Use of IndiGO individualized clinical guidelines in primary care

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ABSTRACT

Objective To determine if IndiGO individualized clinical guidelines could be implemented in routine practice and assess their effects on care and care experience.

Methods Matched comparison observational design. IndiGO individualized guidelines, based on a biomathematical simulation model, were used in shared decision-making. Physicians and patients viewed risk estimates and tailored recommendations in a dynamic user interface and discussed them for 5–10 min. Outcome measures were prescribing and dispensing of IndiGO-recommended medications, changes in physiological markers and predicted 5-year risk of heart attack and stroke, and physician and patient perceptions.

Results 489 patients using IndiGO were 4.9 times more likely to receive a statin prescription than were matched usual care controls ($p=0.015$). No effect was observed on prescribing of antihypertensive medications, but IndiGO-using patients were more likely to pick up at least one dispensing ($p<0.05$). No significant changes were observed in blood pressure or serum lipid levels. Predicted risk of heart attack or stroke decreased 1.6% among patients using IndiGO versus 1.0% among matched controls ($p<0.01$). Physician and patient experiences were positive to neutral.

Limitations We could not assess the separate effects of individualized guidelines, user interface, and physician–patient discussions. Patient selection could have influenced results. The measure of risk reduction was not independent of the individualized guidelines.

Conclusions IndiGO individualized clinical guidelines were successfully implemented in primary care and were associated with increases in the use of cardioprotective medications and reduction in the predicted risk of adverse events, suggesting that a larger trial could be warranted.

INTRODUCTION

Evidence-based medicine requires integrating individual clinician expertise with the best available external clinical evidence and patient choice.[1] Evidence-based medicine began with the development and application of categorical rules to identify individuals and populations at risk and target them with effective treatment and prevention. Over time, it has evolved to incorporate increasingly detailed criteria to enhance accurate risk identification and treatment targeting. For example, the ATP-3 dyslipidemia guideline uses comorbidities, risk factors, and coronary heart disease risk to sort individuals into risk categories.[2] Individualized clinical guidelines, taking into account individual risk factors and expected benefit from treatment, represent an even more precise application of evidence-based medicine.[3 4]

From the inception of modern evidence-based clinical guidelines, questions have consistently arisen about how best to disseminate and implement them.[5 6] Individualized guidelines heighten these concerns because of the requirement for detailed information about the person to whom they will be applied, for example, individual risk of morbidity or mortality and expected benefits of treatment. Integration of guidelines in electronic health records (EHR) enables the ready availability of information necessary for personalized recommendations,[7] but little is known about the use of individualized guidelines in routine clinical practice.

Demonstrating the potential benefits of individualized guidelines for a specific clinical problem is one challenge that must be met if they are to be used more broadly.[7] A second challenge is clinician adoption. This report examines the feasibility of using individualized clinical guidelines in primary care and provides limited-scale observational data on medication use and cardiovascular risk.

BACKGROUND AND SIGNIFICANCE

IndiGO individualized clinical guidelines are based on the Archimedes model, a full-scale, rigorously validated biomathematical simulation model of human physiology, diseases, behavior, interventions, and healthcare systems.[8–17] IndiGO uses regression equations to predict the likelihood of heart attack or stroke based on individual risk factors: cardiovascular disease history, comorbidities, medication history, biomarkers (low-density lipoprotein (LDL) cholesterol, triglycerides, blood pressure, and body mass index (BMI)), and lifestyle behaviors. Interventions modeled in IndiGO include smoking cessation, weight loss, and preventive medications: simvastatin, lisinopril, atenolol, hydrochlorthiazide, amlodipine, and lisinopril/hydrochlorthiazide.

Using patient-level clinical information in an EHR, IndiGO produces individualized 'benefit scores' predicting risk reduction from maintaining each intervention over 5 years. The score is a weighted combination of the decreased risk of adverse outcomes; weights approximate the expected 5-year reduction in quality of life that would result from each outcome. Known side effects and harms are weighted and subtracted from the benefit score. IndiGO also produces a 'total benefit score' for each individual, the sum of benefit scores for all interventions. Finally, IndiGO predicts individualized 5-year risk of heart attack or stroke under three scenarios: (1) maintaining current interventions for 5 years; (2) discontinuing all current interventions; or (3) maintaining all identified interventions for 5 years. Complete

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details of the predictive modeling have been published.[18] Automated data interchange between the EHR and the biomathematical model updates benefit scores daily, which are displayed in an interactive graphical user interface (GUI).

