original reports abstract

Development and Pilot Implementation of the Genomic Risk Assessment for Cancer Implementation and Sustainment (GRACIAS) Intervention in Mexico

Kathleen R. Blazer, EdD[1]; Yanin Chavarri-Guerra, MD, MSc[2]; Cynthia Villarreal Garza, MD, DSc[3]; Bita Nehoray, MS[1]; Alejandro Mohar, MD[4,5]; Adrian Daneri-Navarro, MD, PhD[6]; Azucena del Toro, MD[6]; Dione Aguilar, MD[3]; Jazmin Arteaga, MD[2]; Rosa Maria Álvarez, MD[4]; Rosa Mejia, BS[1]; Josef Herzog, BS[1]; Danielle Castillo, BS[1]; Maria Fernandez, PhD[7]; and Jeffrey N. Weitzel, MD[1,8]

PURPOSE Genomic cancer risk assessment (GCRA) is standard-of-care practice that uses genomic tools to identify individuals with increased cancer risk, enabling screening for early detection and cancer prevention interventions. GCRA is not available in most of Mexico, where breast cancer (BC) is the leading cause of cancer death and ovarian cancer has a high mortality rate.

METHODS Guided by an implementation science framework, we piloted the Genomic Risk Assessment for Cancer Implementation and Sustainment (GRACIAS) intervention, combining GCRA training, practice support, and low-cost *BRCA1/2* (*BRCA*) gene testing at four centers in Mexico. The RE-AIM model was adapted to evaluate GRACIAS intervention outcomes, including reach, the proportion of new patients meeting adapted National Comprehensive Cancer Network criteria who participated in GCRA. Barriers to GCRA were identified through roundtable sessions and semistructured interviews.

RESULTS Eleven clinicians were trained across four sites. Mean pre-post knowledge score increased from 60% to 67.2% (range 53%-86%). GCRA self-efficacy scores increased by 31% (95% CI, 6.47 to 55.54; $P = .02$). Participant feedback recommended Spanish content to improve learning. GRACIAS promoted reach at all sites: 77% in Universidad de Guadalajara, 86% in Instituto Nacional de Cancerología, 90% in Tecnológico de Monterrey, and 77% in Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Overall, a pathogenic *BRCA* variant was identified in 15.6% (195 of 1,253) of patients. All trainees continue to provide GCRA and address barriers to care.

CONCLUSION We describe the first project to use implementation science methods to develop and deliver an innovative multicomponent implementation intervention, combining low-cost *BRCA* testing, comprehensive GCRA training, and practice support in Mexico. Scale-up of the GRACIAS intervention will promote risk-appropriate care, cancer prevention, and reduction in related mortality.

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INTRODUCTION

Genomic cancer risk assessment (GCRA) is a standard-of-care practice using genetic and genomic tools to identify and manage individuals with inherited cancer risk.[1] Despite evidence that GCRA enables earlier stage at diagnosis or prevention of cancers among *BRCA1/2* (*BRCA*) pathogenic variant (PV) carriers, GCRA services are not well-diffused,[2] particularly in low- and middle-income countries (LMICs) like Mexico, where breast cancer (BC) is the leading cancer cause of death in women and ovarian cancer also has a high rate of mortality.[3-6] There are limited GCRA expertise among healthcare professionals in Mexico and barriers in access to cancer genetic testing for most of the population.

Implementation of GCRA services and *BRCA* testing in Mexico would identify patients with hereditary cancer who may benefit from reduction of new primary cancer risk or targeted therapy[7,8] and also has the potential to reduce cancer burden through cascade testing and cancer screening and prevention for at-risk family members. This may allow for better allocation of limited and cancer screening resources, in alignment with emerging health policies in Mexico.[9]

We implemented *pro bono* GCRA services to address disparities at a Hispanic-serving safety net hospital in

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Although genomic cancer risk assessment (GCRA) is a standard-of-care service in developed nations, access remains limited in Mexico and other low- and middle-income countries. We describe the first project to use implementation science methods to develop and deliver an innovative multicomponent implementation intervention called Genomic Risk Assessment for Cancer Implementation and Sustainment (GRACIAS), combining low-cost *BRCA* testing, comprehensive GCRA training, and practice support.

Knowledge Generated

Roundtables identified limitations in healthcare finance, adequately trained workforce, and population-based registries. GRACIAS resulted in increased reach and sustainment of GCRA services at four major centers in Mexico, and the yield of *BRCA* pathogenic variants was comparable with the yield in US high-risk clinics.

Relevance

GCRA risk stratification could inform allocation of limited resources and result in prevention of cancer. The implementation science developed for GRACIAS may help scale up dissemination of GCRA in Latin America and for application in low-resource settings, including rural communities and safety net hospitals in the United States.

Los Angeles[10-13] and used a community-based clinical research network to collect data and learn from similar low-resource settings across the United States.[10,14,15] This paper describes the development, delivery, and preliminary outcomes of a Genomic Risk Assessment for Cancer Implementation and Sustainment (GRACIAS) implementation intervention in Mexico.

