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Achieving Effective Universal Health Coverage And Diagonal Approaches To Care For Chronic Illnesses

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ABSTRACT **Health systems in low- and middle-income countries were designed to provide episodic care for acute conditions. However, the burden of disease has shifted to be overwhelmingly dominated by chronic conditions and illnesses that require health systems to function in an integrated manner across a spectrum of disease stages from prevention to palliation. Low- and middle-income countries are also aiming to ensure health care access for all through universal health coverage. This article proposes a framework of effective universal health coverage intended to meet the challenge of chronic illnesses. It outlines strategies to strengthen health systems through a "diagonal approach." We argue that the core challenge to health systems is chronicity of illness that requires ongoing and long-term health care. The example of breast cancer within the broader context of health system reform in Mexico is presented to illustrate effective universal health coverage along the chronic disease continuum and across health systems functions. The article concludes with recommendations to strengthen health systems in order to achieve effective universal health coverage.**

Universal health coverage is an explicit goal of health systems strengthening and a cornerstone of health reform.[1] The World Health Organization (WHO) defines *universal health coverage* as ensuring that all people receive the promotive, preventive, curative, rehabilitative, and palliative health services they need, of sufficient quality to be effective, while the use of these services does not expose the user to financial hardship.[2]

Achieving universal health coverage has become especially challenging in the face of the epidemiological transition that has brought an increasingly complex burden of noncommunicable diseases and injuries. This is especially true in low- and middle-income countries, where health systems are weak and where the epidemiological transition has been more rapid than in high-income countries. Low- and middle-income countries face a disease burden associated with poverty and at the same time an emerging burden of chronic diseases that are costly to treat. The rising burden of chronic disease coincides with a rapidly aging population that is stressing societies and their institutions.[3]

Chronic diseases are typically ill defined for the purpose of analyzing an effective health system response. This category includes diseases where treatment spans months or years before death occurs or before reaching a point where the patient is considered no longer at risk of death from that cause. With medical innovation, many diseases that were previously untreatable have been transformed into chronic conditions. HIV/AIDS is a leading example. Hence, in health system design, it is the chronic nature of illness that should be taken into account, not whether a disease is communicable or not.[4]

Chronic conditions pose complex challenges

for health systems, which by the WHO definition include stewardship, financing, service delivery, and resource generation,[5] as their management requires integrated interventions, policies, and programs over time and across and among health care providers and institutions. The requirements for prevention, early detection, treatment, disease management, and palliation of noncommunicable and chronic diseases typically demand stronger primary health care from families, communities, and professional providers. The redesign of health systems to address chronic disease suggests an opportunity to treat patients holistically, across their life cycles, and as productive members of families, communities, economies, and societies.[6]

In low- and middle-income countries' health systems, chronic diseases are addressed as a sequence of acute episodes.[4] Hence, the interaction between various acute events, multiple comorbidities, palliative care, and survivorship care tend to be neglected.[4,7] In the face of increasing life expectancy and aging populations, and the transformation of the disease burden in low- and middle-income countries, the issue of chronicity, or long-term care, is a pressing priority for individuals and health systems in those countries. Noncommunicable diseases accounted for 68 percent of global deaths in 2012, and three-quarters of these occurred in low- and middle-income countries.[8] Indeed, how to address noncommunicable diseases is a paramount issue for the post-2015 development agenda, as the global community defines new development goals.[9] A paradigm shift in thinking is necessary to move from the delivery of episodic care to address the complex array of concerns related to chronicity. Universal health coverage provides the opportunity to retool health systems to introduce care delivery models for chronic conditions[10] that span the care continuum and the life course.

The next section of this article introduces the notion of effective universal health coverage with respect to stages of the care continuum. The following section discusses the segmented approach currently prevailing in many low- and middle-income countries and how the lack of a diagonal response that simultaneously addresses disease and system-specific needs hinders the realization of effective universal health coverage throughout the life course. We then present a case study on how health care reform in Mexico allowed for new approaches to managing and treating breast cancer, to illustrate potential strategies to realize effective universal health coverage. The final section concludes with recommendations for policy makers to address the challenge of chronicity.

Transforming Health Systems To Respond To Chronic Illness

Health systems around the world were designed and deployed to manage disease, ill health, and injury that were quickly resolved; either cure or death was the near immediate outcome. Chronicity poses new demands on each health system function and on the efforts to achieve universal health coverage.[1]

Chronic illnesses—defined by the WHO as conditions that require ongoing health care management over time—today account for the majority of the global burden of disease.[11,12] Effective management of chronic illness requires provision of services across the care continuum, which includes primary prevention, secondary prevention or early detection, diagnosis, treatment, survivorship and rehabilitation care, and palliative and end-of-life care. The overlapping nature of the disease continuum along the life cycle and across stages of disease generates additional complexities.[4,13] Health systems in many low- and middle-income countries mainly focus on a specific component of the care continuum (treatment) while neglecting other components. Systems fail to adequately respond to the various needs of patients and families as they progress through different stages of a chronic disease along the life cycle.