IndiGO's unique strength is identifying two types of individuals: those for whom traditional population-based guidelines indicate treatment but who would benefit too little to justify the side effects or risks, and those missed by population-based guidelines but who would derive considerable benefit. A simulation applying IndiGO to a secondary dataset found that individualized guidelines could lead to improved quality of care and lower costs for patients with hypertension, compared to traditional guidelines.[3] We report here on the initial implementation of IndiGO individualized guidelines in primary care, in which we assessed the feasibility of use in routine clinical practice, integration into shared decision-making, patients' and physicians' experience with their use, and effects on medication use and cardiovascular risk in a small population over a short observation period. We considered assessment of these factors a first step that could lead to a full-scale trial or to further refinement in practice.

MATERIALS AND METHODS

Design and setting

Our quality improvement project used a matched control observational design in two clinics employing 10 primary care providers (PCP) in Kaiser Permanente's Hawaii region (KPHI). All providers at these sites used IndiGO. KPHI serves 224 000 members with a hospital on Oahu and 15 clinics across three islands. A comprehensive integrated EHR, KP Health Connect, contains all patient information.[19 20]

Implementing IndiGO individualized guidelines

IndiGO individualized guidelines were implemented by automated daily extraction of relevant clinical information for all KPHI adult members from KP Health Connect. After applying IndiGO calculations, risk and benefit scores were embedded in the panel support tool, a population management module of KP Health Connect, where PCP accessed them.[21–24]

To encourage acceptance by practicing physicians and organizational leadership, algorithms were set such that all interventions that would be recommended by existing guidelines would also be recommended by IndiGO. The GUI displayed each member's current 5-year risk of heart attack or stroke and the comparable predicted risk after adopting and maintaining all identified interventions (figure 1). Risk-reduction information was shown for each intervention; selecting interventions as adopted dynamically changed the 5-year predicted risk display.

Participants

Patients were considered eligible for IndiGO use if they had a scheduled primary care visit and their IndiGO total benefit score was in the top third of the KPHI population. PCP then selected individual patients for IndiGO use based on the patient's chief

