borderline hypertension.

Screening approaches with positive evidence in low-resource settings notably include using community health workers (CHWs) to increase screenings in the community. CHWs are effective at improving hypertension outcomes as evident by one study demonstrating they were able to increase the proportion of patients with controlled hypertension by 20% more than the group with usual care.[17,53–55] Further, screening can occur in places people regularly visit, such as barbershops, beauty shops, grocery stores, pharmacies, and churches, improving screening equity. For example, barbershops offering blood pressure checks with haircuts and promoting physician follow-up improved hypertension control among Black men. In one study, this approach improved rates of 8.8% more than the comparison group.[21,56,57] Similarly, cosmetologists can be important health care promoters for women from diverse racial/ethnic backgrounds, and in one study, cosmetologists that promoted awareness of healthy behaviors yielded 46% of clients reporting healthier food consumption.[58] Moreover, the Food Trust—which works with policymakers, neighborhoods, farmers, schools, and grocers to provide information on healthy decisions, and to ensure availability of affordable, nutritious food—is partnering with corner stores to check blood pressure and basic health.[59]

Strategies for Management

For example, Kaiser Permanente implemented a comprehensive hypertension registry program including developing and sharing performance metrics, implementing evidence-based guidelines, medical assistant visits for blood pressure measurement, and single-pill combination pharmacotherapy.[60] The program increased hypertension control by ≈70% across all racial and ethnic groups. An important aspect contributor to its results was creating a model that constantly reports and reviews blood pressure levels at a population level and then works with patients to ensure follow-up based on blood pressure monitoring.

Table 2. Barriers to Implementation of Hypertension- and Atrial Fibrillation-Focused Upstream Stroke Prevention (and Strategies to Overcome Them)

Barriers for Implementation	Strategies to Overcome Barriers, Examples
Regulatory and policy challenges	
Preventive models often not supported by reimbursement mechanisms.	Alternative payment models can encourage care redesign to support prevention.
Lack of patient-centered stroke-related quality measures limits effective tracking.	Tracking patient-centered outcomes (eg, functional status) can aid risk communication and shared decision-making.
Variation by state in scope of practice for nonphysician clinicians and by payers in services they will reimburse.	Developing standards for real-world data applicable to stroke prevention for use as validated real-world evidence.
Implementation in low resource settings	
Low resource settings tend to serve populations with higher rates of HTN and Afib, but financial restraints limit ability to engage in innovative strategies or prescribe/pay for medications.	Expanding Get With The Guidelines-Atrial Fibrillation to ambulatory, outpatient settings would move atrial fibrillation identification further upstream and support guideline adherence across settings.
SDOH are often acute needs, vary by geography.	Target:BP program offers evidence-based guidance on improving blood pressure management.
	Targeting patients where they are, using health professionals like CHWs can make interventions less costly and more relevant to local needs.
	Identify new payment and financing, such as population-focused payment reforms, grants, or public health funding.
Data limitations	
Lack of rigorously tested surveillance and evaluation tools limits organizations' ability to measure effectiveness.	Wearables and personal technology could help people self-monitor heart health in everyday settings (but evidence is limited and if devices are unaffordable, could worsen inequity).
Variability in access to tools, ongoing interoperability challenges limit tools' impact.	Leverage national data sources and real-world data, incorporate predictive analytics into their functionality, tailor messages, and visually prioritize risk scores.
Limited ability to get real-world data connected to EHR/clinicians.	SMART technology on FHIR allows third party apps to directly provide clinicians with data from apps, integrate into EHR.
Medication adherence and lifestyle change	
Prevention limited by medication adherence.	Patient engagement, empowerment, and education strategies assure patients are knowledgeable of risks, benefits, responsibilities (eg, interactive group online sessions).
Communicating risk to patients is challenging.	Creative messaging that is catchy, attention-grabbing, fun; peer support groups help with translation of risk.
Clinicians often have no data on medication adherence, making targeted approaches difficult.	Wearables, personal technology can engage patients in medication adherence.

Afib indicates atrial fibrillation; CHW, community health worker; EHR, electronic health record; FHIR, Fast Healthcare Interoperability Resources; HTN, hypertension; SDOH, social determinants of health; and SMART, Substitutable Medical Applications and Reusable Technology.

