Implementation Science

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A pragmatic randomized trial to compare strategies for implementing primary HPV testing for routine cervical cancer screening in a large healthcare system

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Abstract

Background Recent updates to national guidelines recommend primary human papillomavirus (HPV) screening for routine cervical cancer screening alongside previously recommended screening options. However, limited guidance exists for implementation approaches that best facilitate cancer screening practice substitution and achieve optimal stakeholder-centered outcomes. We compared "centrally-administered + locally-tailored" (here after referred to as locally-tailored) vs. "centrally-administered + usual care" (here after referred to as centrally-administered) approaches for achieving substitution of HPV and cytology co-testing with primary HPV screening for routine cervical cancer screening to examine the effect of local tailoring on implementation and stakeholder-centered outcomes.

Methods We conducted a pragmatic, cluster randomized trial embedded in the Kaiser Permanente Southern California (KPSC) health system, randomly assigning site groups to study arms at the level of the geographic service area (12 service area randomized). The study took place between 2020–2022. Centrally-administered implementation strategy bundles included physician and staff educational activities. Sites in the locally-tailored arm underwent local needs assessment followed by local selection, tailoring and deployment of implementation strategy bundles. The primary outcome was the proportion of primary HPV screenings among all screenings performed. Secondary stakeholder-centered outcomes included patient (knowledge, emotional reaction, satisfaction, volume of patient inquiries) and provider outcomes (perception, knowledge, acceptance, and satisfaction) measured via repeated surveys or electronic health records. The generalized estimating equation framework and the difference-in-differences approach were used to compare outcomes across study arms.

Results The proportion of appropriate screenings (i.e., use of primary HPV screening) during the post-intervention period was high, with no observed difference between study arms: 98.4% (95% confidence interval [CI] 96.3%-100%)

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for the locally-tailored arm and 99.1% (95% CI: 97.8%-100%) for the centrally-administered arm ($p = 0.34$). There were no statistically or clinically significant differences in patient- and provider- outcomes between study arms.

Conclusions Primary HPV screening was feasible and demonstrated high fidelity in all KPSC service areas. The locally-tailored practice substitution approach and centrally-administered practice substitution approach both achieved near complete uptake of primary HPV screening. Further, similar effects on stakeholder-centered outcomes were observed for both approaches. However, generalizability of our findings may be limited due to unique features of our integrated health system.

Trial registration NCT04371887. Registered 30 April 2020, URL: https://clinicaltrials.gov/study/NCT04371887?cond=primary%20HPV%20screening&rank=5.

Keywords Locally-tailored, Implementation approach, Practice substitution, Pragmatic trial, Constrained choice implementation, Cervical cancer screening, Primary HPV screening, Embedded research

Contributions to the literature

- Conducted head-to-head comparison of two implementation approaches for practice substitution.
- Described approaches to locally-tailored implementation strategies.
- Demonstrated the value of "constrained choice implementation" to achieve guideline-concordant practice substitution in an integrated health care environment.

Background

Widespreadadoption of cervical cancer screening practices in the United States (US) and other developed countries has been an important public health triumph. While screening with the Papanicolaou (Pap) test (a cytology test) is effective in reducing the burden of cervical cancer, recent evidence documents greater effectiveness of screening strategies that focus on persistent infection with high-risk human papillomavirus (hr-HPV) [1, 2], which causes virtually all cervical cancers [3]. h-HPV testing is more sensitive for detection of severe precancerous lesions than cytology [4–12], and is as effective as the cytology and HPV co-testing strategy [13–15]. Based on this evidence, effective cervical cancer screening programs can primarily rely on hr-HPV testing, with reflex cytology testing only for certain HPV test results. This strategy, labeled Primary HPV screening, also requires fewer tests and costs less per screened woman than co-testing [16]. In 2018, the U.S. Preventive Services Task Force updated its recommendation for routine cervical cancer screening to include primary HPV screening alongside previously-recommended approaches for routine cervical cancer screening for women age 30–65 years. Professional societies such as the American Society for Colposcopy and Cervical Pathology, the Society of Gynecology Oncology, the American College of Obstetrician and Gynecology, and American Cancer Society have released similar recommendations [17–19].

Although interest in substituting primary HPV testing for stand-alone Pap testing and co-testing is growing, recent publications suggest that the transition to primary HPV screening might encounter barriers at multiple levels. These include incomplete physician knowledge and confusion regarding the new guideline recommendations [20, 21], physician concern about missing cancer [22], patient attachment to the widely-known Pap test, low acceptance of primary HPV testing, and infrastructure requirements [20, 23–25]. To date, insufficient guidance exists regarding how to design and deploy practice substitution strategy bundles to successfully de-implement older practices and replace them with newer practices [26, 27]. This is particularly relevant in cervical cancer screening, where an ever-evolving evidence base, development of new technologies and resulting changes in clinical practice guidelines have necessitated frequent changes in clinical practices [28].

Efforts to substitute newer evidence-based practices in patient care settings have historically relied on a centralized, "one-size fits all" approach involving one or more discrete implementation strategies deployed in a bundle across all participating sites. The one-size fits all approach can be effective in achieving desired changes [29] but often fails to produce reliable or consistent change across sites [30]. Such variability is thought to be caused by heterogeneity in the underlying implementation barriers and in local contextual features such as settings and staff [31]. Local tailoring of implementation strategies and bundles has been recommended to respond to variation in local barriers and context [32, 33]. Evidence from head-to-head comparisons of locally-tailored approaches vs. conventional "one-size fits all" approaches is needed to confirm the value of local tailoring for various types of implementation and de-implementation, including practice substitution [34].

In response to the new recommendations for cervical cancer screening, Kaiser Permanente Southern California (KPSC) decided to implement primary HPV screening to replace its existing co-testing method for routine cervical cancer screening for women aged 30–65. We leveraged and supported this health system initiative by conducting a head-to-head cluster randomized pragmatic trial comparing two practice substitution approaches: a "centrally-administered + locally-tailored" (hereafter referred as "locally-tailored") versus a "centrally-administered + usual care" (hereafter referred as "centrally-administered") approach to facilitate adoption of primary HPV screening for routine cervical cancer screening and optimize stakeholder-centered outcomes. As this research was embedded within a large health care delivery system, our results could inform the decision making of clinical and health system leaders interested in selecting, tailoring and deploying optimal implementation strategy bundles to achieve successful de-implementation and substitution.