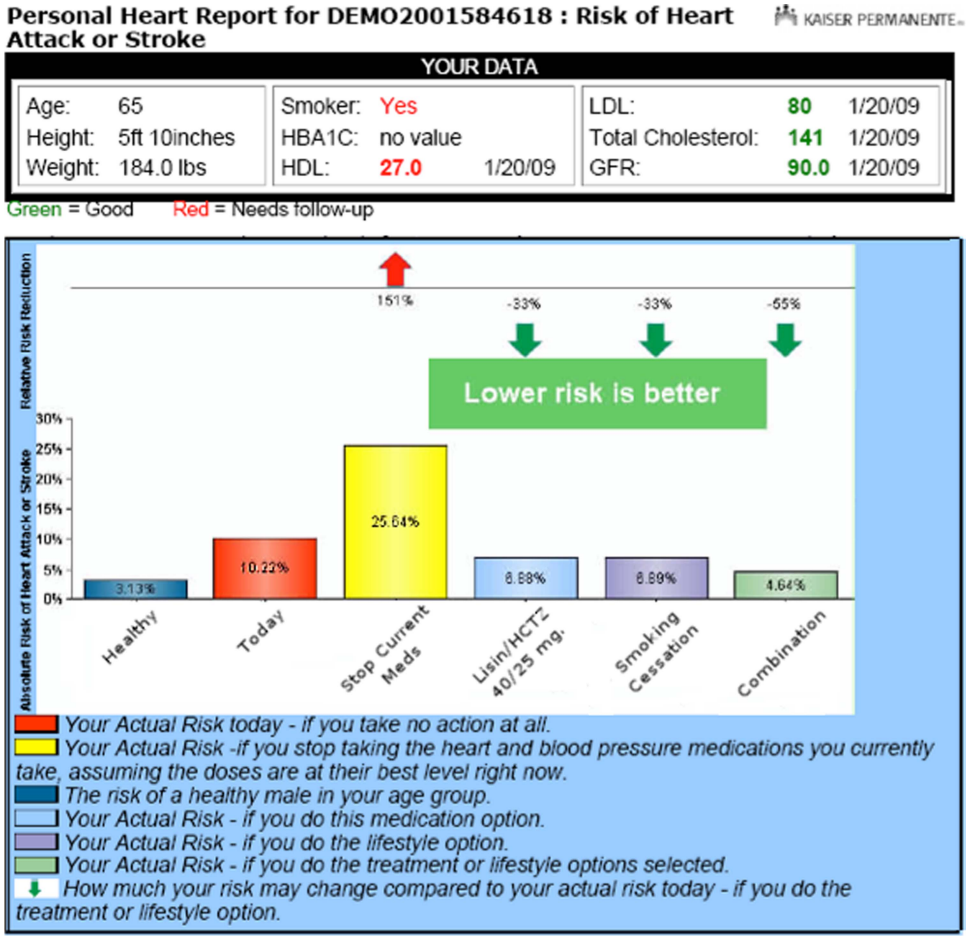

Figure 1 Screenshot of IndiGO graphical user interface. GFR, glomerular filtration rate; HBA1C, hemoglobin A 1C; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

complaint and availability of PCP time, and the extent to which PCP believed patients would be likely to accept treatment recommendations. Physicians selected patients with primary care visits between November 2008 and April 2009; for the purposes of this project, patients were followed for 3–6 months.

Selected patients viewed a video explaining individualized guidelines, their benefits and limitations, and the GUI. PCP and patients subsequently used IndiGO in 5–10-min shared decision-making sessions; a printed summary displayed interventions chosen by the member and the predicted 5-year risk with no interventions, with selected interventions, and with all identified interventions. Physicians made treatment recommendations based on existing guidelines, IndiGO benefit scores, and clinical judgment. For example, IndiGO modeling was based on specified medication doses, but physicians tailored doses to individual patient needs. The intervention described in this report thus includes three components: individualized guidelines, a GUI to communicate risk-reduction options to patients and their physicians, and a brief face-to-face discussion of the risk-reduction options.

Propensity score matching

We compared patients using IndiGO at the pilot clinics with those receiving usual care at other clinics. We identified the matched comparison cohort using nearest-neighbor propensity score matching with replacement. We estimated a logistic regression model with IndiGO use as the dependent variable and six matching variables: age; gender; pre-IndiGO history of cardiovascular disease, diabetes, or hypertension; number of primary care visits during the 12 months before IndiGO use; an indicator for the presence or absence of at least one health behavior benefit recommendation; and an indicator for the presence or absence of at least one medication recommendation.

Outcome measures and statistical analysis

The primary outcome measures were prescribing and dispensing of medications that have been shown to reduce the risk of heart attack or stroke: statins or other lipid-lowering medications, diuretics, calcium antagonists, β-blockers, and ACE inhibitors or angiotensin receptor blockers (ARB). Because IndiGO often recommends multiple medications, we grouped them by likely indication to simplify the analysis and gauge any general effect on prescribing and dispensing rates. Statins and other lipid-lowering medications were grouped, and we refer to them collectively as 'statins'. Medications and medication combinations intended primarily for hypertension control—diuretics, calcium antagonists, and lisinopril/hydrochlorothiazide—were collectively tracked as 'antihypertensives'. We also included in this category recommendations for any of these medications in combination with a β-blocker, ACE inhibitor, or ARB, which also have antihypertensive effect. We counted separately recommendations for β-blockers alone and ACE inhibitors or ARB alone, because these may be indicated after a myocardial infarction and for chronic kidney disease, respectively. Because β-blockers and ACE inhibitors or ARB could be recommended either to reduce blood pressure or for other indications, IndiGO recommendations for these medications were not amenable to straightforward interpretation and were not analyzed in detail.

Secondary outcome measures included blood pressure and LDL cholesterol levels, BMI, and change in 5-year IndiGO-predicted risk of heart attack or stroke. Data were available from KP Health Connect. Secondary measures also included physician and patient perceptions of individualized guidelines; data were collected during focus groups and a post-project email survey (physicians) and through a pre-post mail survey (patients). We used difference-in-differences methods to evaluate changes in the secondary outcome measures between the intervention group and matched controls, assessing statistical significance with Student's t test. We did not adjust significance tests for multiple comparisons.