Theoretical Approach

We tested the GRACIAS intervention at four Mexican clinics, guided by the Interactive Systems Framework for Dissemination and Implementation (ISF).[16] The ISF helped us understand the various systems (synthesis, translation, support, and delivery systems) involved in new practice implementation and also informed our development of capacity-building tools and resources. We used the RE-AIM Framework[17] to evaluate the impact of the implementation strategies.

METHODS

The process and tools used for developing and assessing the GRACIAS intervention are summarized in Figure 1 and described below.

Participants and Settings

Clinician participants. Clinician scientists identified through networking at academic oncology conferences were identified as champions for delivering GCRA services at their respective Mexican health centers.

Settings. We piloted the GRACIAS intervention at Universidad de Guadalajara (UdeG), which collaborates with two public hospitals (Instituto Jalisciense de Cancerología and the OPD Hospital Civil de Guadalajara) to care for patients with cancer from Jalisco, and Instituto Nacional de Cancerología (INCan) in Mexico City, the largest center and main referral resource for specialized cancer care for the uninsured population. We subsequently added Tecnológico de Monterrey Escuela de Medicina Monterrey (TecSalud), an academic and community health system, and Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (Nutrición) in Mexico City. Nutrición is a national referral center, providing care to $>$ 4,000 mostly uninsured patients annually.

The health system in Mexico comprises insurance for employees, public assistance for the uninsured, and a private sector. Approximately 50% of people are uninsured. All GRACIAS sites serve the uninsured population. Although some general genetics services were available before the GRACIAS intervention, this was primarily empirical cancer risk counseling on the basis of syndromic phenotypes, with limited access to *BRCA* testing.

Patient participants. Patient eligibility for GCRA was adapted from National Comprehensive Cancer Network (NCCN) guidelines and included a diagnosis of BC $\leq$ 50 years, triple-negative breast cancer, or ovarian cancer at any age.[18]

Ethics approval and consent to participate. Patients who received GCRA services in this study were recruited into a shared prospective human subjects Institutional Review Board (IRB; City of Hope IRB# 96144; data coordinating center)–approved cancer genetics registry protocol used across the federated *Clinical Cancer Genetics Community Research Network* (CCGCRN). The protocol was reviewed and approved at each partner institution (IRB# 00007348, INCan, Mexico City; IORG# IORG0006166**,** UdeG, Guadalajara, México). Patients provide written informed consent for collection of baseline and follow-up medical and family history and blood or saliva sample and for recontact to receive genetic test results.

Engagement and Readiness Planning

Guided by the ISF, we initially met with institution leaders and clinician stakeholders at UdeG in 2011, INCan in

