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**ABOUT COVER**

Editor-in-Chief of *World Journal of Clinical Oncology*, Professor Hiten Patel is an expert in the field of Urology and a United Kingdom-trained surgeon who provides both general and specialist urological care. Professor Patel has co-lead the implementation of minimal access surgery, the fast-track/enhanced recovery after surgery (ERAS) program, and robotic surgery within several units, including the Section of Laparoscopy and Robotic Surgery at the University of Rochester Medical Centre (New York, United States), Guy's and St Thomas' NHS Foundation Trust (London, England) and University Hospital North Norway (Tromsø, Norway). He is passionate about applying simulation training to help educate teams within the field of surgery, surgical techniques, new technologies, and enhanced recovery. (L-Editor: Filipodia)

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## Healthcare delivery interventions to reduce cancer disparities worldwide

James C Dickerson, Meera V Ragavan, Divya A Parikh, Manali I Patel

**ORCID number:** James C Dickerson 0000-0002-8935-2939; Meera V Ragavan 0000-0002-8991-0259; Divya A Parikh 0000-0002-7432-4601; Manali I Patel 0000-0002-9943-5762.

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**James C Dickerson, Meera V Ragavan,** Department of Internal Medicine, Stanford University, Stanford, CA 94305, United States

**Divya A Parikh, Manali I Patel,** Division of Oncology, Department of Medicine, Stanford University, Stanford, CA 94305, United States

**Manali I Patel,** Center for Health Policy/Primary Care Outcomes Research, Stanford University, Stanford, CA 94305, United States

**Manali I Patel,** VA Palo Alto Health Care System, Palo Alto, CA 94306, United States

**Corresponding author:** James C Dickerson, MD, Doctor, Department of Internal Medicine, Stanford University, Lane Building L154, 300 Pasteur Dr, Stanford, CA 94305, United States. [jdicker@stanford.edu](mailto:jdicker@stanford.edu)

### Abstract

Globally, cancer care delivery is marked by inequalities, where some *economic, demographic, and sociocultural* groups have worse outcomes than others. In this review, we sought to identify patient-facing interventions designed to reduce disparities in cancer care in both high- and low-income countries. We found two broad categories of interventions that have been studied in the current literature: Patient navigation and telehealth. Navigation has the strongest evidence base for reducing disparities, primarily in cancer screening. Improved outcomes with navigation interventions have been seen in both high- and low-income countries. Telehealth interventions remain an active area of exploration, primarily in high income countries, with the best evidence being for the remote delivery of palliative care. Ongoing research is needed to identify the most efficacious, cost-effective, and scalable interventions to reduce barriers to the receipt of cancer care globally.

**Key Words:** Intervention; Cancer; Disparity; Health services research; Global oncology; Navigation; Telehealth

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**Core Tip:** Equitable delivery of cancer care requires the study of interventions that can improve access for historically disadvantaged groups. In this review we examine two

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approaches, patient navigation and telehealth, that have been implemented globally to reduce cancer disparities. Navigation has the most robust evidence, largely for improving cancer screening, and telehealth remains an area of exploration, primarily for the remote delivery of palliative care.

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## INTRODUCTION

Despite significant advances in cancer prevention and treatment over the last few decades, disparities in cancer outcomes persist across many nations<sup>[1,2]</sup>. Specifically, cancer incidence and mortality are higher among particular racial and ethnic groups, populations from less developed nations, populations with low incomes, and those who live in rural areas<sup>[3-6]</sup>. These demographic and sociocultural disparities exist in all phases of cancer care, including prevention, treatment, palliation and survivorship. For example, cervical cancer screening rates are lower among people in many African countries as compared to people living in more affluent western European countries; colon cancer mortality is greater among Hispanic Americans as compared with non-Hispanic whites; and, Black Americans experience higher rates of undertreated pain at the end of life than white Americans<sup>[7-9]</sup>. The roots of these disparities are multifactorial with historical and social context, financial toxicity, access to care, support systems, and health literacy all playing a significant role<sup>[10-13]</sup>. Addressing these disparities in cancer care is a stated goal of many national health agencies and international organizations, such as the National Cancer Institute, the World Health Organization, and the World Bank<sup>[14-16]</sup>.

While many studies have focused on characterizing disparity, fewer have described interventions to reduce them. Within this relatively small body of literature there is great diversity: Information campaigns, outreach programs, patient navigation, phone-based applications, and online stress management tools have been trialed. While some interventions have been shown to reduce gaps in cancer care, the reproducibility, scalability, and generalizability is often not known.

In this narrative review we seek to highlight two broad categories of patient-facing health services interventions that aim to reduce disparities in cancer care globally: Patient navigation (with a focus on community health workers) and telehealth. We additionally comment on the generalizability and scalability of these published approaches. Articles were identified either through hand search or *via* search on CINAHL, EMBASE, MEDLINE, or PubMed using search strings including terms such as “disparity”, “cancer”, “technology”, and “navigation”. We emphasize randomized trials from high income nations, primarily available from the United States, and review data from studies performed in low and middle income countries (LMICs)<sup>[17]</sup>. Lastly, we sub-divide each section by the phase of care, specifically into (1) prevention, screening and early detection; (2) treatment with cancer therapeutics; and (3) palliation and survivorship.

## PATIENT NAVIGATION and COMMUNITY HEALTH WORKERS

In this review, we define “patient navigation” as the process of a patient advocate serving as a guide for patients throughout the cancer care continuum. Patient navigation is one of the most widely studied health services interventions in oncology<sup>[18,19]</sup>. Navigation services are often delivered by non-professionally trained persons *i.e.*, lay or community health workers (CHWs), primarily as they are more cost-effective (in comparison to training a nurse to deliver the care) and can be selected from the community for which the intervention is designed to impact (for example a “Promotora” for Hispanic American communities). Patient navigation programs vary in their approaches of the navigator role, with some programs providing extensive guidance through the healthcare system while others are limited to one or two aspects of care. The most basic form includes the dissemination of information within a

community by a CHW, while the most extensive navigator programs provide assistance with appointments, insurance, and transportation among other activities. Although CHWs have been used in primary and preventative care for over a half-century, CHW delivered navigation services for cancer care have only been seen on a broad scale in the last thirty years<sup>[20-22]</sup>.