The Kaiser Permanente Hawaii Institutional Review Board reviewed the project and determined that it was quality improvement and not human subjects research.

RESULTS

Between November 2008 and April 2009, 29 395 patients had a primary care visit and an IndiGO total benefit score that would make them eligible for IndiGO use; 1915 (6.5%) visited participating sites. Of these, 489 (26%) patients were selected for IndiGO use by their PCP. Propensity score matching produced well-matched comparison groups (table 1).

IndiGO identified 1100 intervention recommendations, an average of 2.2 per patient. Antihypertensive medications and statins were most frequently identified (table 2). The average intervention benefit score among members with a non-zero benefit ranged from 3 to 39. Of IndiGO-identified interventions, 514 (47%) matched guidelines already available as point-of-care decision supports. The remaining 586 identifications (53%) were unique to IndiGO. The proportion of unique to IndiGO identifications ranged from 0% for lifestyle interventions to 89% for adding a β-blocker.

Patients who used IndiGO and had statins recommended received significantly more new statin prescriptions than did usual care patients (39% vs 8%, $p<.01$). Patients using IndiGO with new prescriptions for statins had a non-significant increase in the percentage that picked up at least one dispensing (72% vs 50%, $p=0.10$). Patients using IndiGO who had antihypertensive agents recommended did not receive more physician prescriptions (17% vs 15%, $p>0.20$) but were more likely to pick up at least one dispensing if prescribed (85% vs 67%, $p=0.01$).

No statistically significant differences existed in mean systolic blood pressure, LDL cholesterol, and BMI between baseline and follow-up for patients using IndiGO compared to matched usual care patients. The predicted 5-year risk of heart attack or stroke for patients using IndiGO decreased from 6.7% to 5.1%, a reduction of 1.6%, while predicted risk for usual care patients

Table 1 Characteristics of patients using IndiGO and matched usual care comparison group

	Patients using IndiGO (489)	Matched usual care patients (489)
Age (mean, years)	59	59
Gender (male, %)	66	69
Chronic conditions (diabetes, coronary artery disease, heart failure, or hypertension), %	76	80
Baseline IndiGO data, %		
5-Year heart risk of attack or stroke	6.7	7.5
IndiGO would recommend at least one medication change	95	97
IndiGO would recommend weight loss and/or smoking cessation	43	61*
5-Year heart attack/stroke risk if all interventions sustained	1.7	1.9

*p<0.01.

Table 2 Frequency and type of recommendations for patients using IndiGO

	Frequency of recommendations (% of patients using IndiGO)	Frequency of unique-to-IndiGO identifications (% of all recommendations)
Add a statin medication*	221 (45)	157 (70)
Add an ACE inhibitor or ARB alone†	153 (31)	131 (86)
Add a β-blocker alone‡	42 (9)	38 (89)
Add an antihypertensive agent§	400 (82)	265 (66)
Add daily aspirin	30 (6)	0
Stop smoking	149 (31)	0
Lose 10 pounds	105 (22)	0

*IndiGO recommendations are based on adding simvastatin (40 mg) to a patient's treatment regimen.
†IndiGO recommendations are based on adding lisinopril (40 mg) to a patient's treatment regimen. Recommendations that included an ACE inhibitor or ARB along with hydrochlorothiazide or amlodipine are counted under 'antiphypertensive agents'.
‡IndiGO recommendations are based on adding atenolol (50 mg) to a patient's treatment regimen. Recommendations that included a β-blocker along with hydrochlorothiazide or amlodipine are counted under 'antiphypertensive agents.'
§IndiGO recommendations are based on adding hydrochlorothiazide (25 mg), lisinopril/hydrochlorothiazide (20 mg/12.5 mg), or amlodipine (5 mg) to a patient's treatment regimen.
ARB, angiotensin receptor blockers.

decreased by 1.0% (table 3). The predicted relative benefit was statistically significant (p=0.015).