Multiple pharmacological interventions can reduce stroke risk through hypertension, but people may not take medications regularly. A solution may be cardiovascular polypill approaches[17,61] (a pill ideally containing at least one antihypertensive with rate-controlling properties and one lipid-lowering medication). This strategy has been effective in low-income settings in other countries because of affordability and improved adherence relative to multiple pills. This approach would not currently work in the United States, however, because there are no polypill options available.[62] Development of new polypills would likely result in patented pills with high list prices. It would take many years until a generic option is available and, without an affordable generic, price barriers could exacerbate existing socioeconomic inequities in hypertension and stroke. However, it is conceivable that direct development of a generic polypill could happen if a generic manufacturer received long-term payments to make investment worthwhile or agreement between a coalition of payers to develop an affordable generic. Nonetheless, there are affordable hypertension generics currently available, and in the interim, guideline-adherent hypertension medication therapy should be continued.

For all of the above hypertension strategies, programs will need to determine whether to focus on high-risk patients or the general population. A large Veterans Affairs evaluation found that an intervention for all veterans with hypertension yielded larger quality-adjusted life-years gained (35 517) and strokes prevented (20 940) while a more targeted approach for those with prior cardiovascular disease had less quality-adjusted life-years gained (27 856) and fewer strokes prevented (16 479). However, the more targeted

approach, targeting patients with prior cardiovascular disease and/or multiple risk factors, was more resource efficient in per quality-adjusted life-year gained and stroke prevented.[63]

IDENTIFYING FRONTIER EVIDENCE-BASED STROKE PREVENTION STRATEGIES FOR ATRIAL FIBRILLATION

This section summarizes opportunities and evidence regarding components of a frontier program to push stroke prevention further upstream through predicting, preventing, and managing atrial fibrillation and left atrial disease. These strategies should be used to complement current guidelines for primary stroke prevention related to atrial fibrillation[11] (pulse assessment for patients over 65 years old; depending on valvular versus nonvalvular, CHA_2DS_2-VASc risk score, risk for hemorrhagic complications, patient risk factors, and patient preference for cost and side effects, this can include different long-term oral anticoagulant therapies, aspirin, potential closure of the left atrial appendage, or no treatment).

Strategies for Prediction, Screening, and Prevention

Risk stratification tools in use today can identify who to screen for atrial fibrillation, predict stroke risk in patients with atrial fibrillation, and predict bleeding complications among those on anticoagulants. A systematic review (of 61 studies relevant to predicting thromboembolic risk and 38 to predicting bleeding risk)[64] found that $CHADS_2$, CHA_2DS_2-VASc and the age, biomarkers, and clinical history risk scores, while imperfect, are the most useful tools to predict embolism in patients with atrial fibrillation (with moderate strength of evidence). Additionally, HAS-BLED scores (Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage), while not a tool for decision-making on anticoagulant use, calculate bleeding risk in atrial fibrillation patients on anticoagulants,[64] which can help providers and patients identify modifiable risk factors to reduce bleeding risk.

As previously mentioned, the HAVOC scoring system is a newer risk tool to better identify patients with atrial fibrillation.[49] It has not yet been widely used and requires more research but is a promising frontier for identifying a subset of patients at higher risk relative to other more prominently used risk scores.

Collectively, these tools could be integrated into electronic health records (EHRs) to facilitate rapid, consistent, and accurate screening, and improve clinicians' use of evidence-based treatments. Preliminary research is examining automatic calculations of CHA_2DS_2-VASc in EHRs, finding an adjusted net reclassification index (a measure of improved prediction performance) of 4%,[65] but this currently happens on a hospital level, case-by-case basis. Preliminary data also suggests improvements in prescribing of oral anticoagulants for patients at higher risk.[66] However, further research and validation in additional populations are needed.