Achieving universal health coverage is now an explicit goal of health systems—one that can be achieved only if the complexity of chronic and noncommunicable disease is taken into account.[1] Universal health coverage has been characterized in three dimensions: It aims to cover all beneficiaries (with priority given to vulnerable groups); it provides benefits through an explicitly defined package of health services; and it covers a proportion of direct costs to maximize financial protection and protect individuals and families from catastrophic and impoverishing health expenditure.[7] The path toward universal health coverage is a continual process of striving to cover people as populations grow, as interventions change with the emergence of new science and best medical practices, and as the disease burden evolves. Universal health coverage is achieved through progress along these dimensions in three stages: legislation and affiliation to ensure coverage of all people; provision of access to an expanding benefit package of cost-effective health services in line with economic growth and financial protection; and creation of a means of financial protection that contributes to achieving the highest level of health outcomes and quality.[14]

In the face of the shift in the burden of disease toward noncommunicable diseases and chronicity, effective universal health care must consider

the stages of the chronic disease continuum and the integration of care by health system function at each stage of the continuum, as well as across each health system function by stage. Effective universal health care requires integrating the health systems functions and the components of the chronic care disease continuum.

Diagonal Approach To Health System Strengthening And Integration

Designing a health system specific to each chronic disease would be needlessly costly as well as ineffective, especially for patients who must navigate a divided rather than an integrated system. Extant literature demonstrates why this approach was ineffective when it was applied to the challenge of HIV/AIDS in the 1990s, providing evidence as to why it is also not desirable to create parallel systems for noncommunicable diseases and chronic illnesses.[15]

Preparing systems to provide care across the chronic disease continuum through effective universal health coverage requires a cross-cutting framework. Moving toward effective universal health coverage requires integrating the health systems functions and the components of the chronic disease continuum. The diagonal approach overcomes the barriers between vertical (disease-specific) and horizontal (systemic) approaches by making full use of potential synergies between disease programs and health functions and prioritizing programs that respond to multiple diseases.[16,17] Integration can take place across each stage of the chronic disease continuum spanning prevention to palliation, as well as for multiple diseases both acute and chronic.[4] A diagonal approach to health system strengthening provides holistic care across diseases, while at the same time addressing specific diseases in a manner that reinforces the overall system and each of its functions.[4]

A diagonal response seeks to identify opportunities for optimal use of existing health programs or platforms, including those in other sectors such as education, to address multiple health priorities. The diagonal approach bridges horizontal and vertical interventions for different diseases and breaks down barriers between communicable and noncommunicable diseases to promote a life-course approach.[4]

Health system segmentation and fragmentation are common in low- and middle-income countries and result in an atomized approach that does not exploit linkages across the system. In a diagonal approach, disease-specific, vertical programs are integrated across health system functions as part of a larger blueprint for health systems strengthening. Instead of developing a parallel system for noncommunicable disease and chronic illness, the diagonal approach promotes an integrated response within the overall health system that accounts for the myriad health problems faced by patients during their lives.

A Diagonal Approach For Breast Cancer And For Palliative Care And Pain Control In Mexico

BREAST CANCER IN LOW- AND MIDDLE-INCOME COUNTRIES Breast cancer is the cause of approximately 25 percent of all cancers in women globally.[18] It is the leading cause of cancer-related death of women in most low- and middle-income countries, outstripping cervical cancer in all but the poorest nations and populations.[19,20] The incidence of breast cancer is increasing at alarming rates and in low- and middle-income countries is particularly concentrated among women in younger age groups.[21,22] In Mexico, for example, breast cancer is the second-leading cause of death among women ages 30–54 and the leading cancer-related cause of death.[23,24] Furthermore, survival rates are much lower for poorer women within and across countries—less than 50 percent in low-income countries compared to more than 75 percent in high-income nations.[19] Responding to the challenge of breast cancer in low- and middle-income countries is thus both a health and an equity imperative.

Breast cancer is a disease amenable to both primary, populationwide interventions and secondary prevention through early detection. Appropriate diagnosis is complex and key to effective treatment, which tends to be lengthy, often spanning years of drug regimes. Survivors require medical attention and other types of interventions to enable them to fully participate in their communities—including, for example, reducing stigma in the work setting. Palliation and pain control are important for patients who will die of their disease, as well as during the treatment process. Thus, breast cancer constitutes an ideal "tracer" disease to map an effective health system response along the care continuum, providing informative lessons for other noncommunicable diseases and chronic illnesses.