Methods

Study setting

This study was conducted in KPSC, a large integrated health care delivery system providing care to over 4.8 million members who are broadly representative of the racially, ethnically and socioeconomically diverse residents of Southern California [35]. KPSC members are insured through a variety of commercial, private paid, Medicare, and Medicaid plans, and other low income programs, and represent a wide range of income levels. KPSC delivers care through 15 hospitals and approximately 209 medical offices grouped into 13 medical service areas. The populations served by these medical service areas differed in size and distribution of demographic characteristics and urban/suburban/rural residence. For example, the proportion of Hispanic members in a medical service area ranged from approximately one-third to two-thirds; and the average census block proportion with adults with a college degree ranged from approximately one-fifth to two-fifths. A multidisciplinary HPV Task Force composed of clinical (primary care and ob/gyn physician and nurse leads), administrative, and laboratory leaders as well as health system implementation experts oversaw the health system-led primary HPV screening practice change effort. The HPV Task Force designed and delivered the centrally-administered implementation strategy bundles; the Task Force collaborated with members of the research team to design and carry out the locally-tailored activities in the second study arm (detailed below).

Study design and study participants

This was a prospective, cluster randomized programmatic trial conducted through a research-practice partnership to compare the effects of a locally-tailored versus centrally-administered practice substitution approach to facilitate adoption of primary HPV screening. We measured several system-level implementation outcomes and additional stakeholder-centered outcomes. The study randomization unit was the medical service area. All service areas received the centrally-administered implementation activities comprised of clinician-targeted educational webinars and socialization of the practice change through existing communication networks of clinicians and administrators in preparation for the roll out of primary HPV screening, as well as provision of patient-facing materials to facilitate patient education and explanation. After the region-wide launch of primary HPV screening, sites randomized to the locally-tailored arm participated in a structured process to select, tailor and deliver implementation strategy bundles responding to local needs and circumstances. Sites randomized to the centrally-administered arm did not receive any additional implementation strategies and followed established practice in leveraging the centrally-administered activities to achieve practice change (see Fig. 1 for study activities and study timeline). This manuscript follows the CONSORT guideline for reporting randomized trials.

One service area served as the pilot site for the locally-tailored approach and the remaining 12 service areas were randomized to the two practice substitution approaches. We used matched-pair cluster randomization: the 12 service areas were first matched in pairs on the following factors using a SAS algorithm (SAS Institute Inc) and then randomized: [36] number of clinics within a medical center (a proxy for the difficulty of disseminating information and achieving buy-in and support throughout the entire service area); current cervical cancer screening rate (a proxy for the level of attention and culture related to cervical cancer screening); and average waiting time (in days) for an obstetrics/gynecology appointment (a proxy for provider capacity).

The identification of relevant implementation approaches and the design of the evaluation were guided by the Consolidated Framework for Implementation Research (CFIR) [37] and the Theoretical Domains Framework (TDF) [38–40]. We used CFIR to identify relevant organizational and additional contextual factors to guide design of the practice substitution bundles as well as evaluation design and methods, including variable selection, collection of qualitative and quantitative data, and analyses. We used TDF to guide selection of practice substitution strategies targeting clinician knowledge, attitudes, beliefs and practice change, and methods for qualitative data collection and analysis. The KPSC IRB reviewed and approved the study.

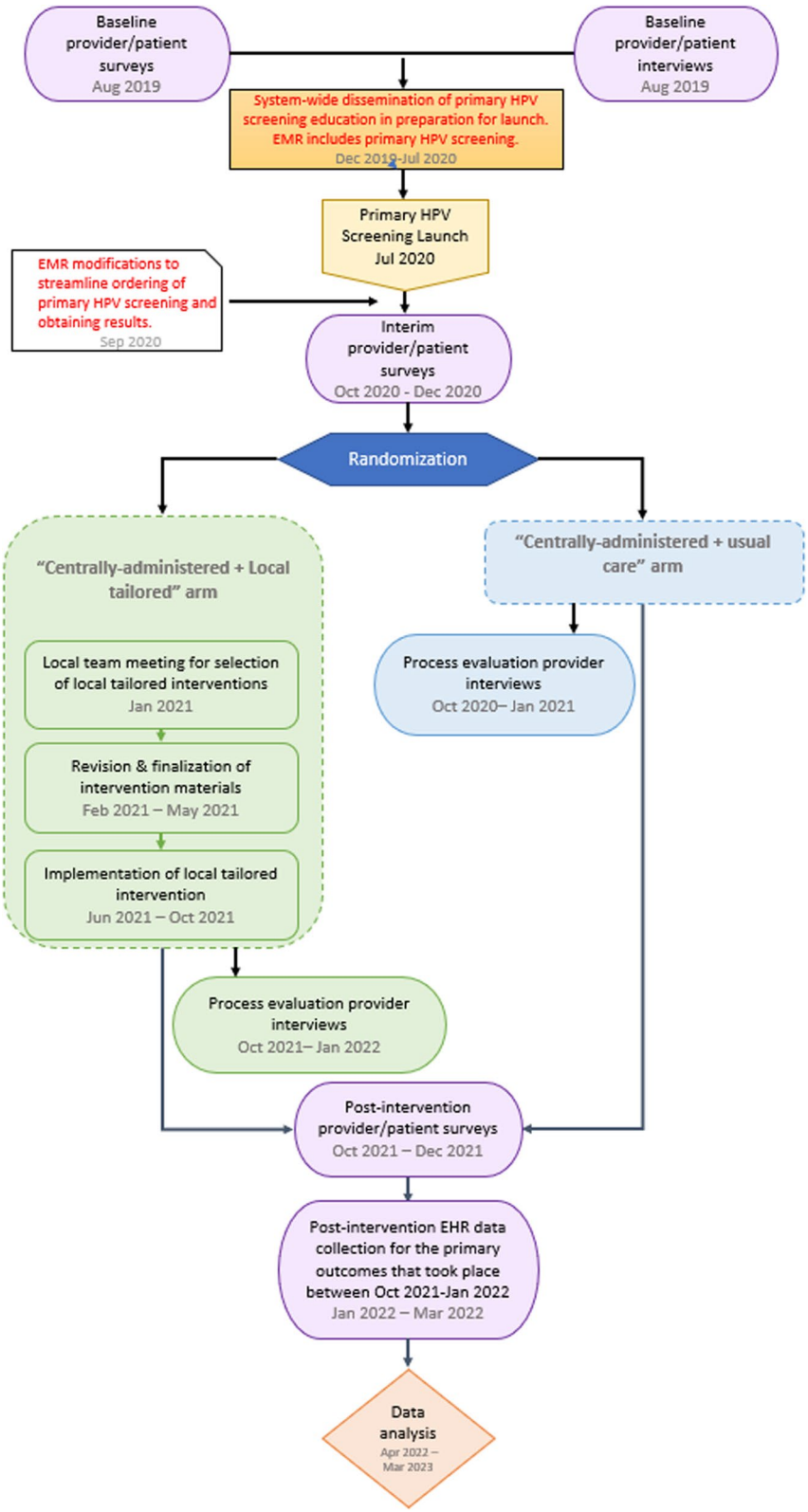

Fig. 1 Timeline of intervention and data collection by implementation strategy arms

All primary care and obstetrics/gynecology departments from KPSC's 13 service areas participated in the study. Implementation activities were delivered at the service area level, involving all physicians, licensed vocational nurses (LVN), medical assistants, administrators, and all women aged 30–65 years who received cervical cancer screening during the study period.