There is limited evidence that remote technology and wearable devices that screen for atrial fibrillation directly improve clinical outcomes, but there is increasing interest in their use as a patient-facing screening tool that can also encourage patient awareness of rhythm and rate.[67] One popular example is the Apple Watch. One study found 57% of participants who received an alert sought medical care.[68,69] Other innovative examples are emerging, such as underwear for detecting atrial fibrillation.[70] For wearables to reliably identify atrial fibrillation and reduce stroke risk, they will need to improve the sophistication of signal processing, coding algorithms for QRS detection, and real-time recognition of arrhythmia onset, as well as integrate wearable data into clinician-facing platforms.[68,69,71] Further, longer-term and larger population-level research is needed to improve the accuracy (sensitivity and specificity) of ECG recordings from wearable devices and the timeliness of reading, interpretation, and feedback to patients and clinicians. For example, one study of the Apple Watch[71] identified a substantial proportion of individuals with nonclinically meaningful arrhythmias which can cause added burden on the health system and bring negative psychological consequences for patients.[72–75]

Finally, diseases of the left atrium, notably left atrial enlargement, lead to multiple prevalent cardiovascular pathologies, including both atrial fibrillation[76] and stroke as well as myocardial ischemia and heart failure. Cardiologists generally acknowledge, for example, that the left atrial appendage, not the fibrillating atrium itself, is the most common site for cardiac thrombus formation, with literature reviews on the topic noting that left atrial appendage flow patterns causing cardiac emboli can occur in normal sinus rhythm, potentially explaining unexplained strokes.[77] Understanding how to screen left atrial disease at a population level would be a valuable contribution and could have multiplicative effects (preventing stroke directly as well as preventing stroke risk factors). Hand-carried ultrasound devices can be used by noncardiologist clinicians to screen for left atrial enlargement with high specificity[78] for further cardiologist follow-up. Machine learning approaches based on electrocardiograms during normal sinus rhythm may also detect patients with a high likelihood of atrial fibrillation.[79,80] If these techniques are paired with quick pulse and blood pressure screenings, population-level hypertension, and left atrial disease screening can be combined. Other left atrial disease screening approaches include electrocardiographic markers, such as P wave terminal force velocity in lead V1,

ectopy, and PR interval, and serum biomarkers, including NT-proBNP[77,81–83] (N-terminal pro-B-type natriuretic peptide, which may plausibly predict need for anticoagulation use for primary prevention of stroke).[84] Clinical trials testing anticoagulation for secondary prevention of stroke in patients with atrial cardiopathy are ongoing,[85] and trials in primary prevention could follow. Further research into left atrial disease prevention strategies is required.

There are other medical risk factors for atrial fibrillation that do not yet have proven prevention strategies, such as obstructive sleep apnea.[86] These require future research.

Strategies for Management

Evidence-based therapeutics exist for atrial fibrillation prevention and management and can be managed by primary care physicians (sometimes coordinating with cardiologists and anticoagulation clinics). Because some therapies have burdensome side effects, physicians must carefully weigh patient preferences, limiting the ability to make a population health level recommendation. We thus only provide a brief overview of therapeutic options. Some medications reduce symptoms of atrial fibrillation (such as β-blockers and digoxin) but do not prevent stroke. One evidence-based preventive medication class is direct-acting oral anticoagulants, which are at least as effective and safe as warfarin for patients with nonvalvular atrial fibrillation, with similar safety and benefits across patient subgroups.[87] Direct-acting oral anticoagulants are easier for patients since they do not require regular attendance of clinics (like warfarin). A device option is the Watchman™ Left Atrial Appendage Closure Implant,[88] a permanent heart implant in patients who cannot tolerate long-term oral anticoagulants. Though not tested as a front-line nonpharmacological option among those eligible for oral anticoagulants, Watchman™ can reduce the risk of bleeding compared with oral anticoagulants with no increased stroke risk, thereby minimizing need for anticoagulant medication therapy.[33,89]

Noting the serious aforementioned caveats regarding cardiovascular polypill availability in the United States, if an avenue to directly creating a generic polypill came to fruition, some have recommended its customization to include stroke prevention compounds related to atrial fibrillation,[90] but further research and thought is needed.

Standardized, high-quality data is central to efforts to improve atrial fibrillation management and monitor stroke incidence in at-risk populations. One option is Get With The Guidelines-AFIB, a hospital-based program of monitoring and guideline adherence,[91] although this program has not had widespread adoption. Similarly, the American College of Cardiology has an Atrial Fibrillation Ablation Registry.[92] While limited in scope, this registry encourages use of data for decision-making, captures real-time metrics to compare performance with peers, and supports development of evidence-based data on performance and outcomes. Expanding these data efforts would increase the ability to track atrial fibrillation patients over the time before stroke occurs. Moreover, there is opportunity to expand both programs beyond inpatient settings to outpatient and ambulatory settings, including after stroke. These could be useful complements to AHA Get With The Guidelines-Stroke,[93] in which 2000 United States hospitals participate, covering a substantial majority of hospitalized stroke discharges and has seen improved quality of care; one study found clinically meaningful improvements in all 7 measures examined.[94,95] Similarly, evidence from the Get With The Guidelines-Heart Failure registry indicates their ability to promote equitable care as one study found composite metrics of quality of care and outcomes improved similarly between Hispanics and whites (up to around 70%–90%).[96,97]