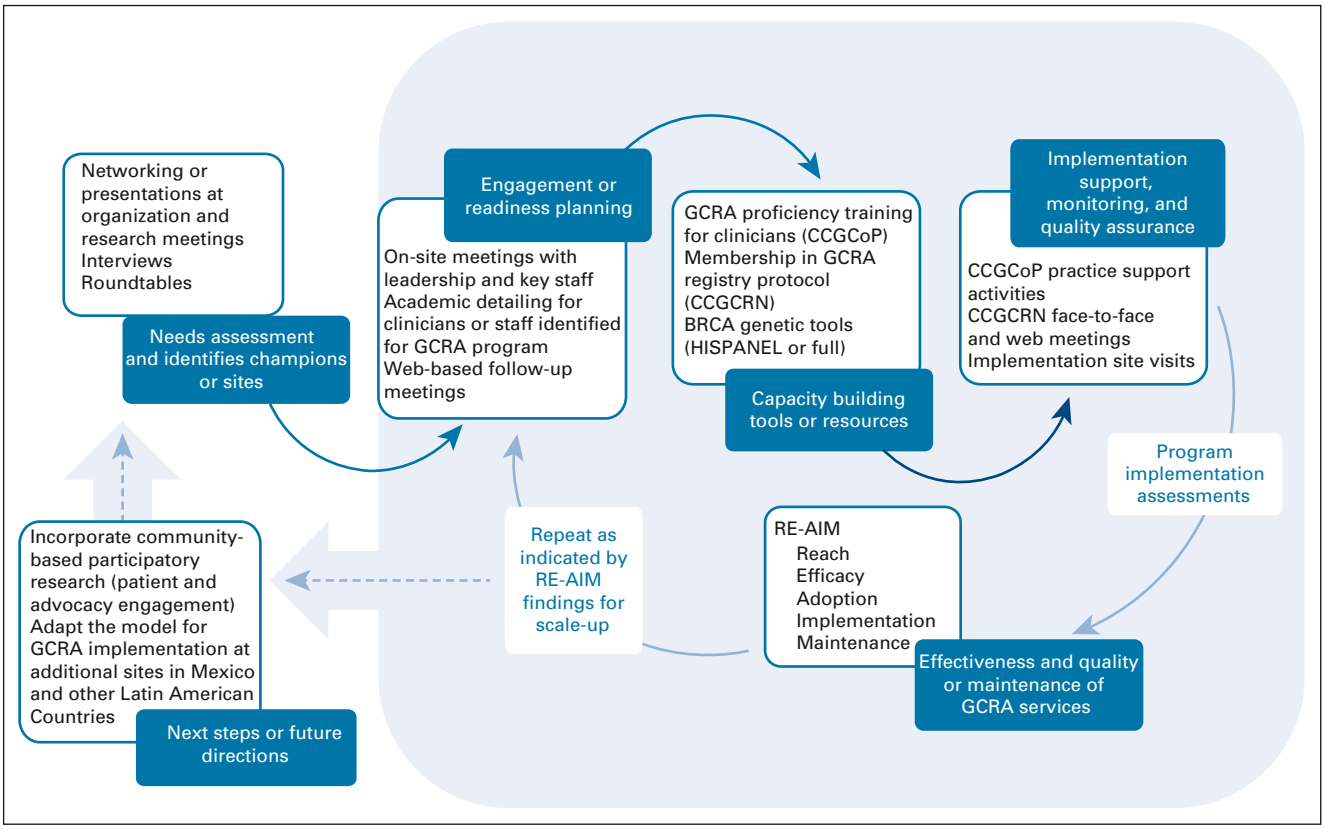

FIG 1. GRACIAS project. The key components and iterative process for implementing the pilot GCRA intervention in Mexico. CCGCoP, Clinical Cancer Genomics Intensive Course and Community of Practice; CCGCRN, Clinical Cancer Genomics Community Research Network; GRACIAS, Genomic Risk Assessment for Cancer Implementation and Sustainment; GCRA, genomic cancer risk assessment.

2012, TecSalud in 2014, and Nutrición in 2015 to (1) assess the organizational infrastructure of each institution, including pre-existing genetic services; (2) determine the patient pools eligible for GCRA; (3) assess materials, staff, and services needed for GCRA practice; and (4) work with leadership to identify common goals and clinicians for GCRA training. We also met with two patient advocacy groups in Mexico to build awareness about the potential benefits of GCRA for patients with BC and their families and to explore their information and resource needs: CIMA,[19] a nonprofit organization aimed at reducing BC mortality in Mexico and Oncoayuda,[20] which is dedicated to improving quality of life among cancer survivors.

Capacity Building Tools or Resources

Informed by our initial visits to UdeG and INCan, we adapted the following established resources to incorporate into the GRACIAS intervention:

The Clinical Cancer Genomics Intensive Course and Community of Practice. Since its inception in 2001, this award-winning[21] NCI-funded (R25CA171998) initiative combines distance learning, face-to-face workshops, and ongoing web-based practice support for GCRA clinicians.[22,23] More than 1,200 clinicians from all 50 US states and 27 countries completed the course[22-25] and became members of the Clinical Cancer Genomics Intensive Course and Community of Practice (CCGCoP). Adaptations: Funding from the Breast Cancer Research Foundation and Avon (grant No. 02-2013-044) supported the participation of Mexican physicians.

The CCGCRN. The CCGCRN is a consortium of 45 community-based and academic oncogenetic practices. The shared registry protocol collects family history, biospecimens for genomic testing, and clinical outcomes data and allows clinicians to provide clinically actionable research results to patients. Progeny Web (Progeny Software LLC, Delray Beach, FL) is the CCGCRN relational database and serves as a pedigree drawing tool for clinical use at all participating sites. Adaptations: Registry consent and protocol documents were translated to Spanish and approved by the IRB for each site according to institutional policies and national regulations, including Mexico's Federal Commission for Protection against Sanitary Risk to obtain a permit for batch shipment of patient biospecimens.

Low-cost BRCA genetic testing. We developed a 115-PV *BRCA* panel (HISPANEL) that identifies recurrent *BRCA* PVs among Hispanics for $20 US dollars per case.[26-28] HISPANEL-negative patients are screened with full *BRCA* gene sequencing with a researcher-designed next-generation

sequencing assay and for copy number variants in *BRCA1* by multiplex ligation–dependent probe amplification (MRC-Holland, Amsterdam, the Netherlands). No *BRCA2* copy number variants were detected among 1,627 participants (manuscript under review). HISPANEL (77% sensitivity) and full *BRCA* sequencing were used sequentially as a low-cost[29] approach to support GCRA (Fig 2).

Implementation Support, Monitoring, and Quality Assurance

We conducted the following activities to provide expert guidance, assess quality, and help identify and address barriers to implementing and sustaining GCRA services.

Clinical practice and research support. Clinicians who completed GCRA training were provided access to practice support resources of the CCGCoP (eg, web-based discussion boards and interprofessional case review conferences) and met with the research team quarterly via web conference and once in person at annual CCGCRN meetings to promote networking and collaborative research.