Practice substitution strategies and bundles

The substitution of primary HPV screening for Pap testing and co-testing in a health system required system-level, non-tailorable infrastructure changes (e.g., to laboratory and electronic health record [EHR] and information technology policies and design), as well as tailorable implementation strategies such as physician and staff training/support and patient education. The implementation strategies and their inclusion in both comparators are described below and additional details are available in the study protocol [41].

Comparator 1

The locally-tailored implementation approach involved a structured process encompassing (1) site-specific assessment of local needs followed by convening of a local site team to (2) review the needs assessment data and (3) select from a pre-developed menu of implementation strategies (*forms*) grouped by core function and matched to specific needs, followed by (4) deployment of the resulting tailored bundle of implementation strategies at each site [31, 42]. Two levels of local tailoring were used in this study: (1) selection of core functions based on the highest-ranked local needs/barriers identified; and (2) selection of one or more forms (e.g., email communication or hardcopy handout) to carry out each core function to fit the site context.

Comparator 2

Sites randomized to the centrally-administered arm did not receive support from the research team nor use a systematic needs assessment process to guide local tailoring, but some sites may have augmented the centrally-administered implementation activities with minimal local activities.

Study outcomes and data collection

The primary outcome of interest was the proportion of screening visits by women aged 30–65 in which primary HPV screening was conducted. This outcome was measured at the service area level in a three-month window (Oct 2021-Jan 2022) using data from the KPSC EHR. A greater than 5% difference was pre-specified as clinically important by clinical experts on the project. Of note, following the initial roll out of primary HPV screening and after the trial design had been finalized, HPV Task Force leaders decided to facilitate adherence to the new clinical policy through redesign of the health system's EHR-based cervical cancer screening ordering screens: the health system removed the option to order co-testing for routine screening and listed HPV screening as the only option for routine screening, retaining co-testing as an available option only for patients with a prior abnormal history.

In addition to uptake of a new clinical practice, stakeholder buy-in and satisfaction are critical features of successful implementation: clinician or patient reluctance or dissatisfaction with a planned change can contribute to low rates of initial and/or sustained practice change, and to other adverse outcomes even if practice change is mandated. Acceptability by key stakeholders is thus a critical implementation outcome [43]. To this end, we measured patient- and provider-centered outcomes identified or defined by members of our stakeholder advisory committee as secondary outcomes (Fig. 2). Patient-centered outcomes included knowledge about HPV and HPV testing, acceptance of primary HPV screening, emotional reactions (stigma and embarrassment) to a positive HPV test result, satisfaction with the screening experience, all measured through patient survey (see Appendix Tables 2 and 3 for survey questions). Patient email inquiries about cervical cancer screening, a proxy for patient confusion or unaddressed questions, were also measured from the EHR. Provider-centered outcomes included beliefs about the efficacy of the new test, resistance or acceptance of primary HPV screening (physician only), familiarity with screening guidelines (physician only), knowledge of the follow-up guidelines (physician only), as well as acceptability, appropriateness, and feasibility of primary HPV screening, and satisfaction with the practice substitution process, all measured by provider survey (see Appendix Table 5a/5b for survey questions).

Tertiary outcomes included extent of provider delivery of patient education about cervical cancer screening, and within the locally-tailored arm only, fidelity, sustainment and scalability of the locally-tailored approach. Tertiary outcomes were measured using provider survey and are discussed in the publicly accessible final report from the Patient-Centered Outcomes Research Institute (PCORI) website.

Patient and provider surveys were administered at three time points: 1) pre-implementation (*before* centralized educational activities and implementation of primary HPV screening), (2) interim (post-rollout, three months after the system-wide roll out of primary HPV screening); and (3) post-intervention (two months after the research-led implementation strategy bundles were delivered). Women who tested HPV-negative were