RECOMMENDATIONS FOR A PROGRAM TO PREDICT AND PREVENT STROKE

Table 1 synthesizes evidence and recommendations from the previous sections to highlight key components of a frontier program aimed at upstream stroke prediction and prevention. Recommendations are organized thematically for hypertension and atrial fibrillation across 3 domains: screening and predicting risk, medication and device therapy, and using data, technology, and existing infrastructure to track patients.

BARRIERS TO IMPLEMENTATION (AND STRATEGIES TO OVERCOME THEM)

This section discusses key implementation barriers for the stroke prevention program framework and identifies strategies to overcome those barriers (summarized in Table 2).

Barrier: Regulatory and Policy Challenges

Fee-for-service reimbursement presents challenges for upstream stroke prevention. While fee-for-service models do cover relevant generic medications and some screening and follow-up (such as for hypertension), they are not flexible enough to support ideal care models for upstream stroke prevention (such as supporting care coordination and CHWs). Moreover, fee-for-service inherently encourages higher volume instead of prospective care planning and prevention. Integrating preventive strategies into clinical settings will require

understanding how to do so within existing (or new) payment reform mechanisms.

Another regulatory and policy challenge is identifying and implementing measures that gauge key aspects of stroke care quality, which are important for quality improvement and value-based care. There are many different stroke measures in used today.[98,99] Get With The Guidelines—Stroke made great progress developing and refining quality measures for stroke, though these measures are not always widely used. There are multiple challenges in quality measures today. First, there is lack of consensus on which patient-reported stroke outcome measures to use, and future measures should place greater weight on patient preferences and goals.[98,99] Second, current measures are not always endorsed by the same set of organizations or necessarily aligned between payers and settings.[98,99] Greater measure alignment and more patient-focused measures will help with improving stroke care and outcomes while minimizing the administrative effort of collecting and reporting measures.

Lastly, variation in state laws and regulations can limit the ability to widely implement some proposed strategies. For example, state variation in scope of practice for nonphysician clinicians limits their effective use in the provision of care.[100] Pharmacists vary in their ability to independently prescribe, modify, or monitor pharmaceutical therapies, even though these care models have shown success for use of antihypertensives and improved blood pressure.[101] Similarly, restrictive scopes of practices for advanced practice nurses and physician assistants could affect management of hypertension,[102] especially given limited availability of primary care in rural and low-income areas.

Strategy for Regulatory and Policy Challenges: Alternative Payment Models

An increasing percentage of total health care dollars are moving away from fee-for-service reimbursement and through Alternative Payment Models (APMs)—now 36%, up from 25% 4 years ago.[103] APMs encourage care redesign that would benefit stroke prediction and prevention. They provide greater flexibility for investment in care coordination, team-based care, remote monitoring, and behavioral tools. Further, APMs extend care delivery flexibility to encourage team-based care emphasizing the use of nonphysician clinicians (such as CHWs for community hypertension screening)—recommendations of this practical framework.

There are some studies on potential impact of APMs on stroke or cardiovascular outcomes. Accountable Care Organization payment arrangements are associated with reduced length of stay in Skilled Nursing Facilities after hospitalization for stroke[104] and increased hospice enrollment after hospitalization for ischemic stroke,[105] signaling improved quality of end-of-life care. Recent evidence from the Medicare Accountable Care Organization program found that cardiologist involvement in Accountable Care Organizations was associated with lowered costs of patients with cardiovascular disease for the same level of care quality.[106] It would be valuable for APMs to also include neurologists, who impact stroke prevention.[107]

While there are some cardiovascular care focused payment models, they tend to focus on efficient management of specific acute events or procedures and not on preventing the events and procedures in the first place.[108] Longitudinally focused payment arrangements that build off of infrastructure of more widespread, primary care focused APMs may help.[109] In addition, APMs with linked stroke prevention performance measures (like hypertension screening and control rates, health coaching, and prescription fills) would further encourage health care organizations to focus on important upstream stroke risk factors.