### **Prevention, screening and early detection**

The role of patient navigation in oncology was first described in the 1990s in a single-institution, landmark study in New York City<sup>[22]</sup>. A hospital in Harlem found that the five-year breast cancer survival rates among their predominantly Black patient population was 39%, considerably lower than the national five-year survival rate of 65% among white women. This difference was felt to be driven by later stage diagnoses in Black women<sup>[23]</sup>. To address this, the Harlem Hospital developed the “Cancer Control Center of Harlem,” a program comprised of numerous free clinics to provide breast cancer screening in conjunction with a patient navigator program. Navigators assisted eligible uninsured patients in applying for health insurance, made follow-up appointments for abnormal mammograms and breast biopsies, helped transcend financial barriers to access ambulatory clinics, and served as communicators of information regarding screening and diagnosis in a culturally sensitive manner. Implementation of this CHW patient navigator program resulted in increased rates of earlier stage cancer diagnoses among Black women from 6% to 41% and decreased late stage breast cancer diagnoses from 49% to 21% between 1964-1986 and 1995-2005<sup>[24]</sup>.

The Harlem Hospital program was the first to describe the impact of a patient navigator study in improving rates of cancer screening in the United States, leading to the adoption of patient navigator programs across other institutions and integration into government policy<sup>[25]</sup>. In the mid-2000s, increased funding for navigation interventions from the National Cancer Institute through the Patient Navigation Research Program led to a number of randomized controlled trials (RCTs) in the United States (Table 1)<sup>[26]</sup>. Many of these RCTs examined the effect of navigation on cancer screening, and most reported improvements in the screening rate. As an example, in Percac-Lima *et al*<sup>[27]</sup> patients ( $n = 1223$ ) overdue for colorectal cancer (CRC) screening at a single urban community health center in Chelsea, MA were randomized to either a navigation intervention or usual care. Navigation was led by a community health worker who sent patients an introductory letter and then contacted the patient by phone or in person multiple times. Navigators provided education on the importance of screening, as well as assistance with scheduling, transportation, and applying for insurance. The primary endpoint, the percentage of patients that received CRC screening at nine months, was met. Specifically, 27% of those in the navigation group received screening in comparison to the 12% in the control group ( $P < 0.001$ )<sup>[27]</sup>. Improved CRC screening rates with navigation have also been demonstrated in other patient populations (Table 1).

Marshall *et al*<sup>[28]</sup> examined the effect of navigation on mammography rates. Black women with Medicare insurance in Baltimore, MD ( $n = 1905$ ) were recruited from both the community and a primary care clinic affiliated with an academic medical center. The intervention group received navigation in the form of education, “coaching”, and assistance with arranging appointments. The control arm received a pamphlet on mammography. With a median follow-up of eighteen months, the primary outcome, patient reported mammography in the last two years, was met with 93% reporting mammography in the intervention group *vs* 88% in the control group ( $P < 0.001$ ). While the overall effect size appears modest, when patients out of compliance with screening recommendations at study entry were examined alone, the effect was more robust: 73% were up to date in the intervention arm *vs* 46% in the control at study exit ( $P < 0.001$ )<sup>[28]</sup>.

Some trials examined the effect of navigation on time to follow-up for an abnormal cancer screening test. In the United States, three of four RCTs (Table 1) showed improvements in follow-up. In a retrospective analysis of all the patients ( $n = 10521$ ) in nine studies funded by the Patient Navigation Research Program in the United States, there was large variability in the results – some sites reported up to 20% improvement in follow-up of abnormal screens while other institutions saw no meaningful difference with navigation. The largest improvements were seen in centers with low baseline follow-up, echoing the suggestion that focusing resources on the most at risk populations may yield the greatest improvements<sup>[29]</sup>.

Table 2 shows patient navigation and CHW interventions in LMICs. Notably, this excludes a large body of non-peer reviewed reports from governments, the World Health Organization, and the World Bank. Interventions in LMICs often highlight limitations in resources<sup>[30,31]</sup>. For example, the largest breast cancer screening studies

**Table 1 Randomized trials from the United States focusing on navigation interventions to improve outcomes in cancer care for historically marginalized populations**