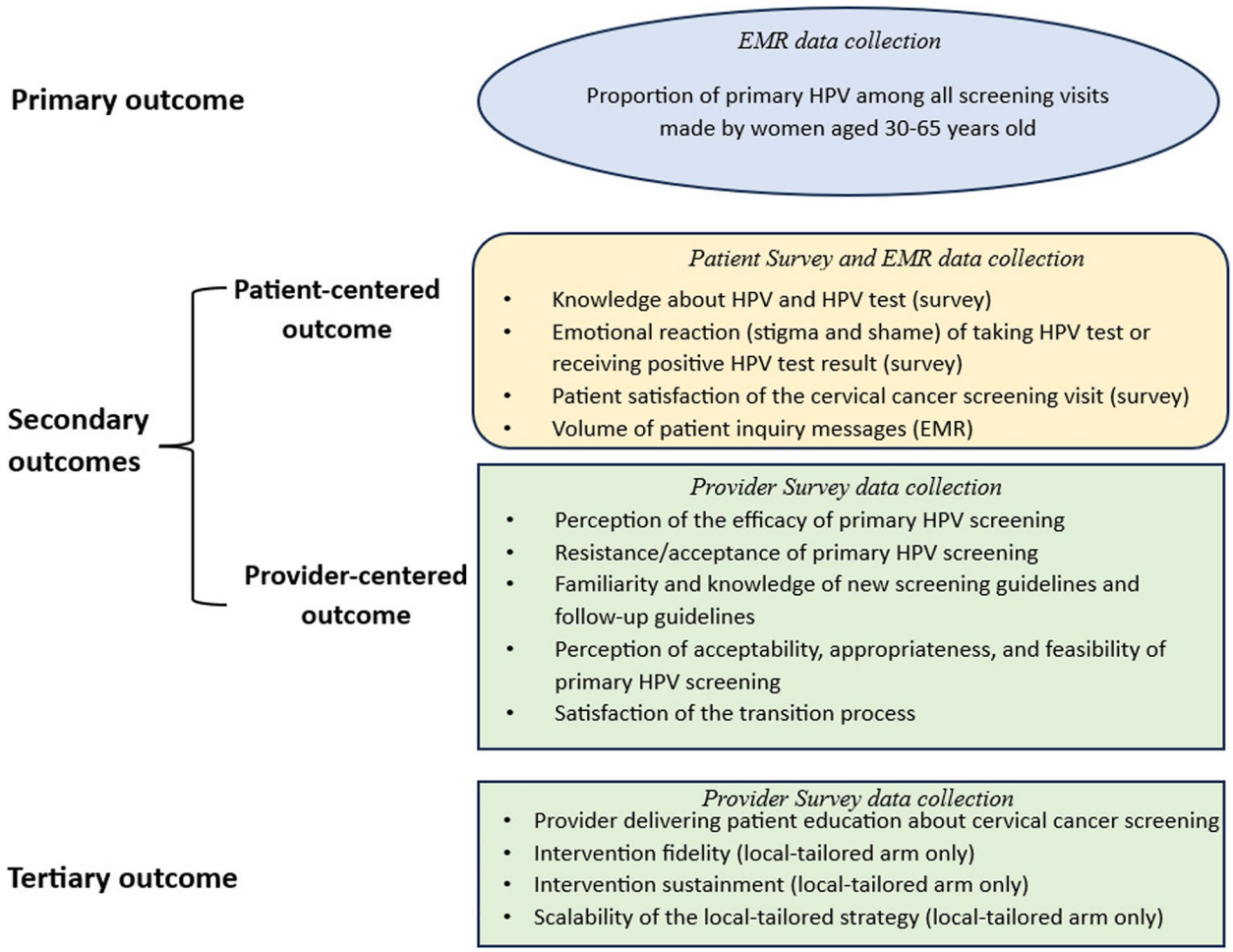

Fig. 2 Summary of study outcomes and methods of data collection

included in the survey. Survey questions were adopted from validated instruments (e.g., patient HPV knowledge score and stigma and shame about HPV [44–46]; provider implementation outcome measures [47]) or published measures when possible [48], while others were developed based on stakeholder input. Provider surveys were administered on-line, whereas on-line and mailed survey methods were employed for patient surveys.

For patient email inquiries about cervical cancer screening, measured via EHR data, the baseline data collection window was 10/19/2019–01/18/2020 (*before* centralized educational activities started in May 2020 and roll-out of primary HPV screening in July 2020) and the post-intervention data collection window was 10/19/2021–01/18/2022. An electronic algorithm was developed to capture email messages from patients inquiring about the cervical cancer screening test or test results. Chart review was performed to help develop this algorithm and validate its accuracy.

Qualitative interviews were also conducted as part of this study in two phases: baseline interviews and post-implementation process evaluation interviews (Fig. 1). Interviews were conducted with physicians, nurses, and administrators from the primary care and ob/gyn departments, and for baseline interviews, also with women between ages 30 to 65. The interview data collection methods and findings have been reported elsewhere [22].

Covariates

KPSC's EHR and administrative databases were used to measure patient-, provider- and system-level characteristics including patient age, race/ethnicity, neighborhood income and education level, preferred language, primary home service area, and length of membership; provider age, sex, race/ethnicity, specialty, and years of practice at KPSC, and the number of clinics in each service area.

Analytical approaches

Analysis for the primary outcome compared the average between-arm difference over the three-month observation period. We computed the proportion of primary HPV screening among all screening visits at the service area level. The proportion was estimated as (# of primary HPV screenings in the observation period)/(total # of screening tests performed in the observation period, i.e., [# of primary HPV screenings in the observation period +# of co-testing performed in the observation period for screening purpose]). The number and proportion of co-tests performed for screening purpose was estimated based on site-specific chart review (50 charts randomly selected for manual review from all co-testing orders occurring in each service area—300 total charts reviewed) with sampling weights applied to estimate the weighted proportions of co-tests performed for screening and subsequently the number of co-tests for screening [49]. We also used the sampling weights to calculate the variance of the total number of co-tests performed for screening and obtained 95% confidence limits. Statistical testing comparing the two arms was performed using Z statistics accounting for the design effect.

For all secondary outcomes, we first calculated the distributions of the demographic characteristics of study subjects included for each secondary outcome, overall and by study arm. For each outcome, we estimated changes in each outcome from baseline to post-intervention within each arm, and the difference-in-differences (DID, the main parameter of interest) between the two arms. We used the Generalized Estimating Equations (GEE) framework for marginal models, with different link functions to address the different types of outcomes allowing for clustering. An additional random effect was included to account for the matched design. We adjusted for patient age, race/ethnicity, and years of prior KPSC membership for patient-centered outcomes, and provider age, sex, race/ethnicity, and years of practice at KPSC for the provider-centered outcomes. We accounted for the survey sampling design and survey response by calculating design and response weights as the inverse of the selection or response probabilities.

For patient email inquiries, in order to account for the effect of individual physicians and to facilitate the DID approach, we included only physicians who performed cervical cancer screening in both the baseline and the post-intervention periods (85% of all physicians) and performed a minimum of five cervical cancer screenings in the study windows (74% of all physicians who performed screening in both baseline and post-intervention). We used the same analytical principles as described above, with log-Poisson models with robust standard error. We adjusted for provider department, gender, race/ethnicity, and years of experience in KPSC, and provider-level averages of patient age, race/ethnicity, years of KP membership, and neighborhood deprivation index (NDI) quartile. We encountered very few instances of missing covariate data (< 5% for all covariates). All analyses were conducted in SAS statistical software Version 9.4; Cary, North Carolina, USA.

Results

Primary outcome

Appendix Table 1 shows the number of providers and women screened by primary HPV screening in the study intervention and data collection window. All service areas were found to have a very high proportion of appropriate screenings at post-intervention [the proportion of primary HPV screening (as opposed to co-testing) among all screening visits], ranging from 97.6% to 99.6% (Table 1). The overall proportion was estimated to be

Table 1 Estimated proportion of primary HPV screening among all screening visits by service area and study arms in the post-implementation data collection period

Locally-tailored		Centrally-administered	
Service Area	**Estimated proportion of primary HPV screening among all screening visits**	**Service Area**	**Estimated proportion of primary HPV screening among all screening visits**
Service area 1	99.7%	Service area 7	98.4%
Service area 2	99.5%	Service area 8	99.6%
Service area 3	98.6%	Service area 9	98.6%
Service area 4	99.4%	Service area 10	98.9%
Service area 5	98.9%	Service area 11	97.6%
Service area 6	98.7%	Service area 12	98.6%
Combined	98.4% (96.3-100%)[a]	Combined	99.1% (97.8-100%)[a]

[a] 95% confidence interval

98.4% (95% confidence interval [CI] 96.3%− 100%) for the locally-tailored arm and 99.1% (97.8%− 100%) for the centrally-administered arm (p-value = 0.34). The absolute difference in the proportions between arms did not reach the pre-specified clinically meaningful level (i.e., 5%).