Implementation site visits. Site visits were conducted by research team leaders to understand the processes, facilitators, and barriers to GCRA services, assess and provide feedback to site leaders and administrators on the quality and fidelity of GCRA services, and provide academic detailing to raise awareness and promote referral to GCRA services.

Roundtable Forums

Two roundtable discussion forums were conducted by the research team. The first was in March 2014 in the City of Hope campus with Latin American physicians to consider the state of GCRA services in Latin America. The second was in January 2020 in Mexico City with participants from the GRACIAS pilot sites and candidate GCRA implementation sites, focused on context-specific themes. The sessions were conducted in Spanish and recorded, transcribed, and translated into English for thematic analysis by three bilingual cancer genetics clinician-researchers.

Effectiveness and Quality or Maintenance of GCRA Services

Table 1 shows the instruments used to document the progress and outcomes of the intervention.

Data Analysis

The RE-AIM model was adapted to provide systematic evaluation of GRACIAS intervention outcomes as follows: *Reach*, the proportion of the target patient population (anonymized data on new patient registrations at participating sites, meeting adapted NCCN criteria) vs. profile of enrolled patients referred for GCRA; *Effectiveness,* the number of patients who completed GCRA and received *BRCA* test results and the number identified as *BRCA* carriers; *Adoption,* the number of organizations and providers who engage in the facilitation of GCRA; *Implementation,* successful delivery of GCRA practice (measured by observation of genetics consultations and informed consent process, patient pedigree, clinical characteristics, and genetic test results documentation); and *Maintenance*, the extent to which the delivery is sustained over time. Identification of barriers to GCRA implementation was obtained through semistructured interviews and feedback from clinicians, administrators, and staff during site visits and meetings.

Survey data were entered into Microsoft Excel 2013 (Microsoft, Redmond, WA) and audited for accuracy. Descriptive statistics were computed for demographic, yes or no, and rating scale items. Quantitative data were analyzed using Fisher's test or χ^2 statistics, with a two-sided P value of $< .05$ considered significant (SPSS 14.0 New York). Paired *t*-test assessed baseline to postcourse changes in physician knowledge. Coding and thematic analysis of open-ended responses were conducted by three researchers through a series of iterations. Qualitative findings were triangulated with quantitative outcomes to increase the depth and support the validity of quantitative findings.[30]

RESULTS

Training Outcomes

Eleven healthcare professionals (six geneticists, two oncologists, one gynecologist, one general physician, and one genetic laboratory clinician) age 26-35 years, with 1-5 years of clinical practice experience, participated in the CCGCoP training from 2011 to 2017. The mean knowledge score increased from 60% (range 53%-75%) at baseline to 67.2% (range 53%-86%) postcourse. Two participants did not demonstrate significant increase in knowledge score and self-reported challenges with written English language proficiency. Open-ended feedback also suggested that content in Spanish would improve the learning experience. Professional self-efficacy (SE) scores related to GCRA knowledge and skills increased by 29.4% (95% CI, 3.29 to 16.3; $P = .005$). The median self-efficacy increased 0.69

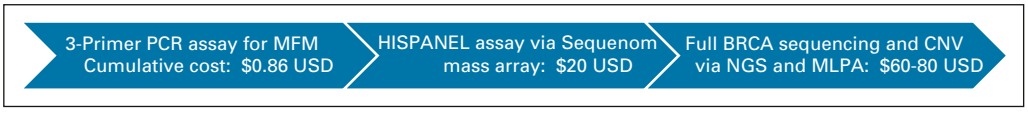

FIG 2. Low-cost *BRCA* genetic testing process. CNV, copy number variant; MFM, Mexican founder mutation; MLPA, multiplex ligation-dependent probe amplification; NGS, next-generation sequencing; PCR, polymerase chain reaction; USD, US dollars.

points, from 3.73 at baseline (range 1.94-4.54) to 4.42 (range 4.03-4.78) postcourse.

RE-AIM Outcomes

Reach and effectiveness. A 2-year window of patient accrual for each site is depicted in Figure 3 and summarized in Table 2. At UdeG, 190 of 247 patients were accrued in the first year of implementation in 2012 (77% reach), with 20 *BRCA* PVs detected among 190 tested (10.5%). UdeG accrual was subsequently interrupted because of personnel limitations (the only GCRA-trained clinician went out on personal leave) and protracted regulatory challenges with Federal Commission for the Protection against Sanitary Risk. GCRA accrual at INCan was 640 of 747 patients from 2013 through 2014 (86% reach), with 105 *BRCA* PVs detected among 634 tested (16.6%). Interim analysis demonstrated that reach at INCan was significantly greater than that at UdeG ($P = .0013$).

