

1 **Title**

2 Barriers and facilitators to implementation of cancer treatment and palliative care
3 strategies in low and middle income countries: systematic review

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22 **Abstract**

23 **Objectives**

24 To appraise improvement strategies adopted by low and middle income countries to
25 increase access to cancer treatments and palliative care; and identify the facilitators
26 and barriers to implementation.

27 **Methods**

28 A systematic review was conducted and reported in accordance with PRISMA
29 statement. MEDLINE, CINAHL and the Cochrane Library databases were searched.
30 Bias was assessed using the Standards for Quality Improvement Reporting
31 Excellence, and evidence graded using the Australian National Health and Medical
32 Research Council system.

33 **Results**

34 Of 3069 articles identified, 18 studies were included. These studies involved less than
35 a tenth (n=12, 8.6%) of all low and middle income countries. Most were case reports
36 (58%), and the majority focused on palliative care (n=11, 61%). Facilitators included:
37 stakeholder engagement, financial support, supportive learning environment, and
38 community networks. Barriers included: lack of human resources, financial
39 constraints, and limited infrastructure.

40 **Conclusions**

41 There is limited evidence on sustainable strategies for increasing access to cancer
42 treatments and palliative care in low and middle income countries. Future strategies
43 should be externally evaluated and be tailored to address service delivery; workforce;
44 information; medical products, and technologies; financing; and leadership and
45 governance.

46 **Keywords**

47 Neoplasms, Surgery, Radiotherapy, Chemotherapy, Palliative Care, Low and middle

48 income countries

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49 **Introduction**

50 Many low and middle income countries (LMICs) are ravaged by significant
51 socioeconomic and healthcare challenges, including a rapid escalation in non-
52 communicable diseases (NCDs), particularly cancer (Meara et al. 2015). Between
53 1990 and 2013, the 70% increase in cancer mortality occurred in LMICs, with 196.3
54 million disability-adjusted life years lost (Global Burden of Disease Cancer
55 Collaboration et al. 2015). Globally, cancer incidence is projected to increase to 22.2
56 million new cancer cases by 2030, and LMICs will bear the major burden (Bray et al.
57 2012).

58 To date, the focus has been on cancer prevention and screening strategies in LMICs
59 (Hanson et al. 2015; Raesima et al. 2015). But to improve survival and quality of life,
60 equitable access to cancer treatment and palliative care is imperative (Knaul et al.
61 2011). However, many LMICs lack: national policies; infrastructure; skilled workforce;
62 financial resources; technology; and information system for quality cancer treatment
63 and palliative care (Knaul et al. 2011; Ngwa and Ngoma 2016). Currently, 90% of
64 cancer patients in low income countries are unable to access quality surgical care
65 (Meara et al. 2015; Sullivan et al. 2015) and a third of LMICs have no functional
66 radiotherapy services (Abdel-Wahab et al. 2017), while a fifth of those that do have
67 only one radiotherapy machine per five million or more population (Abdel-Wahab et al.
68 2017; Atun et al. 2015; Datta et al. 2014). In most LMICs, late-stage presentation is
69 common and the only treatment option is palliative care (Knaul et al. 2011; WHO
70 2007). Yet, many LMICs are not able to provide the 52 cancer medicines and 22 pain
71 and palliative care medicines on the World Health Organisation's (WHO) List of
72 Essential Medicines (Vanderpuye et al. 2017; Wirtz et al. 2017). Consequently, 80%
73 of people living in LMICs have little or no access to pain relief (Knaul et al. 2017).

74 Given these challenges, innovative, cost-effective, and applicable improvement
75 strategies are urgently needed.

76 High income countries (HICs) able to develop, implement, sustain and scale-up
77 strategies have made progress expanding access to cancer treatment and palliative
78 care. Several systematic reviews focusing on access to cancer treatment and palliative
79 care in HICs have documented: i) facilitators such as: drive for quality clinical
80 outcomes; strong political commitment; continuity of care; financial resources;
81 educational opportunities; and patient need for care; and ii) barriers such as: lack of
82 knowledge; lack of awareness and support; competing priorities; and pervasive
83 misconceptions about treatment quality (Chamberlain et al. 2016; Lockett et al. 2013;
84 Obeidat et al. 2011; Thompson et al. 2017).