Secondary patient-centered outcomes

For the patient surveys, a total of 1,266 (36% response rate, mean age 45) and 949 (31% response rate, mean age 48) survey responses were received from the baseline and the post-intervention survey invitations, respectively. Weighted patient characteristics of the survey respondents are shown in Table 2.

No significant DID was found between study arms for any patient-centered outcome evaluated (Fig. 3 and Appendix Table 2). Further, no significant change between baseline and post-intervention time periods was noted for patient-centered outcomes measured at both time periods within each arm. For the HPV knowledge score that ranges from 0–6 (6 being the highest knowledge), the overall mean score was 2.7 (standard deviation [SD] 1.5) at baseline and 2.5 (SD 1.5) at post-intervention. For women's acceptance of primary HPV screening, overall, 6.1% of the women viewed primary HPV screening as an acceptable screening modality at baseline, compared with 5.1% in the post-intervention period. For the stigma score ranging from 1–5 (5 being highest stigma), the overall mean score was 1.5 (0.8) and 1.9 (1.1) for taking the HPV test and testing HPV positive at baseline, respectively, compared with 1.5 (0.9) and 1.8 (1.2) post-intervention, respectively. For embarrassment about taking the HPV test, 21.3% of respondents overall reported embarrassment at baseline, compared with 19.9% in the post-intervention period. For embarrassment about testing HPV positive, 49.9% reported embarrassment at baseline compared with 46.9% in the post-intervention period. For patient satisfaction of the screening visit (score 1–5, 5 being the highest satisfaction),

Table 2 Characteristics of patient survey respondents included in the analysis (HPV-negative women only)

	Baseline Survey Respondents				**Post-intervention Survey Respondents**			
	Total (n = 1266)	**Centrally-administered (n = 786)**	**local-tailored (n = 480)**	***p*-value**	**Total (n = 949)**	**Centrally-administered (n = 510)**	**local-tailored (n = 439)**	***p*-value**
Age, Mean (SD), yrs	44.5 (10.6)	44.8 (10.6)	44.0 (10.4)	0.21	48.1 (10.5)	48.4 (10.5)	47.8 (10.5)	0.38
Race/Ethnicity n(%)				< 0.01				0.19
White	526 (41.5%)	349 (44.4%)	177 (36.9%)		253 (26.7%)	147 (28.8%)	106 (24.1%)	
Black	89 (7.0%)	69 (8.8%)	20 (4.2%)		46 (4.8%)	31 (6.1%)	15 (3.4%)	
Hispanic	432 (34.1%)	245 (31.2%)	187 (39%)		505 (53.2%)	259 (50.8%)	246 (56%)	
Asian	122 (9.6%)	69 (8.8%)	53 (11%)		87 (9.2%)	44 (8.6%)	43 (9.8%)	
Pacific Islander	9 (0.7%)	4 (0.5%)	5 (1%)		3 (0.3%)	1 (0.2%)	2 (0.5%)	
Native Am Alaskan	2 (0.2%)	1 (0.1%)	1 (0.2%)		2 (0.2%)	0 (0%)	2 (0.5%)	
Multiple	5 (0.4%)	3 (0.4%)	2 (0.4%)		2 (0.2%)	1 (0.2%)	1 (0.2%)	
Other	31 (2.4%)	20 (2.5%)	11 (2.3%)		13 (1.4%)	5 (1%)	8 (1.8%)	
Unknown	50 (3.9%)	26 (3.3%)	24 (5%)		38 (4%)	22 (4.3%)	16 (3.6%)	
Census-block median annual income, $, Mean (SD)	87,029.6 (31,880.7)	87,795.6 (32,601.0)	85,779.0 (30,660.8)	0.33	77,801.2 (30,382.6)	77,291.4 (29,227.6)	78,412.4 (31,738.9)	0.99
% of adults with college degree in census block, Mean (SD)	31.1 (18.1%)	32.8 (19.2%)	28.3 (15.6%)	< 0.01	26.7 (17.4%)	27.3 (17.8%)	25.9 (16.7%)	0.29
Preferred Language n(%)				0.98				0.60
English	1258 (99.4%)	781 (99.4%)	477 (99.4%)		663 (69.9%)	360 (70.6%)	303 (69.0%)	
Spanish	8 (0.6%)	5 (0.6%)	3 (0.6%)		286 (30.1%)	150 (29.4%)	136 (31%)	
Years of enrollment in the past 10 years, Mean (SD)	5.0 (3.6)	5.0 (3.7)	5.0 (3.6)	0.79	5.9 (3.8)	6.0 (3.8)	5.9 (3.8)	0.69