More research is needed to design a stroke prevention-focused payment model. However, a framework for a heart failure focused longitudinal APM was recently published,[109] and the components of this article's framework serve as a starting point to similarly develop a model. Both heart failure and stroke are significant enough population health issues that their APMs could be integrated into existing primary care focused models.

Barrier: Implementation in Low-Resource Settings

Low-resource settings (eg, rural, urban safety net, or smaller, physician-led practices) often have the most need to address inequities. However, financial constraints may limit their capacity to implement strategies that higher revenue health systems have more capital to pilot, or prescribe and pay for emerging medications. In addition to challenges implementing in lower-resourced settings, health improvement opportunities and health care resource capabilities vary at local levels, making it difficult to scale programs, and different populations (rural versus urban; young versus old; prestroke versus stroke; patient preferences) require unique approaches.

Strategy for Low-Resource Settings: Leveraging Existing Cardiovascular Quality Improvement Infrastructure

Organizations should leverage existing infrastructure to improve implementation and sustainability of a stroke prevention program. To expand the data infrastructure available, AHA could integrate Get With The Guidelines-Stroke and Get With The Guidelines-AFIB and expand to ambulatory and outpatient settings to move atrial fibrillation identification further upstream. For hypertension, Target:BP,[110] a collaboration between AHA and

the American Medical Association, could be leveraged to improve prediction and prevention. Target:BP provides tools and resources to develop a plan for improving and measuring improvement in blood pressure. It also recognizes organizations with superior performance. These expanded data sources should increase usage and new development of patient-centered quality measures related to stroke.

Strategy for Low-Resource Settings: Maximizing the Health Care Workforce

Health care organizations can leverage clinicians beyond physicians, including Nurse Practitioners (NPs), Licensed Clinical Social Workers (LCSWs), Physician Assistants (PAs), and community pharmacists. Expanding the workforce increases opportunities for health coaching, screening for hypertension and other upstream stroke medical factors, and screening for social and behavioral barriers. Many of these professionals are extensively trained and experienced in patient communication and can effectively explain to patients their medications' purpose, mechanism, and side effects. APMs are needed to reimburse and encourage the services these professionals provide. In addition, differing health information technology platforms allow or restrict which clinicians can document in the EHR, which could limit use of nonphysician clinicians.

CHWs play an important role in stroke prevention by using knowledge of the community, being culturally competent, and meeting patients where they are.[111] Especially in low-resource settings such as federally qualified health centers and rural health clinics,[112] CHWs can help with stroke risk reduction and management, especially by encouraging medication adherence and self-measure blood pressure monitoring training. CHWs provide more face time to patients, helping to improve patient engagement, at a lower cost than a physician. In Canada, paramedics have played a similar role and improved hypertension through weekly visits to subsidized senior living facilities, but this approach is difficult for the US system, even through new payment models.[113]

There are additional examples of how CHWs improve stroke prevention.[17,53–55] One international example, SMARThealth India, allows CHWs in low-resource settings to collect patient information, such as blood pressure and glucose level, via mobile devices to upload to an EHR.[114] CHWs make a referral to a physician, who provide a diagnosis and management plan. The program increases access to screening facilities by engaging in treatment at home during convenient times.[115] Similarly, the trial PANACEA-HF (Propagation ANalysis for Arrhythmogenic Conduction Elimination to Prevent Atrial Flutter and Fibrillation) looked at self-care and nonadherence of heart failure patients and found community-based workers have great opportunity to engage patients in education.[116] The study also found that patients and caregivers are willing to be counseled by CHWs on health beliefs and habits.

Strategy for Low-Resource Settings: Targeting Patients Where They Are

There are multiple evidence-based approaches to meet patients in their communities, which may be especially useful for low-resource areas where transportation can be a major barrier to accessing care. Well attended events like the Heart Walk, the AHA's event that raises funds for stroke and heart disease, or frequently visited places like YMCAs can host blood pressure screenings. Mobile clinics are another way patients can review blood pressure levels with health professionals. In mobile clinics in Massachusetts, screenings and counseling on blood pressure reduced blood pressure resulting in a 44.6% reduction in relative risk of stroke.[117] By bringing care to underserved communities, rather than waiting for individuals to seek care, mobile clinics create awareness and improve knowledge of stroke risk. Another proven community-based strategy is through barbershops; studies conducted in Los Angeles, CA are now being replicated nationally with support from the Centers for Disease Control and Prevention.[21,118]