Differences between the two sites included more trained personnel at INCan (five) versus UdeG (one) and an earlier site visit at INCan (after 1 year of GCRA services *v* after three years at UdeG), wherein academic detailing by study leaders increased awareness of the new GCRA services, and clinical proctoring and site assessments facilitated process improvements. A 20% increase in accruals followed each site visit. Consequently, we incorporated annual site visits for all new sites. Accrual at TecSalud from 2016 to 2017 was 313 of 347 patients (90%), with 53 *BRCA* PVs detected among 304 tested (17.4%), and 178 of 233 patients were accrued at Nutrición from 2018 through 2019 (76%), with 17 *BRCA* PVs detected among 125 tested (13.6%). Table 3 summarizes the characteristics of the accrued patients at the respective sites, with greatest yield of *BRCA* PVs at sites (INCan and TecSalud) with younger age and more patients affected with cancer; two of six patients over 60 years with triple-negative breast cancer had a *BRCA1* PV. All sites met or exceeded the benchmark of 6%-15% yield reported in published studies of high-risk clinics using NCCN testing criteria.[7,28,31-35]

Adoption. Beyond the four GRACIAS sites reported here, we have engaged seven additional candidate sites representing a cross section of clinical practices supported by Ministry of Health or other public health insurance or nongovernmental organizations (Table 4). The candidate sites include communities with largely indigenous populations.

TABLE 1. GCRA Outcomes Assessment Instruments

Instrument or Data Source	Measures or Purpose	When Administered
Primary outcomes data sources		
GCRA Patient Cancer Risk Questionnaire	Demographics, cancer and non-cancer health history, health beliefs, and behaviors of patients receiving GCRA. Purpose: *Baseline Data for Reach*, *Compliance,* and *Effectiveness* assessments	Preinitial GCRA session
GCRA Case Report Form	Patient characteristics, genetic test results, and clinical outcomes (uptake of recommended screening and prevention cares). Extracted from medical record by site clinicians or support staff. Purpose: *Reach*, *Compliance*, and *Effectiveness*	12, 18, and 30 months postinitiation of GCRA services
Secondary outcomes data sources		
GCRA Program Capacity Site Visit Evaluation	Seven domains related to implementation, maintenance, and barriers to delivery of GCRA services. Completed by the research team during site visits. Purpose: assess *Capacity*, *Implementation*, *Compliance*, *Sustainability*, and *Barriers*	During each site visit
GCRA Clinical Assessment	12 domains of GCRA procedural knowledge and clinical skills. Documents direct assessment of clinician competence while proctoring clinician GCRA encounters. Purpose: assess *Fidelity*, *Acceptability*, and *Compliance*	
GCRA Proficiency Training Assessments and Evaluations[a]		
GCRA Knowledge Test	Knowledge related to seven essential content domains in GCRA. Purpose: Assess Provider *Readiness and Acceptability*	Baseline, immediate postcourse
Professional Self-Efficacy Survey	Clinician confidence related to knowledge and skills to perform GCRA. Purpose: Assess Provider *Readiness* and *Acceptability*	Baseline, immediate, and 12-month postcourse
Professional Development Activities Tracking	Longitudinal postcourse engagement with the CCGCoP for professional development and practice support. Purpose: Assess Provider *Readiness*, *Engagement*, *Satisfaction*, and *Barriers*	Ongoing postcourse tracking
GCRA Training Program Evaluations	Participant feedback about the course experience and value to GCRA practice. Purpose: Assess *Satisfaction* and *Acceptability* of the GCRA intervention	During course and immediate postcourse

Abbreviations: CCGCoP, Clinical Cancer Genomics Intensive Course and Community of Practice; GCRA, genomic cancer risk assessment.
[a]Course instrument and data analysis descriptions are previously published.[22-25]

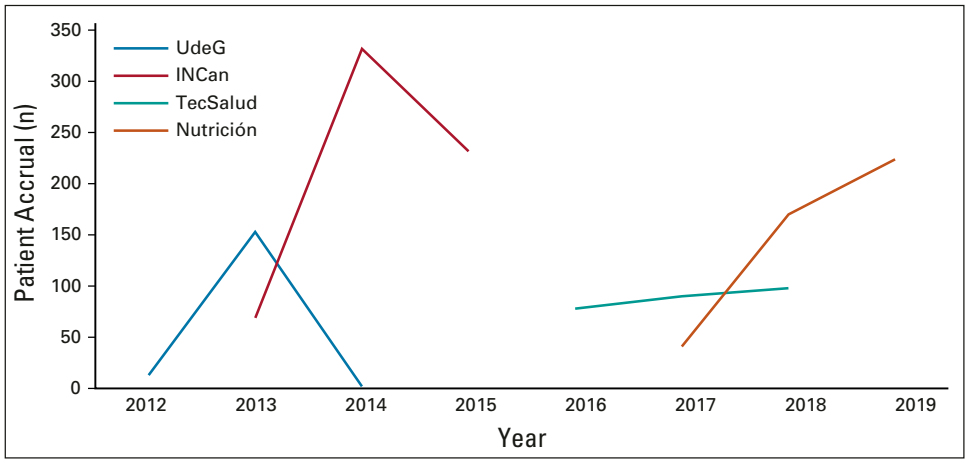

FIG 3. Two-year window of patient accrual for each site. INCan, Instituto Nacional de Cancerología; Nutrición, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; TecSalud, Tecnológico de Monterrey Escuela de Medicina Monterrey; UdeG, Universidad de Guadalajara.