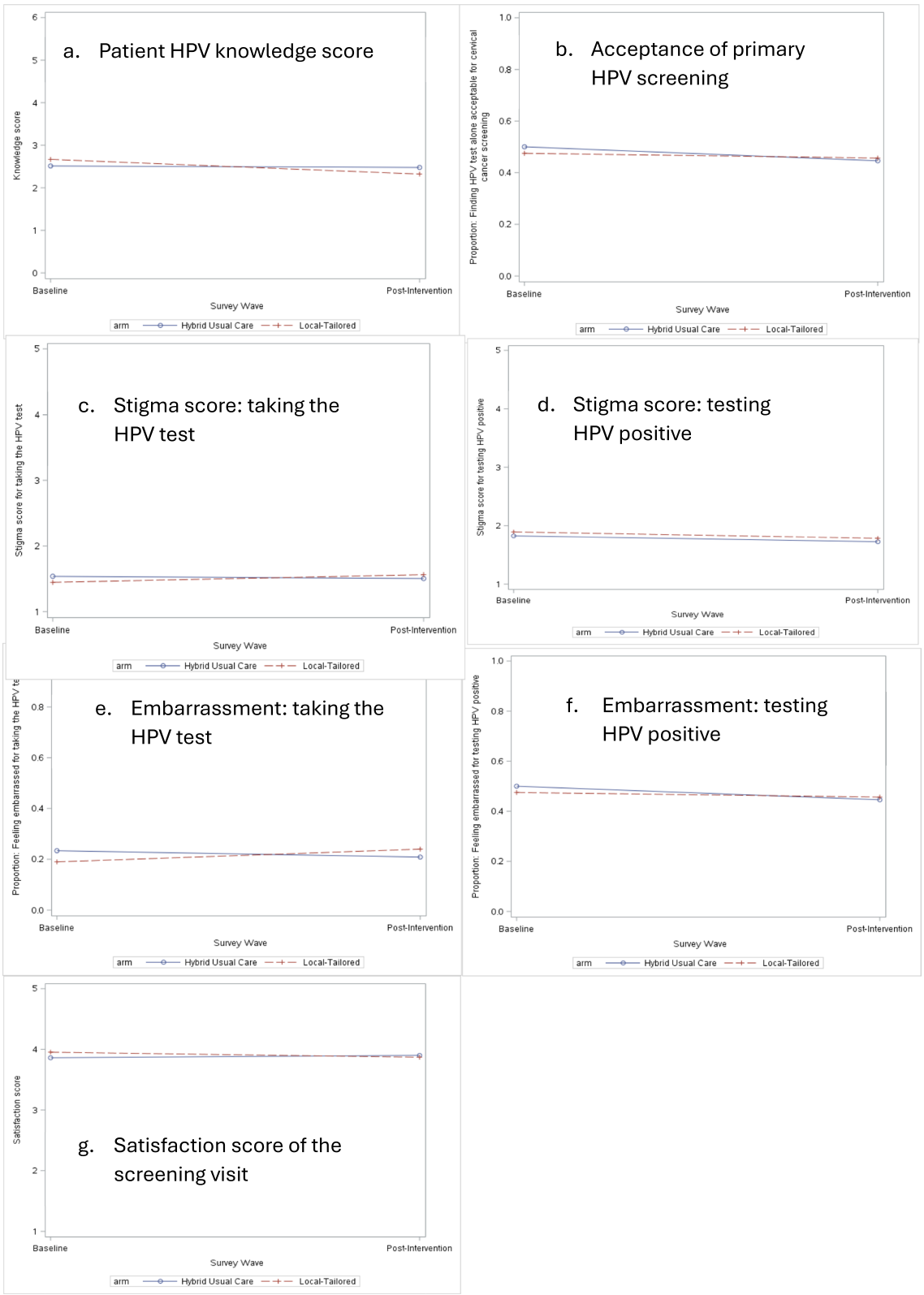

Fig. 3 Baseline and post-intervention patient-centered outcomes by randomization arm

the mean score was 3.9 (0.8) at baseline and 3.9 (0.9) post-intervention.

For the patient email inquiries, a total of 1,294 physicians were included in this analysis (694 in the centrally-administered arm and 600 in the locally-tailored arm, 70% family medicine/internal medicine and 30% obstetrics/gynecology). These physicians screened a total of 24,150 women in the baseline period and 25,464 in the post-intervention period. In both arms, there was a significant decrease between the baseline and post-intervention periods in the number of patient email inquiries regarding screening (Appendix Fig. 1). The patient message volume (i.e., # messages per physician per 10 screened women) at post-intervention was 76% ($p < 0.01$) of that at baseline for the locally-tailored arm, and 71% ($p < 0.01$) for the centrally-administered arm. The DID (measured as ratio of the ratios), however, was not statistically significant (DID = 1.06-fold, $p = 0.59$).

For all patient-centered outcomes, findings are similar between study arms within each time point. Findings are also similar from both the crude and adjusted analyses.

Secondary provider-centered outcomes

For the provider surveys, a total of 588 (23% response rate) and 1,032 (20% response rate) survey responses were received from the baseline and the post-intervention data collection, respectively. The mean age of survey respondents was 44 (baseline) and 45 (post-intervention) for physicians and 38 (baseline) and 41 (post-intervention) for LVNs/MAs. About half of the physician respondents and the majority of the LVN/MA respondents were female (~ 90%). About 80% of the respondents were based in family medicine/internal medicine (Appendix Table 4a/4b).

No significant DID was found between study arms for any provider-centered outcome evaluated. Survey responses were also similar between study arms at each wave of survey. For perception about the effectiveness of primary HPV screening, 66.6% of the providers considered primary HPV screening very effective for screening women aged 30–65 at baseline, compared with 74.2% in the post-intervention period. For the physicians, there was a significant increase in this proportion between baseline and post-intervention, yet for nurses, a significant decrease was observed for the locally-tailored arm but not for the centrally-administered arm (Fig. 4 and Appendix Table 5a/5b). For acceptance of primary HPV screening (physician only), 6.6% of the physicians selected primary HPV screening as an appropriate screening method for women aged 30–65 years at baseline, compared with 48.5% in the post-intervention period. For familiarity with the screening and follow-up guidelines (physicians only), overall, 27% and 11% of the physicians reported being very familiar with the screening and follow-up guidelines at baseline, respectively, compared with 19% and 13% in the post-intervention period (Fig. 4 and Appendix Table 5a/5b). For knowledge with the follow-up algorithm (physicians only), overall, 8.5% of the physicians answered all three questions correctly, compared with 10.2% in the post-intervention period.

Overall, 89% of the providers reported being satisfied with the transition process. The proportion was similar between arms. In the adjusted model, the practice substitution approach (locally-tailored vs. centrally-administered) was not significantly associated with provider satisfaction (OR = 0.91 for "satisfied" for the locally-tailored arm compared with the centrally-administered arm, $p = 0.75$ for this different). Responses to individual survey items regarding provider experience about the transition process are shown in Appendix Table 6.

For all provider-centered outcomes, findings are similar between study arms within each time point. Findings are also similar from both the crude and adjusted analyses.

Discussion

In this study we compared effects of locally-tailored vs. centrally-administered practice substitution approaches on implementation and stakeholder-centered outcomes. The centrally-administered approach is considered the reference approach since it is the standard approach used by KPSC and we were interested in evaluating the potential benefit of adding local tailoring to facilitate cervical cancer screening practice substitution. We found that the rate of appropriate screening (i.e., the proportion of primary HPV screening among all screenings) for women aged 30–65 years was high across all service areas 15 months after the transition, with no benefit observed for the locally-tailored approach on the rate of appropriate screening or on the secondary patient- or provider-centered outcomes.

A powerful system-level implementation approach was deployed at KPSC soon after the initial roll-out of primary HPV screening: system leaders redesigned the test ordering screens in the EHR to eliminate the option for providers to select non-recommended approaches for screening. This approach was designed to facilitate adherence and reduce confusion triggered by the newly released 2019 ASCCP management guidelines specifying the recommended testing approach for patients with an abnormal screening history. The two test options offered in the redesigned EHR order screen were "test for routine screening (HPV with cytology reflex)" and "test for abnormal follow-up (HPV and cytology)." We believe that this EHR redesign was the primary driver of the very high uptake of primary HPV screening and the lack of difference between study arms in the primary outcome of interest: the very high uptake (> 98%) in the reference