All participating PCP completed the post-survey. The majority rated IndiGO as very useful for educating patients about health risks (80%), very helpful in involving patients in decision-making (60%), or in helping them make the best clinical decisions for patients (60%) and usually or always helpful with treatment recommendations (60%). However, 90% of physicians reported they lacked time to use IndiGO with all patients who could benefit. PCP expressed belief in IndiGO's long-term effectiveness at influencing patients towards needed behavior changes, and indicated that they found IndiGO most effective with patients who were non-adherent to medication recommendations, presented for care during a 'teachable moment', or rarely made in-person clinic visits.

Among 1005 members completing the pre-IndiGO survey, 817 (81%) completed the post-survey; 196 had used IndiGO and 621 had not. They did not differ significantly in demographics or self-reported health status. Among IndiGO-using members, 170 (87%) found the GUI 'very' or 'somewhat' easy to understand. They were significantly more likely to report that their PCP or healthcare team had asked about their health goals, helped them with a specific plan for their care, or asked them to take a preventive medication, change their diet, exercise more, or stop smoking (table 4). No significant differences existed between groups in confidence to manage health conditions, belief in the importance of actively managing their healthcare, knowing how to prevent complications, knowing recommended lifestyle choices, having been asked to take insulin, perceived ability to follow recommended medication or lifestyle changes, assessment of how much their doctor helped them in the past 6 months, or overall rating of healthcare.

DISCUSSION

Our project is, to the best of our knowledge, the first to document the implementation in primary care of individualized clinical guidelines derived from biomathematical simulation modeling. Patients using IndiGO were 4.9 times more likely to receive a prescription for guideline-recommended statin medications, compared to a matched usual care comparison group,

Table 3 Changes in medication prescribing, medication dispensing, physiological markers, and predicted 5-year risk of heart attack or stroke in 489 IndiGO-using patients versus 489 matched patients at usual care sites

	Intervention group		Matched patients not using IndiGO		p Value
Medication prescribing—new prescriptions					
Statins	191 (39%)		40 (8%)		<0.01
Antihypertensive agents*	83 (17%)		73 (15%)		0.39
Medication dispensing—at least one dispensing for new prescriptions					
Statins	138 (72%)		20 (50%)		0.76
Antihypertensive agents*	71 (85%)		49 (67%)		0.01
	Baseline	Follow-up	Baseline	Follow-up	
Physiological markers					
LDL cholesterol*	114	106	114	109	0.37
Systolic blood pressure†	134	125	137	131	0.07
Predicted risk					
Predicted 5-year risk of heart attack or stroke	6.7%	5.1%	7.5%	6.5%	0.015
Predicted risk reduction from baseline to follow-up	1.6%		1.0%		

*Antihypertensive agents include hydrochlorothiazide (25 mg), lisinopril/hydrochlorothiazide (20 mg/12.5 mg), or amlodipine (5 mg), as well as any of these in combination with atenolol or lisinopril.
†LDL and blood pressure values exclude 121 patients who were not reassessed between IndiGO use and the end of follow-up.
LDL, low-density lipoproteins.

Table 4 Statistically significant differences in patient experiences of care†

	Patients using IndiGO (n=196)		Patients not using IndiGO (n=621)	
	Baseline	After follow-up	Baseline	After follow-up
In the past 6 months, did this doctor or this doctor's care team… ('definitely yes' or 'somewhat yes' responses, %)				
Ask you about your health goals?	66	88*	71	69
Help you with a specific plan for what you can do to improve your own health?	78	89**	79	78
In the past 6 months, did this doctor or this doctor's care team ask you to… ('yes' responses, %)				
Take blood pressure medication or change the blood pressure medication you are taking?	58	77*	59	57
Take cholesterol-lowering medication or statins?	53	75*	52	52
Take small daily doses of aspirin?	45	73*	44	47
Change your diet?	48	60*	42	41
Exercise more?	66	79*	61	59
Stop smoking?	38	46**	32	32

*p<0.05.
**p<0.01.
†No significant differences were found between groups on nine other survey items, covering belief in the importance of actively managing their healthcare, knowing how to prevent complications, knowing recommended lifestyle choices, having been asked to take insulin, perceived ability to follow recommended medication or lifestyle changes, assessment of how much their doctor helped them in the past 6 months, or overall rating of healthcare.

and those with new prescriptions were at least as likely to pick up their medications. Patients using IndiGO were not significantly more likely to be prescribed an antihypertensive medication, but those with new prescriptions were 30% more likely to pick up at least one dispensing. No between-group differences were found in systolic blood pressure, LDL cholesterol, or BMI. The predicted 5-year risk of heart attack or stroke, if observed risk factor changes were maintained over that time, decreased significantly more among patients using IndiGO. The absolute reduction in predicted risk was modest, but meaningful in that it applies to leading causes of death. PCP reported benefits to IndiGO in terms of shared decision-making and patient education. Compared to non-users, patients using IndiGO reported benefits in eight items related to goal setting, care planning, and medication and health behavior recommendations, but not in nine items assessing other aspects of their care experience.