	Ref.	Population	Cancer type	Navigator type	Time point	Outcome	Result (intervention vs control)	Location
Screening	Jandorf <i>et al</i> <sup>[91]</sup> (2005) <sup>a</sup>	Hispanic (82% of <i>n</i> = 78)	CRC	Lay navigator <i>vs</i> usual care	6 mo	Screening rate	Endoscopy: 16% <i>vs</i> 5% ( <i>P</i> = 0.019)   FOBT: 42% <i>vs</i> 25% ( <i>P</i> = 0.086)	New York, NY (urban)
	Tu <i>et al</i> <sup>[92]</sup> (2006) <sup>a</sup>	Chinese Americans ( <i>n</i> = 210)	CRC	Education + FOBT card <i>vs</i> usual care	6 mo	FOBT rate	70% <i>vs</i> 28% ( <i>P</i> < 0.05)	Seattle, WA (urban)
	Christie <i>et al</i> <sup>[93]</sup> (2008) <sup>a</sup>	Hispanic (71% of <i>n</i> = 25)	CRC	Lay navigator <i>vs</i> usual care	3 mo	Colonoscopy rate	54% <i>vs</i> 13% ( <i>P</i> = 0.058)	New York, NY (urban)
	Percac-Lima <i>et al</i> <sup>[27]</sup> (2009) <sup>a</sup>	Low income ( <i>n</i> = 1223)	CRC	Lay navigator <i>vs</i> usual care	9 mo	Screening rate	27% <i>vs</i> 12% ( <i>P</i> < 0.001)	Boston, MA (urban)
	Ma <i>et al</i> <sup>[94]</sup> (2009) <sup>b</sup>	Korean Americans ( <i>n</i> = 167)	CRC	Lay navigator <i>vs</i> usual care	12 mo	Screening rate	77% <i>vs</i> 11% ( <i>P</i> < 0.001)	NR
	Phillips <i>et al</i> <sup>[95]</sup> (2011) <sup>b</sup>	African American (47% of <i>n</i> = 3895)	Breast	Lay navigator <i>vs</i> usual care	9 mo	Mammography rate	87% <i>vs</i> 76% ( <i>P</i> < 0.001)	Boston, MA (urban)
	Lasser <i>et al</i> <sup>[96]</sup> (2011) <sup>a</sup>	Low income ( <i>n</i> = 465)	CRC	Lay navigator <i>vs</i> usual care	12 mo	Screening rate	34% <i>vs</i> 20% ( <i>P</i> < 0.001)	Boston, MA (urban)
	Myers <i>et al</i> <sup>[97]</sup> (2014) <sup>a</sup>	African American ( <i>n</i> = 764)	CRC	Mailed FOBT and reminder +/- lay navigation	12 mo	Screening rate	44% <i>vs</i> 32% ( <i>P</i> = 0.001)	Philadelphia, PA (urban)
	Braschi <i>et al</i> <sup>[98]</sup> (2014) <sup>a</sup>	Hispanic ( <i>n</i> = 392)	CRC	Culturally tailored lay navigation <i>vs</i> standard navigation	NR	Colonoscopy rate	82% <i>vs</i> 79% ( <i>P</i> > 0.05)	New York, NY (urban)
	Enard <i>et al</i> <sup>[99]</sup> (2015) <sup>a</sup>	Hispanic ( <i>n</i> = 303)	CRC	Lay navigator <i>vs</i> mailed information	16 mo (average, not pre-specified)	Screening rate	44% <i>vs</i> 32% ( <i>P</i> = 0.04)	Houston, TX (urban)
	Braun <i>et al</i> <sup>[100]</sup> (2015) <sup>a</sup>	Hawaiian and Filipino (90% of <i>n</i> = 488)	Multiple <sup>c</sup>	Lay navigator <i>vs</i> usual care	NR	Screening rate	Pap: 57% <i>vs</i> 36% ( <i>P</i> = 0.001)   Mammogram: 62% <i>vs</i> 42% ( <i>P</i> = 0.003)   Prostate: (54% <i>vs</i> 36% ( <i>P</i> = 0.008)   CRC: 43% <i>vs</i> 27% ( <i>P</i> < 0.001)	Hawai'i (rural and urban)
	Marshall <i>et al</i> <sup>[28]</sup> (2016) <sup>a</sup>	African American ( <i>n</i> = 1905)	Breast	Lay navigator <i>vs</i> pamphlet	18 mo (average, not pre-specified)	Screening rate	93% <i>vs</i> 88% ( <i>P</i> < 0.001)	Baltimore, MD (urban)
	Percac-Lima <i>et al</i> <sup>[101]</sup> (2016) <sup>a</sup>	Non-adherent patients ( <i>n</i> = 1612)	Multiple <sup>c</sup>	Lay navigator <i>vs</i> usual care	8 mo	Percentage of patients up to date on all screens	10% <i>vs</i> 7% ( <i>P</i> < 0.001)	Boston, MA (urban)
	Degroff <i>et al</i> <sup>[102]</sup> (2017) <sup>a</sup>	Low income ( <i>n</i> = 843)	CRC	Lay navigator <i>vs</i> usual care	6 mo	Screening rate	61% <i>vs</i> 53% ( <i>P</i> = 0.021)	Boston, MA (urban)
	Thompson <i>et al</i> <sup>[103]</sup> (2017) <sup>a</sup>	Hispanic ( <i>n</i> = 443)	Cervical	Video + lay navigation <i>vs</i> usual care	7 mo	Screening rate	53% <i>vs</i> 34% ( <i>P</i> < 0.001)	Washington and Oregon (rural)
Ma <i>et al</i> <sup>[104]</sup> (2019) <sup>b</sup>	Korean Americans ( <i>n</i> = 925)	CRC	Lay navigator + group teaching + FIT card <i>vs</i> usual care	12 mo	Screening rate	69% <i>vs</i> 16% ( <i>P</i> < 0.001)	NR	

Diagnostic resolution	Ell <i>et al</i> <sup>[105]</sup> (2007) <sup>a</sup>	Hispanic ( <i>n</i> = 204)	Breast	Social worker navigation <i>vs</i> usual care	2 mo	Completion of follow-up testing	90% <i>vs</i> 66% ( <i>P</i> < 0.001)	Los Angeles, CA (urban)
	Ferrante <i>et al</i> <sup>[106]</sup> (2008) <sup>a</sup>	African American and Hispanic (87% of <i>n</i> = 105)	Breast	Lay navigator <i>vs</i> usual care	N/A	Mean time to diagnosis (days)	25 <i>vs</i> 43 ( <i>P</i> = 0.001)	Newark, NJ (urban)
	Raich <i>et al</i> <sup>[107]</sup> (2012) <sup>a</sup>	72% non-white ( <i>n</i> = 993)	Multiple <sup>d</sup>	Lay navigator <i>vs</i> usual care	12 mo	Completion of follow-up testing	88% <i>vs</i> 70% ( <i>P</i> < 0.001)	Denver, CA (urban)
	Lee <i>et al</i> <sup>[108]</sup> (2013) <sup>b</sup>	Hispanic (60% of <i>n</i> = 1039)	Breast	Lay navigator <i>vs</i> usual care	N/A	Time to diagnosis	2.0 mo <i>vs</i> 1.7 mo ( <i>P</i> > 0.05)	Tampa, FL (urban)
Treatment	Ell <i>et al</i> <sup>[40]</sup> (2009) <sup>a</sup>	Low income ( <i>n</i> = 487)	Breast and Gynecological	Lay navigator + social worker <i>vs</i> usual care	12 mo	Chemotherapy completed as scheduled	Breast: 62% <i>vs</i> 75% ( <i>P</i> = 0.47)   Gyn: 63% <i>vs</i> 46% ( <i>P</i> = 0.13)	Los Angeles, CA (urban)
Palliation	Fischer <i>et al</i> <sup>[49]</sup> (2018) <sup>a</sup>	Hispanic ( <i>n</i> = 223)	All	Lay navigator doing at least 5 home visits + educational packet <i>vs</i> usual care	Enrollment till end of life	Advance care planning, pain scores, hospice use	Documentation: 65% <i>vs</i> 36% ( <i>P</i> < 0.001)   Pain reduction ND ( <i>P</i> = 0.88)   Hospice use ND ( <i>P</i> = 0.58)	Colorado (urban and rural)
	Patel <i>et al</i> <sup>[50]</sup> (2018) <sup>a</sup>	Rural veterans ( <i>n</i> = 213)	All	Lay navigator discussing advanced care planning <i>vs</i> usual care	6 mo	Advanced care planning documentation	Documentation: 92% <i>vs</i> 18% ( <i>P</i> < 0.001)	Palo Alto, CA (urban and rural)

If a study had comparisons at multiple points (*i.e.*, three months and six months) only the final time point in each study is reported.

<sup>a</sup>Randomized Controlled Trial.

<sup>b</sup>Cluster Randomized Trial.

<sup>c</sup>Breast, Prostate, Colorectal, and Cervical.