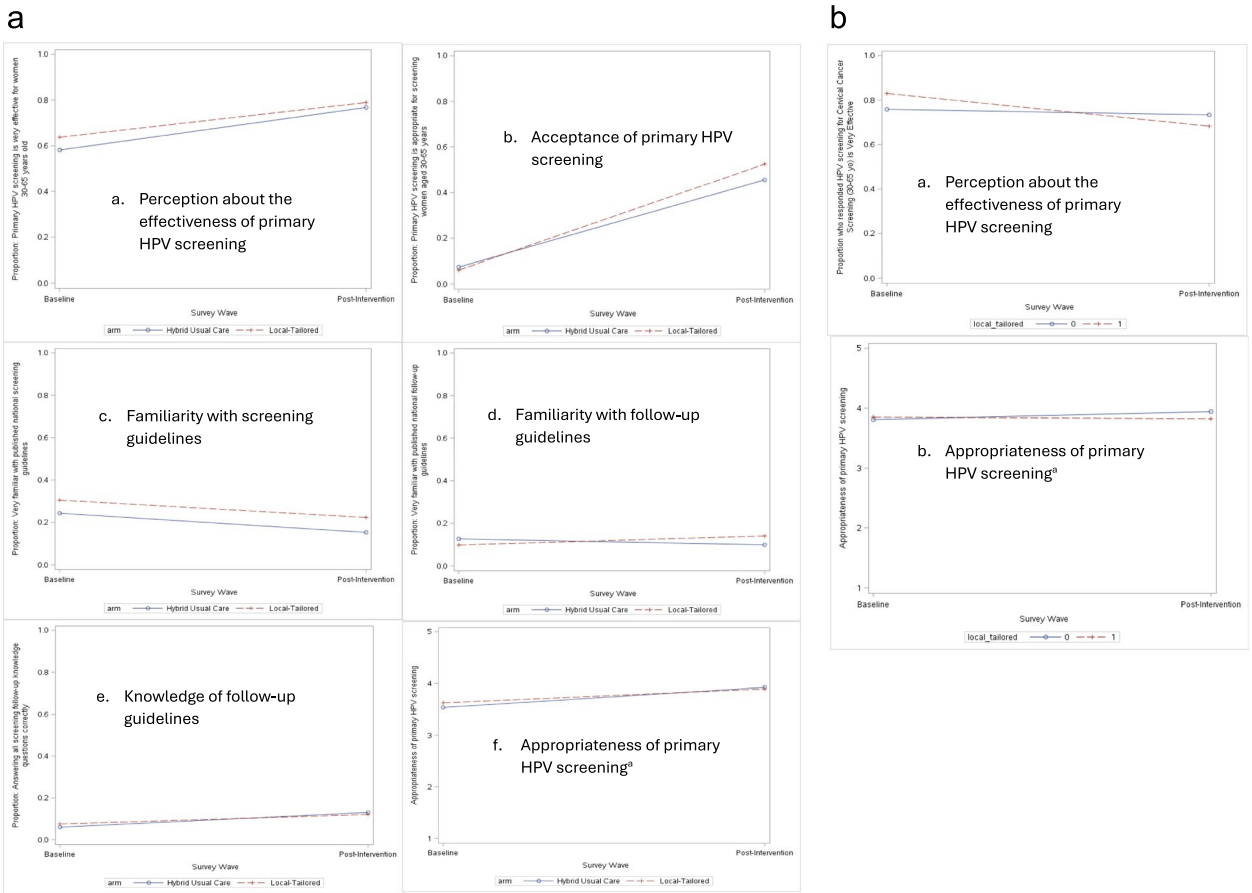

Fig. 4 a. Baseline and post-intervention provider-centered outcomes by randomization arm – physicians. [a]Data and figures for acceptance, appropriateness, and feasibility are similar. Only figure for appropriateness is shown here to avoid redundancy. **b**. Baseline and post-intervention provider-centered outcomes by randomization arm – LVN/MA

arm precluded the detection of statistically significant improvement in the locally-tailored arm (ceiling effect, since the uptake cannot exceed 100%), although any magnitude of improvement from 98% would not be considered clinically important.

The "constrained choice implementation" approach, accomplished through a simple change in the EHR test ordering screens, produced very high rates of practice change in our study. This approach warrants further research, both to identify and evaluate additional forms of constrained choice implementation and to carefully study harms and other unintended consequences. As an implementation strategy, constrained choice implementation is feasible for various health care settings. Additional forms of constrained choice implementation may include policy-level changes (e.g., prohibiting outdated practices [50] or mandating desired practices), elimination of reimbursement for outdated practices or conditioning reimbursement for specific practices on delivery of desired supplementary practices, use of formularies restricting prescribing choices, and withdrawal of resources required to deliver an outdated service. However, adverse effects on clinician, staff, and/or patient satisfaction may result from mandating a practice change (e.g., by removing previously-used practice options) when key stakeholders do not support the change. Measurement of unintended consequences and harms is recommended for all types of clinical research, and therefore harms should be measured as secondary outcomes in all implementation studies [51, 52]. In studies of constrained choice implementation where high adoption of the practice change is expected, harms should be considered as the primary outcome.

We also observed null findings on all stakeholder-centered outcomes; as such, it is important to understand if the null findings might be due to low fidelity to the locally-tailored implementation approach. We measured the fidelity via the provider and patient

survey using a set of questions for awareness, use, and perceived value for each approach/function. Survey results suggested a reasonable uptake (21–60%) of the locally-tailored implementation strategies and a high perceived value of these strategies for clinical practice. However, respondents in our provider interview reported lower rate of recall of use and lower perceived value of these implementation strategies.

It should be noted that the COVID- 19 pandemic had a significant impact on multiple aspects of the study, particularly for the locally-tailored arm. The pandemic reduced the availability of providers to attend educational meetings and local-tailoring meetings. The pandemic also led to temporary stoppage of all in-person department or staff meetings, which likely resulted in less penetration of the locally-tailored implementation activities, or making them less effective in influencing stakeholder-centered outcomes.

Of note, we had a considerable time lag (~ 4 months) between local team meetings and delivery of implementation strategies. This is mainly due to the additional tailoring requests that required organizational approval, such as the introduction of smart phrases in the EHR system. It is possible that providers might have moved their attention away from this practice change and/or gradually accepted the new practice during this time even without additional implementation strategies (which would still argue against the value of local-tailoring since its superiority over non-tailored approaches, even if observed, could be temporary). Based on these experiences, planning activities to conduct local-tailoring should account for the variable availability and priorities of local teams and administrators and consider the uncertainties when allowing a larger scope of local tailoring. This could be proactively managed to a certain extend by limiting the scope of implementation strategy tailoring, and/or by engaging a larger number and types of clinical stakeholders upfront.