The clinician roundtable sessions were held after GRACIAS implementation at the first two sites (UdeG and INCan) in March 2014 and again after implementation at the next two sites (TecSalud and Nutrición) in January 2020. The first was attended by 15 physicians from Mexico (including the clinician champions from the first two GRACIAS sites), Brazil, Colombia, Peru, and Puerto Rico. Findings revealed that clinicians from each country shared common barriers to GCRA implementation, including (1) lack of patient and provider knowledge about GCRA, (2) lack of providers with training or expertise to deliver GCRA, (3) lack of insurance coverage and high patient out-of-pocket costs for GCRA testing, (4) insufficient institutional and government infrastructure or policy to support GCRA programs, and (5) the need to publish GCRA outcomes and develop an evidence base documenting efficacy in their own populations to influence healthcare policy toward building GCRA services.[36]

The second roundtable was attended by 16 clinicians representing eight sites in major population centers in Mexico (including the four pilot GRACIAS sites) to explore the current status of GCRA services in Mexico, barriers to GCRA practice, and potential solutions. Clinician champions from five of the seven candidate sites also participated, demonstrating a high level of commitment to adopt GCRA. Findings paralleled the issues noted in the first session (eg, lack of insurance coverage and high patient out-of-pocket costs) and revealed additional concerns, based in part on political changes directly affecting public health finance and the termination of Mexico's signature safety net program (Seguro Popular). The session was conducted in the backdrop of active civil protest by physicians and patients with pediatric cancer and their families regarding new limitations in access to treatment.[37,38] Participants cited the need for trained GCRA clinicians outside the capital city, particularly in underserved areas. GRACIAS participants reflected that their experience with the program was integral to implementation of GCRA in their centers.

Implementation and maintenance. Proctoring of GCRA sessions during site visits revealed appropriate (1) documentation of family history data as multigeneration pedigrees, (2) delivery of genetic counseling and informed consent, (3) interpretation and disclosure of genetic test results, and (4) provision of risk-appropriate management recommendations and referrals for high-risk care. Participating sites created practical adaptations to the protocol, such as transitioning from handwritten to direct entry of pedigrees and risk factor data into the electronic database during the GCRA session, leveraging clinician fellows to triage GCRA patients and administer clinic questionnaires, and addressing challenges with patient literacy and inefficiencies with the postal system. Overall, there was fidelity

TABLE 2. GRACIAS Implementation and Genetic Testing Outcomes by Institution

Site	UdeG	INCan	TecSalud	Nutrición
Time to IRB approval, months	6	6	1	2.5
IRB approval date	November 2011	November 2012	March 2015	June 2017
Enrolling period	2012-2013	2013-2014	2016-2017	2018-2019
Reach targeted population,[a] No. (%)	190 of 247 (77)	640of 747 (86)	313 of 347 (90)	178 of 233 (76)
Prevalence of *BRCA* PVs, No. (%)	20 of 190 (10.5)	105 of 634 (16.6)	53 of 304 (17.4)	17 of 125 (13.6)

Abbreviations: GRACIAS, Genomic Risk Assessment for Cancer Implementation and Sustainment; INCan, Instituto Nacional de Cancerología; Nutrición, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; PV, pathogenic variant; TecSalud, Tecnológico de Monterrey Escuela de Medicina Monterrey; UdeG, Universidad de Guadalajara.

[a]Eligibility: breast cancer ≤ 50 years and triple-negative breast cancer or ovarian cancer at any age.

TABLE 3. Characteristics of Accrued Cases at Each GRACIAS Site

Site	UdeG	INCan	TecSalud	Nutrición
Sex, female/male	186/4	637/3	306/7	175/3
Affected/unaffected[a]	160/30	640/0	312/1	162/16
Avg. age at diagnosis of BC, years (range)	41.3 (26-76)	38.3 (19-76)	39.1 (18-72)	42.8 (22-86)
Triple-negative BC	29	145[b]	116	67[b]
OC (after BC)	3	37 (9)	5 (3)	16 (4)

Abbreviations: BC, breast cancer; GRACIAS, Genomic Risk Assessment for Cancer Implementation and Sustainment; INCan, Instituto Nacional de Cancerología; Nutrición, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; OC, ovarian cancer; TecSalud, Tecnológico de Monterrey Escuela de Medicina Monterrey; UdeG, Universidad de Guadalajara.

[a]Unaffected with or without family cancer history.

[b]Cases > age 60 years at diagnosis (*BRCA* positive status): 2 (1) INCan; 4 (1) Nutricion.

of laboratory sample handling across sites, but common challenges included correct tube selection, costs for supplies, sample storage, support staff, and shipping.