85 Understanding barriers and facilitators across policy, healthcare organisation and
86 community are essential to inform access strategy implementation (WHO 2002a). Few
87 systematic reviews in this area have focused on LMICs, which continue to hamper
88 strategy implementation required to optimise cancer treatment and palliative care
89 efforts. Accordingly, the aims of this systematic review were to: appraise improvement
90 strategies adopted by LMICs to increase access to cancer treatment and palliative
91 care; and identify the facilitators and barriers to implementation.

92 **Methods**

93 A systematic review conducted and reported in accordance with the Preferred
94 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement
95 (Moher et al. 2009).

96 **Eligibility criteria**

97 Included studies were: all conducted in countries categorised by the World Bank
98 Group (2017) Classification as being 'low income', 'middle income', 'developing', 'less
99 resourced' or 'limited resourced'; published in an English peer-reviewed journal since
100 1990; reporting empirical data related to the impact of a strategy, intervention or
101 programme designed to improve access to cancer surgery, radiotherapy, cancer
102 medicines and/or palliative care. An 'access improvement strategy' was defined as
103 any programme, plan, intervention or policy implemented to ensure cancer surgery,
104 radiotherapy, chemotherapy, other essential cancer medicines, and/or palliative care
105 services were more available, accessible, adequate, affordable, and appropriate.
106 Studies focusing exclusively on cancer prevention or early detection were excluded.

107 **Information sources and search strategy**

108 Search terms were devised from relevant Cochrane Reviews (Dudley and Garner
109 2011; Kredo et al. 2013). A combination of Medical Subject Headings (MeSH) and
110 keywords for LMICs, cancer, treatment modalities and healthcare delivery were used.
111 Table ESM 1 in the Online Resource shows the detailed search strategy.

112 Between 4th April and 6th May 2017, three electronic databases – MEDLINE (EBSCO),
113 CINAHL (EBSCO) and the Cochrane Library, were searched for relevant articles.
114 These were selected, as they provide indexing for extensive international journals and
115 regularly updated with relevant resources covering health topics. Reference lists of
116 relevant articles were hand searched to identify additional articles. Articles were
117 exported to, and managed in, EndNote X8 software.

118 **Study selection**

119 After removal of duplicates, all titles and abstracts were screened against the eligibility
120 criteria (AD). Ten percent of the articles were screened by a second reviewer (TL),
121 with 98.5% agreement being reached. Ineligible articles were removed. Full-text of all
122 potentially relevant articles were retrieved, and further eligibility and quality
123 assessments were undertaken by AD alone, with discussions among the wider team
124 as necessary.

125 **Data items and collection process**

126 Data were extracted into a standardised data collection form using Microsoft Excel
127 2016 (AD) guided by a modified Standards for Quality Improvement Reporting
128 Excellence (SQUIRE 2.0) tool (Ogrinc et al. 2016).

129 **Quality assessment**

130 The quality of the studies was also assessed based on SQUIRE (AD). The Australian
131 National Health and Medical Research Council approved rating system was used to
132 rank the level of evidence.

133 **Synthesis**

134 The multi-level WHO Innovative Care for Chronic Conditions (ICCC) framework was
135 adopted as the analytical framework for this review (WHO 2002a). This framework
136 details the essential building blocks for action at the: micro (patient and family), meso
137 (healthcare organisation and community) and macro (positive policy environment)
138 levels for developing, and re-designing healthcare systems globally (refer Fig. 1)
139 (WHO 2002a). The ICCC framework also integrates the six building blocks identified
140 by the WHO as being necessary for strengthening health systems globally, namely:

141 service delivery; health workforce; information; medical products, vaccines and
142 technologies; financing; and leadership and governance (stewardship) (WHO 2007).

143 Due to the range of designs and outcomes involved, a narrative synthesis using
144 approaches described by Popay and colleagues (2006) was adopted. Included studies
145 were independently coded by two reviewers (AD and TL) to map strategies against
146 the ICCC framework levels. Any discrepancies were resolved through discussion.

147 **Results**

148 The initial search identified 3063 articles, with another six identified during hand
149 searching. After removal of duplicates and screening, 138 articles underwent a full-
150 text review. Nineteen articles met inclusion criteria, with one study reported across two
151 publications (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009) (refer Fig. 2).

152 **Study characteristics**

153 Evidence on strategies for increasing access to cancer treatments and palliative care
154 came from 12 different LMICs, mostly African nations. Table ESM 2 in the Online
155 Resource shows the strategies in the included studies.