In the case of breast cancer, the cancer divide—disparities in cancer morbidity and mortality between the rich and poor as a result of differentials in access to health care and socioeconomic factors—is evident at each stage of the disease continuum. Poor women face exposure to risk factors and lack of awareness about healthy lifestyles; inadequate access to information and screening interventions to promote timely detec-

How to address noncommunicable diseases is a paramount issue for the post-2015 development agenda.

tion; poor diagnostics that lead to costly and ineffective treatment; lack of access to appropriate treatments; increased social and psychological suffering associated with the disease; and limited survivorship care, which is worsened by stigma and discrimination that is magnified by gender inequity. Appalling levels of limited access to pain control and palliative care compounds needless suffering through the course of the disease and at the end of life.[19]

HEALTH REFORM IN MEXICO In 2003 Mexico underwent a remarkable health reform, reported in 2005 in this journal, to ensure social protection for health care through explicit entitlements.[25] The reform established the individual right to health care through the provision of universal access to an essential package of services with financial protection.[14] The reform introduced the System of Social Protection in Health that includes a publicly funded health insurance scheme, the Seguro Popular de Salud (Popular Health Insurance), to cover personal health interventions targeted to the poor. The new structure of financing is based on progressive subsidies from general taxation and public financing. Conditions requiring high-cost and specialized interventions were aggregated into a Fund for Protection against Catastrophic Expenses. The number of covered diseases and interventions has increased steadily and considerably over time, including a growing list of cancers.[14]

As of 2012 the Seguro Popular had affiliated and covered more than fifty million Mexicans who were previously uninsured and by 2015 further expanded coverage to reach more than fifty-six million people. Prior to the Seguro Popular, only salaried individuals and their dependents had access to publicly funded health insurance coverage through Mexico's social security system. All other segments of the population (that is, self-employed, underemployed, or unemployed) had limited access to health services based on inconsistent budgetary allocations, forcing most of this population—mainly poorer Mexicans—to rely heavily on out-of-pocket payments for basic health services and medicines.[25] Catastrophic health expenditures impoverished many families.[14,26]

Improvement of quality of care throughout the health system served as one of the pillars of the reform, with health services delivery channeled only through accredited public and private providers.[14] A regulatory body—the Comisión Federal para la Protección contra Riesgos Sanitarios (Federal Commission for the Protection against Sanitary Risks)—was created to manage service quality and other processes, including implementing safety and efficacy standards and undertaking approval of drugs and medical technologies and control of hazardous substances.[14]

FINANCIAL PROTECTION, PREVENTION, AND TREATMENT FOR BREAST CANCER IN MEXICO The 2003 Mexican health reform incorporated financial protection for breast cancer treatment, yet challenges to achieving effective universal health care persist. Two examples are early detection, which is specific to breast cancer, and palliative care, which is relevant to all life-threatening diseases and patients suffering from pain.

As of 2007 all Mexican women diagnosed with breast cancer have access to treatment with financial protection. All women who were uninsured prior to health reform have the legal right to a generous package of treatment services that includes costly and effective drugs such as trastuzumab for Herceptin receptor positive (HER2+) disease. Yet the effectiveness of increased access to treatment has been attenuated by limited access to early detection and diagnostic facilities, as well as by lack of follow-up and ongoing survivorship and palliative care. A diagonal approach has been recently applied to address some of these gaps and experiences, as discussed below.

SECONDARY PREVENTION (EARLY DETECTION) OF BREAST CANCER Early detection of breast cancer is widely considered to increase the chances of cure and extend healthy life expectancy. Yet in most low- and middle-income countries, late detection is a major concern.[27]

Secondary prevention through awareness building and screening is critical to early detection. In the absence of appropriate health care infrastructure, mammography screening in low-resource settings is difficult and in any case is not a useful screening device for women younger than age forty. In low- and middle-income countries, where the majority of cases are detected in premenopausal women, other options must be considered. Access to breast self-awareness

training and clinical breast exams at the primary level of care continues to hold promise for early detection.[28]

A key focus of the reform in Mexico was to increase financial protection and strengthen the primary level of care to anchor the health system. Yet early detection of breast cancer continues to be a challenge. Data from the National Health and Nutrition Survey of 2012 show that only one in five Mexican women ages 40–69 reported having an annual mammogram or breast clinical exam.[29] In the poorest quintile, the figure is a little more than 10 percent, while in the wealthiest, it is approximately 30 percent.[29] Hospital-based reports suggest that the majority of cases continue to be detected at later stages, especially in poorer states and municipalities, and that mortality rates are high and increasing despite better access to treatment that can save lives.[22,30,31]

In the face of this challenge, a multi-institutional group was established, spearheaded by civil society and working with the Seguro Popular, the National Institute of Public Health of Mexico, and state governments. This group provided training for an extensive primary care network of community health workers, nurses, and primary care physicians. The training focused on early diagnosis through breast health awareness and clinical breast exams, as well as triaging symptomatic and high-risk cases with family history. The training modules and materials were formally evaluated, and the published results show that both professional and part-time community health workers increased their knowledge in a variety of areas and that this knowledge was retained for several months following the initial training.[32] The training modules were refined and then offered to nurses and physicians, and an online version is now available that has been made accessible nationally through the Mexican Social Security Institute. More extensive training on survivorship and pain and palliative care is now under way.