CCGCoP practice support resources were used by clinicians from all GRACIAS sites, who presented and received feedback on GCRA cases during CCGCoP web-based case conferences, and 73% (8 of 11) of site clinicians have attended one or more of the City of Hope annual cancer genomics update conferences (range 1-3). Genetic test results have been incorporated into newly established multidisciplinary tumor boards at each site, wherein hereditary case management is discussed among oncologists, surgeons, gynecologists, and psychologists.

Academic detailing conducted by the research team during site visits enhanced stature, awareness, and institutional support for their GCRA programs. Site champions continue academic detailing. For example, the Nutrición site incorporates content about GCRA in grand rounds at local hospitals and in their residency program to increase patient referrals, enhance awareness of the program, and increase the pool of clinicians interested in GCRA.

On the basis of continuous follow-up from 2012 to 2020, all 11 clinicians who received GCRA training continue to provide GCRA services. The UdeG geneticist completed training in 2011 and initiated GCRA in 2012. After the UdeG team was encouraged to train additional clinicians, a genetics intern completed GCRA training in 2016, enabling more sustained services. Independent of the pilot program since 2016, five of the seven trained clinicians, and three additional geneticists, continue to practice GCRA at INCan. Two clinicians left INCan to initiate GCRA services at other institutions; one recruited a geneticist who completed the GCRA training, and they started a new program at TecSalud. All four sites remain active after GRACIAS implementation, with a range of continuous GCRA activities of 2-8 years (average 5.5 years).

DISCUSSION

Although GCRA is a standard-of-care service in the United States and other developed nations,[1,39] access remains limited in Mexico and other LMICs. The introduction of the ISF[16] to identify systems and support capacity building, and RE-AIM[17] to evaluate progress and outcomes, provided a systematic framework for the GRACIAS intervention. To our knowledge, this is the first time that dissemination and implementation methods have been used to promote GCRA services.

The GRACIAS intervention resulted in increased reach and sustainment of GCRA services at all sites. The yield of *BRCA* PVs across all four sites was comparable with the yield in high-risk clinics in the United States that follow NCCN

TABLE 4. Candidate GCRA Implementation Sites

	Healthcare Coverage		
Site Name, City	Seguro Popular	MOH, Public	NGO
Centro Oncologico Estatal (ISSEMYM), Toluca (two reps at roundtable)[a]	X	X	
Center for the Study and Prevention of Cancer (CEPREC), Oaxaca[a]			X
Fundación Rodolfo Padilla Padilla (FRPP) A. C., Leon, Guanajuato[a]			X
Centro Oncologico Internacional (COI), Mexico City[a]	X		X
Hospital General (HGQ), Queretaro	X	X	
Hospital General (HGT), Tijuana	X	X	
Centro Estatal de Cancerologia (CEC) de Chihuahua[a]	X	X	

Abbreviations: GCRA, genomic cancer risk assessment; MOH, Ministry of Health; NGO, nongovernmental organization.

[a]Attended 2020 Mexico Roundtable.

guidelines, with the greatest yield at sites with younger age at diagnosis and more patients affected with cancer.[7,28,40]

More patients were seen for GCRA and the programs were better sustained in the centers where more clinicians were trained and that had earlier GRACIAS site visits, suggesting that these components are helpful for developing workforce depth and institutional commitment. Site visits may influence the allocation of resources and help inform strategies to address barriers. Although the recorded course modules allow learners with limited English language proficiency to view the curriculum repeatedly and at their own pace, a Spanish-language version of the course and outcomes assessments would be an enhancement. Despite language challenges, site visits revealed high competency and quality in the delivery of GCRA services. Post-training engagement with the CCGCoP and the integration of GCRA testing outcomes at multidisciplinary tumor boards enhance the quality of post-GCRA care and increase adoption and engagement by allied subspecialties.

Another important characteristic of the intervention is the potential for further dissemination of GCRA services at other sites by GRACIAS-trained clinicians. Two of the four sites have developed some capacity for research-based *BRCA* testing. However, broader access to GCRA and genetic testing and the full spectrum of risk-appropriate interventions will require national policy change.

Preliminary observations from CCGCRN protocol outcomes highlighted creative strategies used by the new GCRA programs to include risk-reduction surgeries in the cancer treatment plan or use nongovernmental organization resources, philanthropic support, and interinstitutional agreements to manage *BRCA* PV carriers. Formal evaluation of post-GCRA preventive, surveillance, and cascade testing outcomes is ongoing and part of future studies.

BC advocacy groups were enthusiastic about GCRA; however, some members expressed concerns about competition for limited resources for BC screening. They emphasized the need to educate patients and policymakers about the benefits of GCRA.