156 The majority of studies (61%, n=11) focused on increasing palliative care access (Ali
157 2016; Banerjee 2009; Boit et al. 2014; Gafer and Elhaj 2014; Herce et al. 2014;
158 Krakauer et al. 2015; Lal et al. 2015; Paiva et al. 2012; Shamieh and Hui 2015;
159 Tapsfield and Bates 2011; Wang et al. 2013), while a fifth (22%, n=4) focused on
160 strengthening radiotherapy services (Agrawal et al. 2011; Efstathiou et al. 2016; Einck
161 et al. 2014; Galalae et al. 2015). A tenth (11% n=2) focused on improving integrative
162 cancer care (Brown et al. 2017; Nwogu et al. 2016), and only one study focused on
163 improving anti-cancer drug access (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009).

164 **Quality assessment**

165 Apart from one (Wang et al. 2013) randomised controlled trial (RCT), with high cross-
166 group contamination, the studies all generated low-level evidence predominately from
167 case reports (n=11, 61%) (Agrawal et al. 2011; Ali 2016; Boit et al. 2014; Brown et al.
168 2017; Efstathiou et al. 2016; Einck et al. 2014; Galalae et al. 2015; Garcia-Gonzalez
169 et al. 2015; Krakauer et al. 2015; Nwogu et al. 2016; Shamieh and Hui 2015). Overall,
170 the studies were of poor quality. None were underpinned by a conceptual framework
171 or theory; two-thirds (67%, n=12) did not evaluate the strategy (Ali 2016; Banerjee
172 2009; Boit et al. 2014; Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014;
173 Gafer and Elhaj 2014; Garcia-Gonzalez et al. 2015; Krakauer et al. 2015; Nwogu et
174 al. 2016; Shamieh and Hui 2015; Tapsfield and Bates 2011); 44% (n=8) did not
175 describe the methods (Boit et al. 2014; Efstathiou et al. 2016; Einck et al. 2014; Gafer
176 and Elhaj 2014; Galalae et al. 2015; Garcia-Gonzalez et al. 2015; Krakauer et al. 2015;
177 Shamieh and Hui 2015); and less than a third (n=5) had secured ethics approval
178 (Galalae et al. 2015; Herce et al. 2014; Paiva et al. 2012; Tapsfield and Bates 2011;
179 Wang et al. 2013).

180 **Positive policy environment facilitators and barriers**

181 Seven main positive policy environment facilitators emerged as being crucial to the
182 successful implementation of the access improvement strategies (refer Table 1).
183 Stakeholder engagement (Agrawal et al. 2011; Ali 2016; Banerjee 2009; Boit et al.
184 2014; Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014; Gafer and Elhaj
185 2014; Galalae et al. 2015; Garcia-Gonzalez et al. 2015; Herce et al. 2014; Kanavos et
186 al. 2009; Krakauer et al. 2015; Nwogu et al. 2016; Tapsfield and Bates 2011) and
187 financial support (Agrawal et al. 2011; Ali 2016; Boit et al. 2014; Brown et al. 2017;
188 Efstathiou et al. 2016; Gafer and Elhaj 2014; Garcia-Gonzalez et al. 2015; Herce et

189 al. 2014; Kanavos et al. 2009; Nwogu et al. 2016; Tapsfield and Bates 2011) were
190 identified as critical facilitators across all access improvement strategies
191 implementation. Embedding a shared understanding of the project importance and the
192 proposed action(s) and facilitating a sense of co-creation and ownership, were the key
193 primary focus of the stakeholder engagement strategies implemented across the
194 projects. Through the co-creation of a cancer centre, there was an estimated 17%
195 average annual increase in cancer patients accessing care which was observed
196 between 2014-2016 (Nwogu et al. 2016).

197 Five key positive policy environment barriers that impeded the implementation of the
198 planned access improvement strategies were identified. Across four studies, lack of
199 human resources was the most critical barrier to the implementation of access
200 improvement strategies (Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014;
201 Gafer and Elhaj 2014). Several studies acknowledged financial constraints and lack
202 of political commitment as major barriers to implementation (Ali 2016; Nwogu et al.
203 2016). Collectively these identified barriers contributed to: strategy implementation
204 delays (Ali 2016; Gafer and Elhaj 2014); high health professionals workloads
205 (Efstathiou et al. 2016; Einck et al. 2014); and patients experiencing long waiting times
206 to be seen by health professionals (Brown et al. 2017; Nwogu et al. 2016).