<sup>d</sup>Breast, Prostate, and Colorectal. FOBT: Fecal occult blood test; CRC: Colorectal cancer; NR: Not reported.

from LMICs use the clinical breast exam rather than mammography as this was seen as a more scalable and cost-effective option in these nations<sup>[32-35]</sup>. In three large studies, two from India and one from the Philippines, trained CHWs conducted clinical breast exams—each study screened 100000–150000 women—and provided guidance on the next steps after a positive screen. However, a large percentage of patients with a positive screen were lost to follow-up and thus never received a mammogram, biopsy, or visit with a professionally trained health care worker. While in Sankaranarayanan *et al*<sup>[32]</sup> (2011) the follow-up rate was not reported, in Mitra *et al*<sup>[33]</sup> the follow-up rate in Mumbai for abnormal exams was only 68%-78%. In Pisani *et al*<sup>[34]</sup> the follow-up was so poor in the Philippines at 35% that the study was closed early.

In an effort to improve these poor historical follow-up rates, investigators have examined adding navigation training for CHWs. In Bangladesh (*n* = 22337), two groups of CHWs were trained to perform clinical breast exams. One group received an additional day of training on how to identify barriers to follow-up, troubleshoot these obstacles, and accompanied patients to follow-up appointments. The follow-up rate (being seen by a trained medical professional) for abnormal clinical exams by the CHWs improved from 43% to 63% (*P* < 0.01)<sup>[36]</sup>. Similar interventions have been

**Table 2 Patient-facing studies from low- and middle-income countries involving either a navigation or technology-based component of the intervention**

	Ref.	Study design	Country	Cancer type	Intervention type	Time point	Outcome	Result (intervention vs control)	Location
Screening	Thomas <i>et al</i> <sup>[35]</sup> (2002)	Cluster randomized trial	China ( <i>n</i> = 266064)	Breast	Classes teaching self-breast exam with supervised exams every 6 mo vs none	10 yr	Deaths attributable to breast cancer	0.1% vs 0.1% ( <i>P</i> = 0.67)	Factory workers in Shanghai (urban)
	Mittra <i>et al</i> <sup>[34]</sup> (2010)	Cluster randomized trial	India ( <i>n</i> = 151538)	Breast	Lay health care workers doing clinical breast examination vs social worker delivered education	3 rounds of screening at 2-yr intervals	Downstaging at diagnosis	1 <sup>st</sup> round: ND ( <i>P</i> = 1.00)   2 <sup>nd</sup> round: ND ( <i>P</i> = 0.47)   3 <sup>rd</sup> round lower stage at diagnosis ( <i>P</i> = 0.004)	Slums in Mumbai (urban)
	Sankaranarayanan <i>et al</i> <sup>[32]</sup> (2011)	Cluster randomized trial	India ( <i>n</i> = 115652)	Breast	Lay worker clinical breast exam vs education only	3 yr	Stage at diagnosis	Early-stage diagnosis: 44% vs 25% ( <i>P</i> = 0.023)   Advanced-stage diagnoses: 45% vs 68 ( <i>P</i> = 0.005)	Thiruvananthapuram, Kerala (suburban)
	Ma <i>et al</i> <sup>[109]</sup> (2012)	Cluster randomized trial	China ( <i>n</i> = 453)	Breast	Education + lay navigation vs printed materials	6 mo	Screening rate	73% vs 5% ( <i>P</i> < 0.001)	Employees in Nanjing (urban)
	Shastri <i>et al</i> <sup>[110]</sup> (2014)	Cluster Randomized Trial	India ( <i>n</i> = 151538)	Cervical	Lay health care workers doing cervical examination vs social worker delivered education	12 yr	Cervical cancer mortality (rate per 100000 person years of observation)	11% vs 16% ( <i>P</i> = 0.003)	Slums in Mumbai (urban)
	Abiodun <i>et al</i> <sup>[111]</sup> (2014)	Cohort trial with control from neighboring area (quasi-experimental design)	Nigeria ( <i>n</i> = 700)	Cervical	Patient education by medical students vs none	3.25 mo	Cervical cancer screening rate	8% vs 4% ( <i>P</i> = 0.038)	Ogun state (rural)
	Rosser <i>et al</i> <sup>[112]</sup> (2015)	Randomized controlled trial	Kenya ( <i>n</i> = 251)	Cervical	Lay health worker 30-minute educational talk vs none	3 mo	Screening rate	59% vs 61% ( <i>P</i> = 0.60)	Homa Bay County (rural)
	Lima <i>et al</i> <sup>[113]</sup> (2017)	Randomized cohort trial	Brasil ( <i>n</i> = 524)	Cervical	Behavioral telephone interview vs educational telephone call	NR	Screening rate	67% vs 58% (NR)	Women without up-to-date screens in Fortaleza (urban)
Diagnostic resolution	Pisani <i>et al</i> <sup>[33]</sup> (2006)	Single arm description of a cluster randomized trial	Philippines ( <i>n</i> = 151168)	Breast	Lay health worker clinical breast exam	2 yr	Follow-up for abnormal screening exam	35% follow-up rate	Manila (urban)
	Ginsburg <i>et al</i> <sup>[36]</sup> (2014)	Cluster randomized trial	Bangladesh ( <i>n</i> = 22337)	Breast	CHW with smartphone +/- additional CHW training to navigate	NR	Follow up care if abnormal CBE	63% vs 43% (no navigation) ( <i>P</i> < 0.0001)	Khulna Division (rural)
	Mishra <i>et al</i> <sup>[114]</sup> (2017)	Retrospective descriptive study	India ( <i>n</i> = 2610432)	Head and Neck	CHWs doing physical exams, counseling patients to stop smoking, and referring patients to an ENT practice if a positive exam	3 yr	Referral to tertiary care center	2610432 screened   10522 (1.1%) quit smoking   3309 (0.13%) referred to tertiary care center of which 1890 (57%) were positive for cancer   1712 (91%) diagnosed were able to start treatment	Gujarat (rural)