These efforts must be done in ways that are culturally competent. An initiative addressing stroke prevention through local culturally competent education is Hip Hop Public Health.[119] It has worked with popular figures such as Michelle Obama and hip hop star Doug E. Fresh to promote health equity and reduce preventable conditions, including stroke, in low-income and underserved communities. In 2005, the program produced the song "Stroke Ain't No Joke," which educates children about healthy living, recognizing emergency situations such as stroke, and know how to call for emergency services. It is crucial to tie meet patients where they are strategies to population-focused payment reforms, or otherwise to grant or public health funding mechanisms, however, to ensure sustainability.

Barrier: Data Limitations

Better population health data tools are needed to target people at risk and understand effectiveness of interventions. Technologies must engage both clinicians and patients, protect patients and their data, accurately record patient data in a timely and convenient manner, and be interoperable with EHRs and personal health records. They must be widely accessible and not costly for all patients or else risk worsening health equity.[120] For example, detection of atrial

fibrillation using mobile telemetry is higher in white patients than Black patients.[121]

Potential Strategy for Improving Data: Wearables

Wearables and other personal technology provide opportunities to measure behavior, health metrics, effectiveness of interventions, while patients go about their normal lives. For example, home-based ECG patches facilitate atrial fibrillation diagnosis.[122] These devices also help collect patient experience and other patient-preferred real-world data applicable to stroke that can be turned into real-world evidence counting toward research and development in trials. Further, wearables present opportunities to visually present risk scores and to use patient alerts to help patients understand health and risks.

Wearables present concerns, however, regarding their ability to influence behavior in high-risk patients. Privacy concerns arise from the use of these technologies and lack of protection for consumers[43] and can cause false positives[71] causing psychological consequences on patients. They could exacerbate health inequity and medical distrust. Leveraging technologies communities have access to, however (such as smartphones, which communities have with relative equity[123]) could help ameliorate this concern, though it is still important to consider that apps requiring high bandwidth can be expensive and many low-income consumers have low bandwidth plans. It is unclear which technologies hold the most promise. Further research is required, especially to understand the contexts under which they work best and how to maximize equitable utilization. When more promising technologies are identified, they need to be included in payment models in ways making them affordable and available to all.

While one concern with using wearables for real-world data is the lack of a pathway from data to EHR, SMART (Substitutable Medical Applications, Reusable Technologies) technology on Fast Healthcare Interoperability Resource allows third-party apps to provide clinicians with data in the EHR from apps.[65] This could enable use of data from smartphone apps to be integrated into the EHR. This applies to stroke prevention—an early look at SMART on Fast Healthcare Interoperability Resource[65] found using SMART technology for automated calculations of CHA_2DS_2-VASc resulted in higher scores and more identified comorbidities than those calculated by clinicians. This could be applied within Get With The Guidelines-Stroke and Get With The Guidelines-AFib programs to link patient data to data from wearables and patient-reported outcomes data using SMART on Fast Healthcare Interoperability Resource to create personalized risk factor assessments.

Barrier: Medication Adherence and Lifestyle Change

Interventions addressing medication adherence for hypertension and atrial fibrillation are critical for prevention of stroke. Risk factors for poor medication adherence among atrial fibrillation patients (and similarly for hypertension patients) include sociodemographic characteristics, lifestyle factors, self-reported poor physical health, mental health, sleep quality, memory decline, inadequate health literacy, using low-dose aspirin, having diabetes mellitus and higher comorbidity burden.[124] Previous stroke can act as a barrier to medication adherence among survivors, as it may limit ability to self-care.[125] The Framingham Study found depressive symptoms might act as a barrier for medication adherence among older participants with hypertension, dyslipidemia, and diabetes mellitus.[126]

As reasons for poor medication adherence vary, tailored intervention approaches have a greater potential to affect nonadherence rates. However, physicians are often unaware of adherence levels and lack adherence data, inhibiting ability to affect outcomes.[127] Physicians require support to attain this information. Additionally, improved adherence behavior typically will not be achieved in a single visit or short-term intervention; interventions must include long-term adherence support efforts.