207 **Healthcare organisation facilitators and barriers**

208 Of the eight healthcare organisation facilitators identified, creating a supportive
209 learning environment was key to increasing integrated cancer care, radiotherapy,
210 and/or palliative care access. Thirteen studies with varying levels of evidence reported
211 creating a supportive learning environment for health professionals to develop
212 specialist and generalist knowledge and skills (Agrawal et al. 2011; Ali 2016; Banerjee

213 2009; Boit et al. 2014; Brown et al. 2017; Gafer and Elhaj 2014; Herce et al. 2014;
214 Krakauer et al. 2015; Lal et al. 2015; Nwogu et al. 2016; Paiva et al. 2012; Shamieh
215 and Hui 2015; Tapsfield and Bates 2011). The RCT reported a significant increase in
216 patients' knowledge of cancer pain and pain control by employing task-shifting strategy
217 ($p < 0.05$) (Wang et al. 2013). Few studies targeted financial hardship and treatment
218 adherence by offering free access to essential cancer and palliative care medicines
219 (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009; Lal et al. 2015). While a significant
220 increase in survival could not be determined in a retrospective review of the outcome
221 of the free drug donation strategy, a three-year survival rate of 66% was reported
222 among 13,568 patients (Kanavos et al. 2009). Access improvement strategies tailored
223 to local resources and conditions generated better acceptance of the changes (Einck
224 et al. 2014; Galalae et al. 2015; Garcia-Gonzalez et al. 2015).

225 Ten healthcare organisation barriers to access improvement strategies
226 implementation were identified, with the majority related to radiotherapy access, such
227 as: limited physical infrastructure (Efstathiou et al. 2016; Einck et al. 2014); lack of
228 radiotherapy equipment (Efstathiou et al. 2016; Einck et al. 2014); and radiotherapy
229 equipment maintenance difficulties (Efstathiou et al. 2016). Untimely delivery of
230 appropriate radiotherapy doses was a major negative consequence. The most
231 challenging aspect of chemotherapy access improvement strategies were: poor
232 internet connectivity, identifying and verifying eligible cancer patients, as well as
233 maintaining communication between strategy providers and health professionals
234 (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009). While a small number of studies
235 suggested that prohibitive cancer treatment cost limited access for cancer patients and
236 their families (Einck et al. 2014; Nwogu et al. 2016), no economic evidence estimating
237 the direct and indirect treatment costs was provided.

238 **Community facilitators and barriers**

239 Two community facilitators that supported the successful implementation of integrative
240 cancer care and palliative care access improvement strategies were identified (Boit et
241 al. 2014; Herce et al. 2014; Nwogu et al. 2016). Across two studies, community
242 networks were important providers of complementary services, such as
243 socioeconomic supports (Boit et al. 2014; Herce et al. 2014). A critical facilitator was
244 mobilising and coordinating community resources. One study acknowledged that
245 establishing a non-governmental organisation (NGOs) offered unique opportunities to
246 mobilised funds and coordinated with other community institutions to foster greater
247 community buy-in of improvement strategies (Nwogu et al. 2016).

248 Culturally-related beliefs, attitudes and practices toward cancer and treatment
249 modalities, was the only community level barrier identified which adversely impacted
250 on communities or individuals' non-acceptance of the radiotherapy and palliative care
251 access improvement strategies on offer (Efstathiou et al. 2016; Gafer and Elhaj 2014).

252 **Discussion**

253 Unfortunately, there is no high-level evidence to recommend any particular strategy to
254 increase access to cancer treatments or palliative care in LMICs. Most strategies have
255 focused on increasing palliative care, and none on increasing access to surgical care,
256 the mainstay of curative cancer care (Sullivan et al. 2015).

257 No strategies to date have been robustly evaluated or have included a health
258 economic evaluation. None have made use of an implementation framework.
259 However, despite limitations in the quality of the studies, the literature yields valuable
260 insights of relevance to policy-makers, financiers and researchers.

261 The included studies revealed numerous facilitators and barriers affecting the
262 successful implementation of access improvement strategies at all three levels of the
263 ICCC framework. These facilitators and barriers were complex and overlapping,
264 concerned with: stakeholder engagement, financial support, supportive learning
265 environment, strong community networks, lack of human resources, financial
266 constraints, and limited infrastructure. These results confirm the complexity of
267 implementing healthcare change, which requires an understanding of: processes of
268 implementation; factors affecting implementation; the introduction of solutions, scale-
269 up, and longer-term sustainability (Nilsen 2015; Peters et al. 2013).