	Riogi <i>et al</i> <sup>[38]</sup> (2017)	Cohort study with retrospective control group	Kenya ( <i>n</i> = 75)	Breast	Cohort of patients cared for by nurses trained to navigate <i>vs</i> historic cohort	1 mo	Completion of follow-up testing	58% <i>vs</i> 24% ( <i>P</i> = 0.0026)	Nairobi (urban)
	Vasconcelos <i>et al</i> <sup>[39]</sup> (2017)	Randomized cohort trial	Brasil ( <i>n</i> = 775)	Cervical	Tying ribbon with appointment date on hand <i>vs</i> education session <i>vs</i> card reminder	2 mo	Return for pap test results	66% <i>vs</i> 82% (education) <i>vs</i> 77% (control) ( <i>P</i> < 0.05)	Fortaleza (urban)
	Chavarri-Guerra <i>et al</i> <sup>[115]</sup> (2019)	Retrospective descriptive study	Mexico ( <i>n</i> = 70)	All	Lay navigator	3 mo	Obtain appointment at cancer center	91% had appointment at 3-mo censor	Mexico City (urban)
	Mireles-Aguilar <i>et al</i> <sup>[116]</sup> (2018)	Retrospective descriptive study	Mexico ( <i>n</i> = 656)	Breast	Media campaigns for navigation program followed by navigation by a nurse if alert activated	NR	Follow-up for self-reported symptomatic breast lesions	69% attendance to appointment   Median time from alert activation to treatment ( <i>n</i> = 22): 33 days	Nuevo Leon state (urban and rural)
Treatment	Li <i>et al</i> <sup>[117]</sup> (2016)	Randomized controlled trial	China ( <i>n</i> = 66)	Bladder	"Enhanced" nursing care including phone follow-ups <i>vs</i> usual nursing care	NR	Follow-up after tumor resection	86% <i>vs</i> 63% ( <i>P</i> = 0.032)	Laiwu, Shandong province (NR)
	Alvarez <i>et al</i> <sup>[45]</sup> (2017)	Retrospective descriptive study	Guatemalan children ( <i>n</i> = 1,789)	All	Multifaceted intervention including transportation, food, shelter, and education/guidance on the importance of completing treatment	N/A	Treatment abandonment (year 2001 <i>vs</i> 2008)	27% <i>vs</i> 7% (NR)	Guatemala City (urban and rural)
	Yeoh <i>et al</i> <sup>[46]</sup> (2018)	Cohort study with retrospective control group	Malaysia ( <i>n</i> = 283)	Breast	Nurses who received additional education in patient navigation <i>vs</i> retrospective cohort	N/A	Treatment abandonment	4% <i>vs</i> 12% ( <i>P</i> = 0.048)	Klang (suburban)
Palliative	Sajjad <i>et al</i> <sup>[118]</sup> (2016)	Parallel cohort trail	Pakistan ( <i>n</i> = 50)	Breast	Nurse delivered education series + nurse delivered support during chemotherapy sessions + nurse phone follow-ups <i>vs</i> none	1.5 mo	Change in global quality of life score	Improvement for the intervention group ( <i>P</i> = 0.020)   No change for historic cohort ( <i>P</i> = 0.111)	Karachi (urban)
	Nejad <i>et al</i> <sup>[119]</sup> (2016)	Parallel cohort trail	Iranian caregivers of cancer patients ( <i>n</i> = 60)	Breast	Nurse delivering 2 in-person education / training sessions + 4 telephone follow-up sessions <i>vs</i> none	NR	Change in caregiver strain index scores	Improved scores for the intervention group ( <i>P</i> = 0.001)	Tabriz (urban)

Low- and middle- income countries status determined at time of study. If a study had comparisons at multiple points (*i.e.*, three months and six months) only the final time point in each study is reported. NR: Not reported; N/A: Not applicable; CBE: Clinical breast exam; CHW: Community health worker; ENT: Otorhinolaryngology (Ears, Nose, Throat).

documented in other LMICs. In Nairobi, Kenya, a clinic offering free clinical breast exams trained nurse navigators using a curriculum developed at the University of Colorado (one of the sites in the Patient Navigation Research Program in the United States). Nurses called and texted patients to remind them of their appointments and provided additional support<sup>[37]</sup>. This intervention resulted in surgical consultation for abnormal breast exams among 58% of women enrolled in the study as compared to the baseline historic rate of 24% (*P* < 0.01)<sup>[38]</sup>.

While many studies report positive results in cancer screening and follow-up of abnormal screening exams with patient navigation, there are some studies that have

not found improvements with navigation. In a study of Brazilian women undergoing cervical cancer screening through Papanicolaou testing at a single urban center ( $n = 775$ ), patients were randomized to either receive a written card with a follow-up date on it (control), education on the importance of returning to the clinic and follow-up for the results (education), or a novel patient navigation method where different colored wristbands with reminders were tied onto the wrists of patients (navigation group). The navigation group had a lower follow-up rate (66%) than both the education group (82%) and the control (77%) ( $P < 0.05$ )<sup>[39]</sup>. This highlights the importance of studying the interventions prior to implementation as not all interventions are acceptable, feasible, or produce the same results given differences in the clinical and cultural context of the healthcare system and the community. There are many features of navigation programs, such as the additional social support, problem solving, human contact, and reminders that are likely to be beneficial in all settings, however they may require local adaptation with exploration of novel techniques and environments to ensure their success.

### **Treatment**

Navigation studies among patients undergoing treatment for cancer are limited. In Ell *et al.*<sup>[40]</sup>, low-income patients ( $n = 487$ ) diagnosed with breast or cervical cancer at an academic hospital in Los Angeles were randomized to either receive usual care (financial counseling, pamphlets, and as needed social work) *vs* lay navigation with automatic social work referral. There was no significant difference in the primary outcome, treatment adherence at twelve months, between the two arms<sup>[40]</sup>.

In multiple studies comparing pre- *vs* post-implementation of a navigator program in the United States, there have been positive effects reported for on-treatment cancer patients. In a unique study designed to increase Black patient participation in lung cancer clinical trials, the University of Alabama trained two Black health workers to serve as patient navigators. The navigators reviewed the purpose of clinical trials with patients, completed a needs assessment to identify barriers to participation in clinical trials, helped refer patients to social workers or other community resources when needed (such as transportation and lodging), accompanied patients to their clinical visit, and called patients to remind them of appointments. Patients who opted for navigation services had a trial completion rate of 75% in comparison to 38% for non-navigated patients<sup>[41]</sup>. In an effort to decrease Black-white disparities in early stage lung cancer, a study at two cancer centers in Pittsburgh and North Carolina used a navigator to proactively reach out to Black patients who missed appointments to identify and resolve barriers to care. The Black-white gap in receipt of curative intent surgery or radiation was eliminated, and treatment rates for Black patient ( $n = 144$ ) rose from 69% to 97%<sup>[42]</sup>. In Texas, a similar proactive lay navigator model for Hispanic patients ( $n = 200$ ) with breast cancer correlated with earlier treatment initiation of 1.9 mo *vs* 2.4 mo for a historical group ( $P = 0.04$ )<sup>[43]</sup>. In South Dakota, a cohort of lay navigated American Indians ( $n = 332$ ) receiving curative intent radiation (all cancer types) were found to have less treatment interruptions (average 2 d of interruption) in comparison to a historical cohort (average 5 d)<sup>[44]</sup>.