Broadly, it is difficult for clinicians to communicate a full understanding of what at-risk means to patients, especially for conditions that develop over decades to cause a downstream event like stroke.[128] There can be legitimate reasons for patients to disagree with taking a particular therapy (such as high out of pocket costs or strong side effects).[129] This has implications for stroke prevention methods as patients may not engage in self-care behaviors necessary for prevention if risk is not communicated effectively. This also means it is harder to engage individuals in lifestyle modification (such as healthy eating and exercise), until an event occurs—after it is too late to intervene or modify behavior.

Strategies for Medication Adherence and Lifestyle Change: Stroke-Related Patient Engagement and Education

When addressing modifiable medical risk factors affecting stroke risk, successful interventions incorporate patient engagement and education techniques for increasing self-efficacy, understanding of the importance of behavior modification, and knowledge of stroke and stroke risk factors. The trial IMPACT-AF (A multifaceted intervention to improve treatment with oral anticoagulants in atrial fibrillation) used a patient education program, with brochures, a website, emails, and social media, to increase use of anticoagu-

lants.[66,130,131] Among study enrollees, the intervention group increased oral anticoagulant use by 12% over 12 months, reducing strokes by 52%. Patient engagement in decision-making in interventions is equally as important but remains a challenge in atrial fibrillation-focused stroke prevention efforts; the use of decision aids can help.[132]

Creative messaging that is tailored to populations, catchy, attention-grabbing, and fun can help patients understand their risk. One low-cost option is online interactive group sessions or webinars, tailored to patients by including a question and answer period where patients obtain information specifically relevant to them within the comfort of their home. Another option is through the SMART on Fast Healthcare Interoperability Resource app, called the Digital Drag and Drop Pillbox.[133] The app uses images to overcome health literacy barriers and provides individualized feedback on learning and skill performance. Moreover, education materials will be suboptimal if they do not take a culturally appropriate perspective. Effective interventions must engage with the community to establish trust and mutual understanding of stroke and stroke risk factors. Peer support groups can help translate risk among members who struggle with similar factors.

Self-measured blood pressure monitoring with clinical support (counseling, online, or community-based support, or other tools) is effective in managing and preventing hypertension by improving engagement through convenience.[21,118,134] However, though blood pressure monitors for home use are generally considered affordable and convenient, additional out of pocket costs can be barriers for low-income populations.

Finally, home-based education can empower patients and provide them with important knowledge on their condition while allowing patients to feel comfortable and relaxed. The home-based education and learning program for atrial fibrillation[135] found home-based educational sessions empowering patients to engage in monitoring their condition reduced unplanned hospitalizations. In this program, a team of a pharmacist and a nurse focused on medications, stroke prevention, healthy lifestyle choices and actions to take when in atrial fibrillation, and sessions culturally appropriate and tailored to individuals.

SUMMARY OF IMPLEMENTATION RECOMMENDATIONS

Based on the above evidence, Table 2 highlights key barriers to implementing an upstream stroke prevention program and identifies potential strategies to overcome them.

CONCLUSIONS

Stroke causes significant mortality and morbidity, and curtails quality of life. The ultimate goal of this work is to illustrate potential components of a frontier program for upstream stroke prevention focused on predicting, preventing, and managing hypertension and atrial fibrillation—paired with implementation strategies for putting that program into place across the United States.

The article is intended to serve as a framework organizations can use to support practical implementation of an upstream stroke prediction and prevention program. A goal of creating this is that it provides enough detail on key strategies without being overly prescriptive—balancing scalability and customization. The framework offers a basic set of strategies that apply to all populations that organizations could tailor to their population. Further, it is designed to be implementable in low-resource settings and to benefit vulnerable populations. Looking across the framework, key implementation strategies for upstream stroke prevention in low-resource settings, in particular, include participating in an alternative payment arrangement to allow greater flexibility for prevention (including to maximize use of nonphysician clinicians, such as CHWs), partner with community organizations to meet patients where they are, and leverage any existing infrastructure or data for population health tracking and management. If multiple stakeholders commit to working together to put this framework into action, there is a real chance to predict, prevent, and manage stroke risk upstream—ultimately preventing substantial stroke morbidity and mortality—while improving stroke health equity.

ARTICLE INFORMATION

*A list of all American Heart Association Predict and Prevent Learning Collaborative members is given in the Data Supplement.

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