270 Financing, partnership, legislative frameworks, policy integration, leadership and
271 advocacy, development and allocation of human resources are key requirements of a
272 positive policy environment (WHO 2002a). This review has highlighted the importance
273 of acquiring the necessary financial support before embarking on any access
274 improvement strategy. Financing of access improvement strategies determines who
275 provides funds, and who exercises influence over the funds. International donors
276 increasing their financing priority have been the key driving force for strengthening
277 palliative care services in LMICs (Ali 2016; Boit et al. 2014; Gafer and Elhaj 2014;
278 Herce et al. 2014; Tapsfield and Bates 2011), while locally based NGOs ability to
279 established international ties is central to mobilising international funds for other
280 cancer treatment initiatives (Nwogu et al. 2016). Donor funding approach for a specific
281 purpose restricts strategy scope and limits the sponsors ability to address unique local
282 needs. This mismatch contributes to poor strategy acceptance at the local level.

283 The private sector's financial participation in the health sector in most LMICs has
284 contributed significantly to the availability of radiotherapy (Efsthathiou et al. 2016),
285 chemotherapy (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009) and integrated

286 cancer care (Nwogu et al. 2016). However, private sector financing approach in LMICs
287 exposes' patients without private health insurance and their families, who make up
288 most of these populations, to extreme financial hardships making it impossible for
289 them to pay or adhere to care. As universal health coverage is yet to be fully realised
290 in most LMICs (WHO and World Bank 2015), medical expenses related to cancer
291 treatments continue to serve as a barrier to the successful improvement strategies
292 implementation (Einck et al. 2014; Nwogu et al. 2016). There is an urgent need to
293 institutionalise an appropriate financing system at the national level that offers the right
294 financial incentives for providers, and protects cancer patients from financial hardships
295 (WHO 2007).

296 Policies at the international, national, and regional levels are major issues in the
297 successful implementation of access improvement strategies. This review identified a
298 paucity of evidence about policy development and implementation to improve access
299 to cancer treatments and palliative care. Recently, WHO (2002a; 2002b) has assumed
300 a more central position in providing supports for policy development process in most
301 LMICs, which is crucial to driving in-country reform. A cancer policy framework helps
302 guide critical decisions and systematic course of actions by governments and other
303 stakeholders, both of which are essential to improving cancer control (Adshead and
304 Thorpe 2008). In LMICs, there remains a significant need for: credible policy agenda
305 setting, realistic policy formulation; timely policy implementation; and periodic policy
306 monitoring and evaluation using a theoretical framework (Exworthy 2008). Successful
307 design and implementation of LMIC cancer control policies requires high quality health
308 services research evidence, long-term commitment of resources, institutional capacity
309 to enhance sustainability and reach of the policy, and co-designed approaches. While
310 most of the cancer control policies developed in HICs offer useful starting points, LMIC

311 policy-makers and supporting partners should consider the context, and power to
312 obtain a full understanding of local policy process (Exworthy 2008).

313 Our findings are consistent with other literature on the need to gain commitment and
314 buy-in from key stakeholders, especially those in positions of authority (Ramaswamy
315 and Gouillart 2010). Meaningful engagement of key stakeholders plays an essential
316 role in achieving commitment at the political and community levels. Participatory and
317 co-design driven approach to implementation will assist in structuring health services
318 to deliver effective, safe, and quality cancer treatments and palliative care.
319 Participatory approach offers stakeholders: a more active and significant role in
320 defining their priorities; diagnosing their challenges; securing funds; and implementing
321 appropriate solutions for service improvement (Bate and Robert 2006).

322 The ICCC framework employs a population health approach including: promoting
323 continuity and coordination, encouraging quality through leadership and incentives,
324 organising and equipping healthcare teams, using information systems, and
325 supporting self-management and prevention (WHO 2002a). The performance of the
326 health workforce drives health system improvement strategies and determines how
327 care is delivered. Developing and strengthening a country-based and country-led
328 health workforce education initiative with appropriate international support is essential
329 (Chen et al. 2004) if a responsive, fair, and efficient health outcome is to be realised.
330 A country-based educational strategy helps reduce the outward migration of skilled
331 health professionals from LMICs to HICs. An essential step towards achieving
332 universal access to quality cancer treatments and palliative care is shifting human
333 resource responsibilities and providing generalist doctors, nurses, allied health
334 professionals, clinical pharmacists and community health workers with the necessary

335 training, assessment tools, and essential medicines to deliver appropriate hospital and
336 home-based care (Knaul et al. 2017; Knaul et al. 2011).