Physicians selected patients for participation, which may have led to the inclusion of patients who were believed to be more amenable to new treatment recommendations or whose visits occurred during periods when physicians had more time for discussion. The matching resulted in significantly fewer obese patients and smokers in the usual care group, relative to IndiGO users. We cannot distinguish between the effects of the individualized guidelines, the GUI, and the 5–10-min discussions that ensued between physicians and patients. The measure of risk reduction was based on the same model as the individualized guideline recommendations, which could introduce confounding. Sample size and project duration did not enable comparison of the stability of interventions over time or actual reductions in adverse events.

Our results shed some light on two hypothesized mechanisms by which individualized clinical guidelines may improve care, namely by enhancing shared decision-making and clinical decision support. Patient participation in decision-making is pivotal to improved adherence, patient experience, and outcomes.[25–34] PCP and patients in our project both reported greater attention to shared decision-making when using IndiGO. Greater engagement, such as the higher proportion of IndiGO-using patients who filled new prescriptions for antihypertensive medications, may have resulted from individualized information about the benefits of risk-reducing interventions.

Individualized guidelines constitute a further evolution in point-of-care clinical decision support, with patient-specific risk-reduction information based on all available information. Clinical decision support improves guideline implementation by increasing user familiarity with guidelines and the underlying decision logic, overcoming inertia, and reducing guideline complexity.[35] Predicted, rather than speculative, risk-reduction estimates may have changed the nature of the PCP–patient conversation. Physicians' estimation of patients' cardiovascular risk, which has historically been primarily subjective, affects evidence-based pharmacotherapy recommendations.[36–38]

Well-documented improvements in prescribing rates have occurred for some preventive medications among patients with diabetes and hypertension.[39–44] The observed increase in statin prescribing rates in our project is consistent with these findings and suggests that the enhanced clinical decision support provided by IndiGO may be an effective mechanism for improving care.

Our limited-scale project demonstrates the feasibility of implementing individualized guidelines in clinical care and suggests benefits, but questions of both effectiveness and efficiency would need to be addressed and understood more fully before individualized guidelines are used on a widespread basis.[7] A controlled trial of adequate size and duration would be required to address clinical issues, particularly whether IndiGO-predicted risk reductions translate into actual reductions in adverse events and whether any unanticipated side effects result. Further assessment of individualized guidelines could also address practical issues we encountered, especially constraints on PCP time. Alternative ways of using individualized guidelines might improve efficiency; for example, nurse care managers instead of PCP could engage patients in using IndiGO. Further efficiencies might result from mass customization: applying individualized guidelines to a large population, identifying patients with similar clinical profiles (eg, those with borderline hypertension or hyperlipidemia accompanied by behavioral risk factors), scripting tailored patient and provider recommendations, and conducting systematic outreach for all patients who fit the profile.

CONCLUSIONS

IndiGO individualized clinical guidelines were successfully implemented in primary care and were associated with increased prescribing and dispensing of some, but not all, cardioprotective

medications. Our assessment indicates that implementation of individualized guidelines in routine clinical care is feasible, and suggests that the intervention, including a GUI and physician–patient discussion, may result in care that reduces the risk of heart attack and stroke. This limited-scale pilot had several limitations. An appropriate controlled trial would be needed to establish the clinical benefits of treatment guided by individualized guidelines, and alternative approaches could be developed to improve efficiency in their use.

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Competing interests Archimedes, Inc., the developer of IndiGO guidelines described in this report, is a fully owned subsidiary of the Kaiser Foundation Health Plan.

Ethics approval The Kaiser Permanente Hawaii Institutional Review Board reviewed the project and determined that it was quality improvement and not human subjects research.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Study data are available on request from the corresponding author.

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