These non-randomized studies collectively suggest that navigation interventions improved follow-up rates and adherence to treatment and correlated with consistent improvements in cancer outcomes for marginalized groups. In LMICs, similarly, multiple non-randomized studies suggest that navigation and CHW interventions can reduce gaps in adherence to treatment follow-up. At a pediatric cancer center in Guatemala City, a comprehensive multidisciplinary intervention was implemented which provided food, transportation, education, and counseling services to both patients and their families. Treatment abandonment fell from 27% to 7% after implementation of the program. Factors associated with higher abandonment rates included distance from the cancer center, age, and indigenous race<sup>[45]</sup>. In Malaysia, an urban state hospital examined the outcomes of navigated breast cancer patients ( $n = 135$ ) in comparison to a historical cohort during early treatment. The intervention resulted in reduced treatment abandonment from 12% to 4% ( $P = 0.048$ )<sup>[46]</sup>. These results from both the United States and LMICs suggest again that interventions targeting the most at risk groups may yield the largest effect size.

### **Palliation and Survivorship**

Navigation interventions to reduce disparities in palliative care and survivorship have not been extensively studied, despite evidence that such disparities exist in the receipt of palliative care<sup>[47,48]</sup>. One program, *Apoyo con Cariño* (Support with Caring) based in clinics across rural and urban Colorado implemented a lay navigator program with the aim of improving palliation in Hispanic patients ( $n = 223$ ) with advanced cancer. In

this program, the navigator made home visits to discuss both advanced care planning and pain/symptom management with the patient. They also helped coordinate contact with the primary oncologist to discuss action plans for uncontrolled symptoms. The study resulted in an increase in the rate of documentation of goals of care, but did not lead to any significant differences in patient reported pain reduction or utilization of hospice services<sup>[49]</sup>. An RCT based at a Veterans Affairs (VA) hospital in California tested the efficacy of a lay health worker-led advance care planning intervention in patients with any type of advanced cancer ( $n = 213$ ). At six months, the study demonstrated greater goals of care documentation and hospice use, and lower acute care use among patients in the intervention as compared to the control. It was also found that this intervention decreased healthcare expenditure for the VA system, suggesting that this may be a cost-effective model from the perspective of the payor<sup>[50]</sup>. Further studies of lay health care worker interventions in low income populations in the United States are ongoing<sup>[51,52]</sup>.

### Summary and future directions

In summary, navigation employed across the cancer care continuum has successfully improved cancer screening rates, follow-up, adherence to treatment, and goals of care documentation. Although the most robust data is from the United States, and is specifically for colorectal and breast cancer screening, a positive impact on cancer care delivery has been seen in both high income countries and LMICs. Gaps in the literature remain regarding the cost-effectiveness of patient navigator interventions which is crucial in informing communities, health systems, and policy in the adoption of navigator programs globally.

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## MOBILE HEALTH AND TELE-ONCOLOGY

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For the purposes of this review, we define telehealth as any form of telecommunication (video, voice only, apps, *etc.*) to support patient's remote access to health care services. These interventions span text message reminders, phone applications for palliation, and decision aides<sup>[53-55]</sup>. Although not as well studied as patient navigation interventions, telehealth interventions have increasingly been investigated to improve cancer care delivery. Access to mobile phones is becoming common in LMICs, including in rural communities, making telehealth a potentially powerful tool to reduce disparities in healthcare delivery<sup>[56-59]</sup>.

### Screening

Several randomized telehealth-based intervention trials have evaluated cancer screening in underserved populations (Table 3). Where navigation trials often focus on care coordination, telehealth interventions largely consist of education (often delivered via multimedia) and assisting patients in decision making<sup>[55,60,61]</sup>. Published studies of telehealth interventions in cancer are also limited to shorter follow-up periods (often 6 mo or less, range 1-15 mo) in comparison to patient navigation studies where 16 of 17 studies (Table 1) had follow-up periods of at least 6 mo (range 3-18 mo).

Among the eight screening RCTs included in Table 3, three reported positive outcomes. Two of these studies were based in urban Indiana and evaluated the impact of an interactive informational computer-based education program on mammography rates for Black women ( $n = 344$  and 181) at six months. In both studies, the intervention group received a computer-based education program that included questions as a mechanism to give a tailored message in response to the participant's knowledge and health beliefs about breast cancer and mammography screening. This was compared to a control group who received pamphlets and a DVD. The first study, with this intervention alone, showed a robust increase in screening rate at study exit (40% *vs* 27%,  $P = 0.024$ ). The second study added a lay navigator to the same educational program and demonstrated a larger effect size on mammography rate (51% *vs* 18%,  $P < 0.01$ ). These studies suggest that the combination of self-learning, electronic modules to patient navigation may be more effective than technology alone<sup>[62,63]</sup>. The third positive trial was conducted in nine urban safety-net clinics in Kansas City, MO. The study randomized patients eligible for CRC screening ( $n = 470$ ) to a generic education intervention (control) or the same education intervention plus a series of "implementation intentions" questions. Both arms used a touchscreen computer at the clinic site to deliver the education, and the intervention arm received a series of questions after the education focused on how the patient could keep track of appointments, prepare for a colonoscopy, and arrange for childcare/transport that day

**Table 3 Randomized trials from the United States examining technology interventions to improve outcomes in cancer care for historically marginalized populations**