337 Implementation was largely affected by essential equipment challenges, particularly
338 radiotherapy. Essential medical equipment, such as linear accelerators and high-
339 dose-rate brachytherapy, are of paramount importance in cancer treatments and
340 palliative care. Access to essential medical equipment provides the required
341 assurance of quality, safety, efficacy, cost-effective, and scientific care delivery (WHO
342 2007). However, most LMICs: lack essential radiotherapy equipment; are faced with
343 periodic radiotherapy equipment breakdowns; or have poor radiotherapy equipment
344 maintenance culture. Given that radiotherapy equipment is expensive to install, it is
345 imperative to develop and implement specific preventive and corrective maintenance
346 schedules, procedures and tasks to reduce unnecessary operational interruptions due
347 to breakdowns. These challenges are part of a broader medical equipment problems
348 in most LMICs. Hence, to improve access to essential medical equipment, there is a
349 need to develop simple, quality, and affordable medical technologies. By designing
350 and engineering tools, and techniques less than 500 nanometers in size, emerging
351 field of nanotechnology offers significant opportunity in overcoming different barriers
352 to cancer treatments (Cuenca et al. 2006). Such technologies can help reduce the
353 size, weight, shielding, and shipping costs of medical equipment. Moreover, the
354 technological advances can lead to a reduction of power consumption necessary for
355 operating the equipment, and limited heat production. There should be greater
356 emphasis on developing solar-powered equipment with high-quality insulation to limit
357 the dependence on national power grid (Atun et al. 2015).

358 The ICCC framework assigns significant emphasis to the community, acknowledging
359 both the individuals living in a place and the place itself (WHO 2002a). Informed and

360 prepared community resources help to promote awareness and reduce stigma,
361 provide leadership and support, and deliver complementary services to ensure better
362 outcomes for chronic care conditions (WHO 2002a). Recognising that community
363 agencies, organisations, institutions, opinion leaders, and concern citizens are major
364 stakeholders in strengthening cancer treatments and palliative care delivery will
365 require promoting acceptance and understanding of the notion of community
366 involvement in health and development (Kahssay and Oakley 1999). The community
367 development literature may prove useful in designing and implementing access
368 improvement strategies. By definition, community development contributes to
369 resource mobilisation, local empowerment, capacity development, and growth of
370 political action through a network of relationships to help include the perspective and
371 experience of grassroots (Helling et al. 2005).

372 **Identified gaps**

373 Investing and expanding surgical and radiotherapy capacity ought to be an important
374 priority for all LMICs. Well-established knowledge of the minimum standards for quality
375 cancer surgery and radiotherapy already exist and include: establishing or adopting
376 national accreditation systems; scaling up surgical and radiotherapy workforce;
377 providing competency license; and aligning surgical and radiotherapy access with
378 universal health coverage (Atun et al. 2015; Meara et al. 2015; Sullivan et al. 2015).

379 Another gap relates to the lack of incentives and rewards available for health
380 professionals in LMICs. Incentives and rewards systems should be created for
381 motivating health professionals. Both financial and non-financial incentives are
382 essential to encourage health professionals to effectively perform, and engage in
383 innovative clinical practice (WHO 2002a).

384 While there is an urgent need to increase the access to best evidence-based cancer
385 care for people living in LMICs, this review highlights the importance of access to:
386 universal health insurance, so that more people who need cancer care can afford to
387 access the care they need; and essential cancer and palliative care medications, as
388 per the WHO lists.

389 **Future directions**

390 There are opportunities to draw valuable lessons from the experience in developing
391 and implementing HIV/AIDS strategies in LMICs, as well as cancer treatment and
392 palliative care strategies in HICs. Key among these lessons are: global mobilisation
393 and investment funds; engagement of pharmaceutical companies; development of
394 simple health technologies; strengthening health workforce capacity; development of
395 a supportive national policy framework; connecting health system with community
396 resources; and community participatory in strategy development (Khumalo-
397 Sakutukwa et al. 2008; Knaul et al. 2011; Muthee et al. 2018; Narayan et al. 2011).
398 Recognising the importance of national policies in cancer control; dedicated financial
399 budgets supporting cancer control; high level of advocacy and community involvement
400 in strategy design; strong political support and acceptability of cancer control
401 strategies; progress in cutting-edge technological advancements; and promoting high
402 quality cancer research and evidence-based treatment, are critical to taking cancer
403 care in LMICs to the next stage of their development (Knaul et al. 2011; Obeidat et al.
404 2011; Thompson et al. 2017).