In addition, it is important to note that primary HPV screening has strong clinical evidence and guideline support, does not change the patient experience of the screening process, and was compatible with existing workflows at KPSC [53, 54]. It did not require staff or physicians to take on new roles and in fact had relative advantage in simplifying the workflow. When barriers to the desired practice substitution were assessed in the locally-tailored arm, most of the needs identified centered around provider education, and there was a large degree of overlap in provider needs and patient-level barriers reported across these sites, as well as the selected intervention core functions. These findings suggested that variability in local needs and context might not be sufficient to warrant local-tailoring, which may also in part explain the lack of difference among the stakeholder-centered outcomes. In addition, the value of tailoring by selecting distinct forms also appeared low for this implementation problem.

In a Cochrane systematic review of the effect of implementation strategies tailored to practice determinants, Baker and colleagues identified 32 cluster-randomized trials comparing tailored interventions to no interventions or interventions not tailored [31]. They found an overall odds ratio of 1.56 for tailored interventions compared with non-tailored intervention or no intervention for the outcome of uptake of recommended practice. However, studies showed variable effectiveness. Surprisingly, the pooled odds ratio was higher for the study that had a reference group of non-tailored interventions than those that used no intervention as the reference (odds ratio = 1.79 vs. 1.48). Overall, the number of studies evaluating tailored interventions remains low, and the certainty of evidence remains moderate, with only 20 studies included in this review incorporating some adjustment to local factors (local-tailoring).

Several recently-published articles contribute to the growing body of knowledge and scientific discussion regarding intervention and implementation strategy tailoring [55–63]. Several researchers encourage greater use of theory in tailoring, although balance should be achieved between information obtained from theory, stakeholder input and contextual analysis [55, 63, 64]. To date, methods for conducting effective tailoring, including methods to identify important influences on professional practices and effective approaches for selecting implementation strategies to address these influences, are still in development and require further study [64]. To our knowledge, the literature is also sparse on comparing implementation approaches for practice substitution in general. Considering the limited knowledge available, our study adds to the overall evidence-base for implementation strategy tailoring and local-tailoring for cancer screening as well as practice substitution and practice change in general. Future research should evaluate approaches to optimize the means and process of barrier/need assessment, local-engagement, and implementation strategy selection and tailoring and should continue to evaluate the value of local tailoring in different implementation scenarios as well as practice substitution and de-implementation scenarios.

There are several limitations to consider when interpreting our results. As mentioned earlier, unexpected delay in delivering the tailored implementation strategies was a limitation of the study. Moreover, as with any survey, self-report and participation bias are always possible, especially with response rates ranging between 20–36%.

Potential participation bias, such that those who were more supportive or unsupportive of the practice substitution may be more likely to respond, calls for caution when interpreting the provider survey findings on their own. That said, we expect such potential bias to be non-differential between study arms. Our patient survey did not include women who screened HPV-positive and thus we could not assess implementation bundle impact on this minority group of women. In addition, the COVID-19 pandemic forced replacement of some in-person data collection via site visits with survey and phone interviews. Further, the pandemic might have shifted the priority and attention of both the providers and patients. As a result, it is possible that some of the patient and provider findings may not be applicable to the post-pandemic period.

As discussed earlier, our study findings regarding the effects of constrained choice implementation are likely generalizable to various types of health systems for similar practice substitution problems. Computerized ordering systems are widely available in developed countries and especially those with high levels of EHR implementation. Other approaches to constrained choice implementation may be available for practice settings lacking computerized ordering, including modifications to reimbursement policies. Our finding of no difference between locally-tailored and centrally-administered implementation may be generalizable only to health systems in which routine, centrally-administered implementation approaches are well-designed and strong; and to systems with relatively homogeneous care delivery sites. KPSC has robust infrastructure for implementation of new innovations which has contributed to higher rates of quality improvement compared to the national average [65]. Further, sites within KPSC may be more homogeneous in their needs and thus less responsive to local tailoring. Implementation problems and settings for which barriers vary significantly and/or sites are more heterogeneous (e.g., community health centers or private practices) may show greater response to local tailoring. That said, policy and program incentives at the national level and advancement in technology have led to significant health system consolidation and growth of large integrated delivery systems in the U.S.. For this reason, our practice substitution experience and recommendations regarding desired implementation bundle features are likely applicable to a growing proportion of the U.S. healthcare system.

Conclusion

We did not find evidence to support our hypothesis regarding barrier heterogeneity and the benefit of local-tailoring for the substitution of primary HPV screening for the previous practice of co-testing. Our findings suggest no additional benefit in the rate of uptake of primary HPV screening or in stakeholder-centered outcomes associated with local implementation bundle tailoring, in the context of what proved to be a highly effective centrally-administered approach to implementation incorporating redesign of the EHR test ordering screen. Given the addional costs associated with performing barrier/need assessment and implementation strategy tailoring, the centrally-administered practice substitution approach appears to be the preferred method for this type of practice change in settings similar to KPSC. Further research is needed to determine whether this conclusion is generalizable to other implementation problems where barriers vary significantly across sites and may benefit from more complex local tailoring of the practice change bundle.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13012-025-01432-9.

Supplementary Material 1.

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Authors' contributions

CRC conceptualized the study, obtained funding, supervised the study conduct and data collection, interpreted study findings, and drafted the initial draft and critically revised this manuscript. NC performed project management, including supervising, coordination, and budget management, contributed to the development of data collection tools and stakeholder engagement, and critically revised the manuscript. EEH provided scientific inputs for the study design and conduct, led the qualitative data collection and analysis, and critically revised the manuscript. ES provided scientific input for the study design and led the statistical analyses. CH performed project management, including supervising, coordination, and budget management, contributed to the development of data collection tools and stakeholder engagement, and critically revised the manuscript. QNM provided scientific inputs for the study design and conduct, assisted with result interpretation, and critically revised the manuscript. MKG provided scientific inputs for the study design and conduct, assisted with result interpretation, and critically revised the manuscript. CEM conducted qualitative data recruitment, collection and analysis, including focus groups and qualitative interviews. MHK provided inputs for the study design and conduct as a stakeholder, assisted with result interpretation, and critically revised the manuscript. PW assisted with stakeholder engagement, recruitment and data collection, and critically revised the manuscript. LHA provided inputs for the study design and conduct as a stakeholder, assisted with result interpretation, and critically revised the manuscript. MH provided scientific inputs for the study design and conduct, and critically revised the manuscript. BIB provided inputs for the study design and conduct as a

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Data availability
Anonymized data that support the findings of this study may be made available from the corresponding author on reasonable request from qualified researchers with documented evidence of training for human subject protections.

Declarations

Ethics approval and consent to participate
The KPSC IRB reviewed and approved the study. Individuals provided consent to participate in the qualitative interviews. Completion of the study survey was considered implicit consent to participate in the study by the individuals who completed the study surveys.

Consent for publication
Not Applicable.

Competing interests
None to disclose.

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