	Ref.	Population	Cancer type	Technology	Time point	Outcome	Result (intervention vs control)	Location
Screening	Miller <i>et al</i> <sup>[120]</sup> (2005) <sup>a</sup>	African American (70% of n = 194)	CRC	Educational multimedia computer program <i>vs</i> nurse instruction on using FOBT card	1 mo	Completed FOBT kit	62% <i>vs</i> 63% ( <i>P</i> = 0.89)	Winston Salem, NC (urban)
	Dignan <i>et al</i> <sup>[121]</sup> (2005) <sup>a</sup>	Native American (n = 157)	Breast	Lay navigator on phone <i>vs</i> lay navigator in person	12 mo	Screening rate	42% <i>vs</i> 45% ( <i>P</i> = 0.83)	Denver, CA (urban)
	Champion <i>et al</i> <sup>[62]</sup> (2006) <sup>a</sup>	African Americans (n = 344)	Breast	Interactive educational computer program <i>vs</i> video <i>vs</i> pamphlet	6 mo	Mammography rate	40% <i>vs</i> 25% (video) <i>vs</i> 32% (pamphlet) ( <i>P</i> = 0.037)	Indianapolis, IN (urban)
	Russell <i>et al</i> <sup>[63]</sup> (2010) <sup>a</sup>	African American (n = 181)	Breast	Interactive educational computer program + monthly lay navigation <i>vs</i> pamphlet	6 mo	Mammography rate	51% <i>vs</i> 18% ( <i>P</i> < 0.001)	Indianapolis, IN (urban)
	Miller <i>et al</i> <sup>[122]</sup> (2011) <sup>a</sup>	African American (75% of n = 264)	CRC	Web-based decision aid <i>vs</i> usual care	6 mo	Completion of CRC screening	19% <i>vs</i> 14% ( <i>P</i> = 0.25)	Winston Salem, NC (urban)
	Greiner <i>et al</i> <sup>[64]</sup> (2014) <sup>a</sup>	Low income (n = 470)	CRC	Computer-delivered information on screening +/- implementation intentions theory-based behavior modification tool	6.5 mo	Completion of CRC screening	54% <i>vs</i> 42%, ( <i>P</i> < 0.01)	Kansas City, KS (urban)
	Fernandez <i>et al</i> <sup>[123]</sup> (2015) <sup>b</sup>	Hispanic (n = 665)	CRC	Interactive educational multimedia on a tablet <i>vs</i> video <i>vs</i> none	6 mo	Completion of CRC screening	10% <i>vs</i> 14% (video) <i>vs</i> 11% (none) ( <i>P</i> = 0.46)	Lower Rio Grande Valley in Texas (rural)
	Valdez <i>et al</i> <sup>[124]</sup> (2019) <sup>a</sup>	Hispanic (n = 943)	Cervical	Kiosk delivered education versus pamphlet	6 mo	Pap rate	51% <i>vs.</i> 48% ( <i>P</i> = 0.35)	Los Angeles, San Jose, and Fresno, CA (urban)
Treatment	Helzlsouer <i>et al</i> <sup>[65]</sup> (2018) <sup>a</sup>	African American (n = 101)	Breast	Web-based navigation program versus list of websites	12 mo	Adjuvant treatment completion	94% <i>vs</i> 86% ( <i>P</i> = 0.24)	Baltimore, MD (urban)
	Percac-Lima <i>et al</i> <sup>[66]</sup> (2015) <sup>a</sup>	Likely to no show (n = 4425)	All	Lay navigator <i>vs</i> usual care	5 mo	No show rate	10% <i>vs</i> 18% ( <i>P</i> < 0.001)	Boston, MA (urban)
Palliation	Bakitas <i>et al</i> <sup>[77]</sup> (2009) <sup>a</sup>	Rural patients (n = 322)	All	Psycho-educational classes followed by monthly tele-health check-ins with advanced nurse practitioner <i>vs</i> usual care	Death or study completion (5 yr)	Quality of life	Intervention > control for quality of life ( <i>P</i> = 0.02) and mood scores ( <i>P</i> = 0.03)   ND in symptom intensity ( <i>P</i> = 0.24)	Vermont (rural)
	Kroenke <i>et al</i> <sup>[75]</sup> (2010) <sup>a</sup>	Low income (n = 405)	All	Telecare management with automated home-based symptom monitoring by interactive voice recording or internet <i>vs</i> usual care	12 mo	Improvement in pain and depression scales	Intervention > control for pain and depression ( <i>P</i> < 0.0001 for both)	Indiana (rural and urban)
	Yanez <i>et al</i> <sup>[76]</sup> (2015) <sup>a</sup>	African American (40% of n = 74)	Prostate	Cognitive-behavioral stress management delivered via web/ tablet <i>vs</i> generic health information via web/tablet	6 mo	Depression scale change	ND ( <i>P</i> = 0.06)	Chicago, IL (urban)
	Anderson <i>et al</i> <sup>[125]</sup> (2015) <sup>a</sup>	African American and Hispanic (n = 60)	Breast	Twice weekly automated telephone calls with patient rating of pain. If pain was elevated, e-mail sent to clinician <i>vs</i> usual care	2-2.5 mo	Reduction in pain severity from baseline	Intervention > control ( <i>P</i> = 0.015)	Houston, TX (urban)
	Ramirez <i>et al</i> <sup>[78]</sup>	Hispanic (n = 288)	Breast, CRC,	Intensified telephone and internet-based patient	15 mo	Change in health-	Intervention > control ( <i>P</i> < 0.05) for female CRC	Chicago, IL and San

(2020) <sup>a</sup>	and Prostate navigation <i>vs</i> "standard" navigation	related quality of life score	patients   Intervention = control ( $P > 0.05$ ) for breast cancer, male CRC, and prostate	Antonio, TX (urban)
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If a study had comparisons at multiple points (*i.e.*, three months and six months) only the final time point in each study is reported.

<sup>a</sup>Randomized Controlled Trial.

<sup>b</sup>Cluster Randomized Trial. FOBT: Fecal occult blood test; CRC: Colorectal cancer; ND: No difference.

if applicable, *etc.* Those in the experimental group achieved a higher rates of screening at 6.5 mo of follow-up in comparison to the control group (54% *vs* 42%,  $P < 0.001$ )<sup>[64]</sup>. These positive trials generally used interventions that focused on both education and behavior. In comparison, the negative trials frequently used tablets or websites to deliver educational media alone. While these negative studies often did demonstrate improvement in knowledge base (often immediately after the intervention), it did not appear to translate to an increase in screening rates with limited follow-up periods (Table 3).

### Treatment

We are aware of only two RCTs investigating the impact of technology on treatment adherence. One trial of predominately Black women ( $n = 101$ ) at a single site in Baltimore, MD aimed to improve treatment adherence to adjuvant therapy for breast cancer with the use of a web-based information tool in addition to phone check-ins by a patient navigator every two weeks. The primary endpoint, adherence at twelve months, was not significantly different between the two groups<sup>[65]</sup>. The second study, Percac-Lima *et al.*<sup>[66]</sup>, used a novel method to identify at risk individuals. All cancer patients at a single academic medical center in Boston predicted to be at risk of being lost to follow-up ( $n = 4425$ ) were randomized to phone navigation *vs* usual care. The intent to treat analysis demonstrated lower no-show rates with navigation (10% *vs* 18%,  $P < 0.01$ ). The study also highlighted the importance of direct contact with patients or their family members: When a family member was reached by the navigator the no-show rate fell to just 3%<sup>[66]</sup>.