405 Applying existing implementation research theories to future strategies designs will
406 assist in strengthening the work undertaken to improve access to cancer treatments
407 and palliative care in LMICs. Further research assessing LMICs' readiness to develop

408 access improvement strategies as an essential precursor to an effective adoption is
409 an important next step. A readiness assessment provides strategy implementers with
410 a preliminary understanding of the barriers and facilitators they are likely to encounter
411 when implementing improvement strategies (Helfrich et al. 2009). To help prioritise
412 actions and mitigate implementation barriers, increased focus on readiness are
413 needed so that evidence base for LMICs capacity, preparedness, commitment and
414 willingness to support cancer treatment and palliative care strategy implementation,
415 sustainability and scale-up is available to assist policy-makers. Such focus is of
416 particularly importance to expanding access to cancer treatment and palliative care in
417 LMICs.

418 **Strengths and limitations**

419 The systematic search of articles and application of an internationally recognised
420 framework are strengths of this review. While this review distilled various facilitators
421 and barriers to the successful implementation from the studies, these were not
422 systematically or explicitly investigated using primary research techniques. The results
423 should be interpreted with caution because the studies included were low-level
424 evidence, at the descriptive level except for one randomised control trial (Wang et al.
425 2013). None of the studies referenced the ICCC framework, which may not be an ideal
426 'fit' for some countries' health systems.

427 **Conclusions**

428 While modest progress has been made to increase access to cancer treatments and
429 palliative care in LMICs, some major gaps still exist. In taking this work forward, LMICs
430 are advised to adopt internationally recognised frameworks, such as the ICCC or the
431 WHO's action framework intended to strengthen health systems to improve health

432 outcomes to assist leaders to assess local population needs and integrate initiatives
433 systematically, engage with the appropriate stakeholders and secure the necessary
434 financial support. It is essential to include an evaluation plan and budget during the
435 development of the access improvement strategy. Needs assessment and design
436 evaluation should be undertaken by an independent evaluator to ensure that a reliable
437 blind outcome-based analysis is generated.

438 **Authors contributions**

439 All the authors contributed to the study design, manuscript development, editing and
440 completion of the manuscript. The article search, and management were performed
441 by AD. Articles screening was completed by AD, and TL independently screened 10%
442 of the articles. Quality assessment and study description were performed by AD.
443 Coding of studies to the ICCC framework was performed by AD and TL. Data reduction
444 was performed by AD and consensus discussions and finalising with JP, TL and SA.
445 Table design was completed by AD, JP and TL.

446 **Legends**

447 **Fig. 1** Innovative Care for Chronic Conditions framework adapted with permission
448 granted by WHO (World Health Organization 2002a)

449 **Fig. 2** Flow diagram illustrating study search and selection in the systematic review
450 on barriers and facilitators to implementation of cancer treatment and palliative care
451 strategies in low and middle income countries

452 **Compliance with Ethical Standards**

453 Conflict of interest: The authors declare that they have no conflict of interest.

454 Funding: No funding was received.

455 Ethical approval: This article is based on a secondary analysis of existing literature
456 and does not contain any studies with human participants or animals performed by
457 any of the authors. Good scientific standards have been followed according to the
458 PRISMA statement.

459 Informed consent: Not applicable

460 **References**

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645 **Table**

646 Table 1 Summary of the facilitators and barriers to implementation of cancer treatment and palliative care strategies in low and middle
 647 income countries, 1990-2017