This study identified limitations in healthcare finance, adequately trained workforce, and population-based registries in Mexico. Currently, only physicians provide genetic services in Mexico, as the profession of genetic counseling does not exist, and other midlevel providers are not involved. These barriers were also reflected in the roundtable sessions and previously reported in other LMICs.[41-43] Post-GCRA clinical outcomes are recorded in Progeny Web by the on-site team annually for the GRACIAS registry, which compensates in part for the lack of population-based cancer registries. Jointly authored peer-reviewed publications and poster presentations (n = 16) illuminate the status of GCRA in Latin America[44] and the genetic epidemiology of hereditary BC in Mexico.[45,46]

The GRACIAS components were demonstrably successful in the pilot project and helped elucidate factors influencing implementation of GCRA in Mexico. Next steps and needs for scale-up include the following:

1. Identify candidate sites representing a cross section of practice settings in other states; GCRA activities were recently initiated in Chiapas (one of the most ethnically diverse and underserved regions), and we engaged candidate sites in Chihuahua and Querétaro.
2. Increase the GCRA workforce through interprofessional CCGCoP training, including mid-level providers—changes in Mexican healthcare policy are needed to integrate mid-level providers into GCRA.
3. Create a Spanish-language version of the course curriculum, as well as knowledge and skills outcomes instruments, to optimize training and better assess respective outcomes.
4. Study the impact of, and explore alternate distance-mediated approaches to, site visits, which are time-, cost-, and labor-intensive.
5. Create interventions to enhance cascade testing and access to risk-appropriate care in partnership with key stakeholders such as site champions, administrators, and public health officials and advocates.
6. Promote national policy change necessary to support economical clinical-grade testing services necessary to sustain GCRA services in Mexico.

In conclusion, to our knowledge, we describe the first project to use implementation science methods to develop and deliver an innovative multicomponent implementation intervention, combining low-cost *BRCA* testing, comprehensive GCRA training, and practice support. Scale-up of the GRACIAS dissemination and implementation intervention will result in measurable prevention of BC and reduction in related mortality. Furthermore, the implementation science developed in this project will help establish a framework for further dissemination of GCRA and other clinical services in Latin America and for application in low-resource settings, including rural communities and safety net hospitals in the United States.

AFFILIATIONS

[1]City of Hope Comprehensive Cancer Center, Duarte, CA
[2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico
[3]Hospital Zambrano Hellion TecSalud, Tecnologico de Monterrey, Monterrey, Mexico
[4]Instituto Nacional de Cancerologia, Mexico City, Mexico
[5]Instituto de Investigaciones Biomédicas, Mexico City, México
[6]Universidad de Guadalajara, Guadalajara, Jalisco, Mexico
[7]UTHealth, The University of Texas Health Science Center at Houston, Houston, TX

[8]Latin American School of Oncology (Escuela Latinoamericana de Oncología), Sierra Madre, CA

CORRESPONDING AUTHOR

Jeffrey N. Weitzel, MD, Latin American School of Oncology 578 Acacia Street Sierra Madre, CA. 91024; e-mail: jnweitzel57@gmail.com.

DISCLAIMER

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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AUTHOR CONTRIBUTIONS

Conception and design: Kathleen R. Blazer, Alejandro Mohar, Maria Fernandez, Jeffrey N. Weitzel
Financial support: Jeffrey N. Weitzel
Administrative support: Bita Nehoray, Rosa Mejia, Jeffrey N. Weitzel
Provision of study materials or patients: Yanin Chavarri-Guerra, Adrian Daneri-Navarro, Dione Aguilar, Rosa Mejia, Jeffrey N. Weitzel
Collection and assembly of data: Kathleen R. Blazer, Cynthia Villarreal Garza, Alejandro Mohar, Adrian Daneri-Navarro, Azucena del Toro, Dione Aguilar, Jazmin Arteaga, Rosa Maria Álvarez, Rosa Mejia, Danielle Castillo, Jeffrey N. Weitzel
Data analysis and interpretation: Kathleen R. Blazer, Yanin Chavarri-Guerra, Cynthia Villarreal Garza, Bita Nehoray, Alejandro Mohar, Josef Herzog, Maria Fernandez, Jeffrey N. Weitzel
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Kathleen R. Blazer
Research Funding: Pfizer

Yanin Chavarri-Guerra
Research Funding: Roche
Travel, Accommodations, Expenses: Pfizer

Cynthia Villarreal Garza
Consulting or Advisory Role: Roche, Novartis, Pfizer, Lilly
Speakers' Bureau: Roche, Myriad Genetics, Novartis
Research Funding: AstraZeneca, Roche
Travel, Accommodations, Expenses: Roche, MSD Oncology, Pfizer

Bita Nehoray
Consulting or Advisory Role: Invitae
Travel, Accommodations, Expenses: Invitae

Adrian Daneri-Navarro
Patents, Royalties, Other Intellectual Property: On December 09, 2020, my university requested PCT/IB2020/061716: NANOPARTÍCULAS PARA EL TRATAMIENTO DEL CÁNCER

Rosa Maria Álvarez
Consulting or Advisory Role: Foundation Medicine
Speakers' Bureau: AstraZeneca

Jeffrey N. Weitzel
Speakers' Bureau: AstraZeneca

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