Over the last three decades there has been tremendous interest in developing tools for delivering oncologic care remotely to improve equitable access to care. Published studies mostly describe implementation, and outcome data are rare. As an example, the oncology group at the University of Kansas has published both descriptions and cost analyses of their tele-oncology practice since the mid-1990s, though these reports have not accompanied by outcome data<sup>[67,68]</sup>. In Queensland, Australia a rural hospital partnered with a tertiary care center over 500 miles away. This partnership allowed for chemotherapy administration for solid tumor malignancies via tele-visits. While treatments were first administered in 2007, retrospective results were not published until 2015. These data did demonstrate similar outcomes for rural patients ( $n = 89$ ) in comparison to a matched group receiving care locally at the tertiary care center ( $n = 117$ ), though given the lag time between implementation and data publication it would

be difficult for other institutions looking at this model to know if it is safe and efficacious until many years after the program started<sup>[69]</sup>. Another descriptive example of a novel technique is at a single remote California cancer clinic. The clinic partnered with an academic medical center 100 miles away to establish a virtual tumor board to ensure evidence-based care for complex cancer cases<sup>[70]</sup>. With the increase in precision medicine and genetic testing, tele-genetics has also arisen as a very important aspect of cancer care delivery. Many institutions, such as the VA, have incorporated telephone-based genetic counseling to improve low-cost access to these services; though again outcome data is limited<sup>[71,72]</sup>.

Technology has been trialed to improve care access among patients living in LMICs, though both patient-facing interventions and outcome data are sparse. More often, technology is used to partner with institutions in more wealthy countries. For example, in Jordan, a partnership with a Canadian institution allowed access to a multidisciplinary care conference for pediatric neuro-oncology care with the use of videoconference to present data. In the Solomon Islands, a pathology group used electronic communication (primarily email) to discuss cases with a group in Switzerland<sup>[73,74]</sup>. Again, these manuscripts describe the process of implementation rather than report on patient outcomes with the interventions. Studying implementation with care is needed as neither the risks and benefits, nor the resource usage, of these techniques is known.

### **Palliation and Survivorship**

Four United States based RCTs have evaluated technology-based interventions to deliver palliative and supportive care among minority and low-income patients with cancer. A multisite study in community oncology practices in Indiana randomized patients with any cancer and a diagnosis of depression or cancer related pain ( $n = 405$ ). The intervention included telephone visits along with online symptom monitoring by a nurse trained to provide relevant treatment options; this was then compared to an arm receiving usual care. Pain and depression scores improved for the randomized group as compared to the control ( $P < 0.01$ )<sup>[75]</sup>. Among predominantly Black patients with advanced prostate cancer ( $n = 76$ ) in a single clinic in Chicago, a cognitive-behavioral stress management tool to reduce symptom burden provided to patients on a tablet computer led to a reduction in depressive symptoms ( $P = 0.06$ )<sup>[76]</sup>. In a population of rural veterans in Vermont with advanced cancer ( $n = 322$ ), a palliative care trained nurse practitioner delivered both education and palliation to patients through monthly telephone calls. For the patients randomized to the intervention group, quality of life and mood improved ( $P = 0.02$ ) but there were no differences in symptom intensity ( $P = 0.06$ )<sup>[77]</sup>. Lastly, the effects of telephone and internet-based patient navigation on quality of life in Hispanic survivors ( $n = 288$ ) was examined. Patients with prostate, breast, or colorectal cancer at two academic medical centers (one in Chicago, IL and the other in San Antonio, TX, United States) were randomized to the control of "standard" patient navigation services, including up to six phone calls with a navigator and print materials from cancer societies, *vs* a specific navigator program delivered solely via the internet and telephone (the LIVESTRONG cancer navigation service) that included three months of navigation services via one-on-one bilingual support over the telephone or internet that helped provide support for emotional coping, education on treatment options, arranging for appointments, and connecting patients to community resources such as social work, psychosocial services, child care, and financial services. At fifteen months, female patients with colorectal cancer had improvement in the primary outcome, the score of a health-related quality of life scale ( $P < 0.05$ ). However, there was no difference between the two arms for male colorectal cancer patients, breast cancer patients, or prostate cancer patients<sup>[78]</sup>.

Outside of the United States, there have been only a small number of studies focused on marginalized populations in high income countries. In a multi-site study from Australia that was focused on newly diagnosed rural patients undergoing curative intent treatment ( $n = 191$ ), patients were randomized to receive a six module online self-guided psychotherapeutic intervention. The goal was to reduce stress and improve quality of life. At six months there was no difference in distress level ( $P = 0.22$ ) or quality of life ( $P = 0.62$ )<sup>[79]</sup>. While these five studies report on randomized data, there are a number of small scale feasibility studies, predominately from the United States, that have examined various technologies, usually in rural populations<sup>[80-87]</sup>.

To our knowledge, no telehealth palliative care trials involving patients in LMICs have been reported. In a 2013 report, seventy-five nations (32% of countries) had no known hospice or palliative care presence<sup>[88]</sup>. Furthermore, the poorest half of the world has access to less than 1% of manufactured opioids<sup>[89]</sup>. The lack of studies in

these nations reflects limited resources and palliative care infrastructure. These unmet needs represent opportunities to improve education, implementation, and policy. Given the limited resources, employing tools such as navigation and telehealth may well be invaluable to increase the penetration of palliative care<sup>[90]</sup>.

### Summary and Future Directions

Technology interventions have been quickly incorporated into aspects of cancer care practice, often due to convenience and cost, rather than robust evidence demonstrating their efficacy in improving outcomes. The tested interventions to date have not consistently been shown to improve outcomes in screening, follow-up, treatment adherence, or palliation. There are some interventions with robust effect size, though the reproducibility remains unknown. Technology represents a bridge to the masses and is likely to be a key tool in expanding access to care in all countries regardless of income level. As technology interventions can be deployed on existing infrastructure (for example, cell phones) the cost could be considerably less in comparison to “traditional” care and even the use of in-person CHWs. Further investigation and investment into studying the impact of technology interventions is needed.

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## CONCLUSION

In this review we examine two themes of health service interventions for cancer care: Patient navigation and telehealth. We describe studies designed to improve disparities, with an emphasis on randomized controlled trials and data generated from LMICs. Available studies in both patient navigation and telehealth have been shown to reduce disparities across the cancer care continuum. Patient navigation has the most robust data, primarily in its role in screening and reducing treatment abandonment. Telehealth remains an active area of exploration to improve access to treatment and palliation for patients living in rural settings, although data on the efficacy of these interventions is limited. Continued investigation, iteration, and dissemination of these interventions, and scalability where feasible, can help to identify and reduce barriers to equitable cancer care receipt globally.

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