ICCC levels	Facilitators	Barriers
Positive Policy Environment	Prepared health professionals (Ali 2016; Banerjee 2009; Boit et al. 2014; Brown et al. 2017; Gafer and Elhaj 2014; Herce et al. 2014; Krakauer et al. 2015; Nwogu et al. 2016; Paiva et al. 2012; Shamieh and Hui 2015; Tapsfield and Bates 2011)	Lack of human resources (Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014; Gafer and Elhaj 2014)
	Financial support (Agrawal et al. 2011; Ali 2016; Boit et al. 2014; Brown et al. 2017; Efstathiou et al. 2016; Gafer and Elhaj 2014; Garcia-Gonzalez et al. 2015; Herce et al. 2014; Kanavos et al. 2009; Nwogu et al. 2016; Tapsfield and Bates 2011)	Financial constraints (Ali 2016; Nwogu et al. 2016)
	Political commitment (Agrawal et al. 2011; Ali 2016; Brown et al. 2017; Efstathiou et al. 2016; Herce et al. 2014; Krakauer et al. 2015)	Limited political commitment (Ali 2016; Nwogu et al. 2016)
	Stakeholder engagement (Brown et al. 2017; Nwogu et al. 2016) (Agrawal et al. 2011; Ali 2016; Banerjee 2009; Boit et al. 2014; Efstathiou et al. 2016; Einck et al. 2014; Gafer and Elhaj 2014; Galalae et al. 2015; Garcia-Gonzalez et al. 2015; Herce et al. 2014; Kanavos et al. 2009; Krakauer et al. 2015; Tapsfield and Bates 2011)	Restrictive pharmacovigilance laws and regulations (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009)
	Positive relationships with international organisations (Ali 2016; Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014; Gafer and Elhaj 2014; Galalae et al. 2015; Krakauer et al. 2015; Nwogu et al. 2016)	Drug importation process challenges (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009)
	Committed champions (Ali 2016; Banerjee 2009; Boit et al. 2014; Gafer and Elhaj 2014; Herce et al. 2014; Krakauer et al. 2015; Nwogu et al. 2016)	
	Strategy aligned with national policy (Efstathiou et al. 2016)	
Healthcare Organisation	Supportive learning environment (Agrawal et al. 2011; Ali 2016; Banerjee 2009; Boit et al. 2014; Brown et al. 2017; Gafer and Elhaj 2014; Herce et al. 2014; Krakauer et al. 2015; Lal et al. 2015; Nwogu et al. 2016; Paiva et al. 2012; Shamieh and Hui 2015; Tapsfield and Bates 2011)	Limited physical infrastructure (Banerjee 2009; Efstathiou et al. 2016; Einck et al. 2014; Gafer and Elhaj 2014)
	Recognition of patients' needs (Banerjee 2009; Brown et al. 2017; Gafer and Elhaj 2014; Garcia-Gonzalez et al. 2015; Herce et al. 2014; Kanavos et al. 2009; Lal et al. 2015; Nwogu et al. 2016; Paiva et al. 2012; Shamieh and Hui 2015; Wang et al. 2013)	Prohibitive treatment costs (Einck et al. 2014; Nwogu et al. 2016)
	Patient symptom management education (Banerjee 2009; Gafer and Elhaj 2014; Herce et al. 2014; Lal et al. 2015; Paiva et al. 2012; Shamieh and Hui 2015; Wang et al. 2013)	Lack of WHO essential pain and palliative care medicines (Gafer and Elhaj 2014)

ICCC levels	Facilitators	Barriers
	Strategy coordinator (Herce et al. 2014; Shamieh and Hui 2015; Tapsfield and Bates 2011)	Fragmented health system (Efstathiou et al. 2016)
	Adherence to evidence-based practice (Einck et al. 2014; Galalae et al. 2015)	Irregular meeting attendance (Agrawal et al. 2011; Brown et al. 2017)
	Strategy tailored to local resources and conditions (Einck et al. 2014; Galalae et al. 2015; Garcia-Gonzalez et al. 2015; Kanavos et al. 2009)	Limited or lack of radiotherapy equipment (Brown et al. 2017; Efstathiou et al. 2016; Einck et al. 2014; Nwogu et al. 2016)
	Information management system (Brown et al. 2017; Nwogu et al. 2016)	Poor internet connectivity (Agrawal et al. 2011) (Garcia-Gonzalez et al. 2015; Kanavos et al. 2009)
	Clearly defined strategy objectives (Agrawal et al. 2011; Brown et al. 2017; Galalae et al. 2015)	Radiotherapy equipment maintenance difficulties (Efstathiou et al. 2016)
		Periodic radiotherapy equipment breakdown (Efstathiou et al. 2016)
		Unstable electricity supply (Efstathiou et al. 2016)
Community	Strong community networks (Boit et al. 2014; Herce et al. 2014)	Culturally-related beliefs, attitudes and practices towards cancer and treatment modalities (Efstathiou et al. 2016; Gafer and Elhaj 2014)
	Mobilisation and coordination of resources (Nwogu et al. 2016)	

648 Explanation of abbreviations: ICCC = Innovative Care for Chronic Conditions

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