Education and awareness-building targeted to women were also promoted by linking outreach activities in various formats to the Oportunidades platform (now called Prospera). Prospera is a social welfare scheme, active since 1997, that offers conditional cash transfers to more than 90 percent of poor, urban, and rural families for the purpose of promoting education, health, and nutrition. Seguro Popular works with and through Prospera to support these families to train female household heads and community health promoters throughout the country on basic information about breast health.[14] In 2008 information on breast health was integrated into the Prospera manuals.[14] Ongoing work is required, however, to evaluate and update the information and to make sure that it is integrated as the program evolves.

Each of these interventions to improve training, education, and awareness constitutes a diagonal approach and builds on overall efforts to strengthen primary care and link to specialized tertiary treatment options, instead of developing parallel systems for early detection of breast cancer. These experiences deserve rigorous evaluation, as they suggest that diagonal strategies for early detection of breast cancer can be implemented through integration into national insurance and social security schemes and that antipoverty, maternal and child health, sexual and reproductive health, and HIV/AIDS programs can serve as platforms for addressing early detection and prevention of noncommunicable and chronic diseases. They also suggest the importance of identifying and analyzing the potential of other platforms for raising awareness and integrating delivery of breast health education and screening, such as schools and places of employment.

PAIN CONTROL AND PALLIATIVE CARE Approximately 94 percent of the global morphine consumption is in high-income countries, which make up 15 percent of the world's population.[22] In Mexico, 3,500 milligrams of morphine-equivalent opioid is consumed for pain relief per patient who dies from HIV or cancer, as compared to more than 300,000 milligrams in the United States.[33,34]

The vast majority of the world's countries have neglected to integrate pain control and palliative care into their health systems.[35,36] More than 5.5 million terminal cancer patients around the world needlessly suffer from moderate to severe pain.[37] With late-stage diagnosis, lack of access to treatment, and low survival rates, palliative care and pain control are key to cancer care in low- and middle-income countries. This is equally true for patients who suffer many other diseases, including HIV, and injuries that involve painful disability.

Until recently, pain control and palliative care in Mexico were not integrated into the health system or considered a priority. The health reform of 2003 largely ignored access to palliative care—a requirement of effective universal health coverage and an integral part of care across the chronic disease continuum. The problem was not unique to the Seguro Popular, as none of the major public providers of health care in Mexico have a strong palliative care and pain control program in place.

As a first step to developing adequate programming for delivery of pain and palliative care, a research and advocacy process was implemented

5.5 million

Suffer from pain

More than 5.5 million terminal cancer patients around the world suffer needlessly from moderate to severe pain.

in 2013 from work on breast cancer spearheaded by Mexican civil society organizations Tómatelo a Pecho (Take It to Heart) and the Mexican Health Foundation. The work quickly became part of a broader initiative to improve access for all patients in need of pain control and palliative care and involves multi-institutional networks working closely with the Ministry of Health and linked to global research and advocacy efforts.[35,38] A diagonal framework was used to guide the health system research and identify barriers across each health function in relation to access to pain control and palliative care. The research produced a substantial list of barriers to access to pain control and palliative care amenable to interventions for each health system function—stewardship, financing, delivery, and resources generation—and hence a framework for action specific to the stage of palliative care and relevant to the needs of patients at other points on the care continuum, especially survivorship (Exhibit 1).

A first step was to review innovative legislation on pain control and palliative care that was passed in 2009 and supplemented in 2013 and identify that this had never effectively translated into action because implementation norms were not developed.[38,39] The analysis identified that Mexico lacked a national palliative care strategy and hence also lacked unified guidance and direction for implementation of palliative care programs and pain control—a key to effective stewardship of the health system. Limited and restrictive regulatory structures as well as lack of institutional oversight for monitoring and evaluation of palliative care were also major hurdles. A strong concern for illicit use of opioids stymied their provision and greatly restricted access to pain medication for both in- and outpatients.

In terms of financing, the Fund for Protection against Catastrophic Health Expenditures made no explicit reference to coverage of pain relief; nor does the social security framework provide a clear guarantee to palliative care. In terms of health services delivery, weak infrastructure and inadequate supply-chain management of opioids, particularly in remote parts of the country, hinder the use of pain medication. Palliative care training for physicians and other key health personnel is limited, resulting in insufficient numbers of qualified professionals to prescribe drugs and provide care. University-level curriculum does not integrate palliative care to promote early training of health personnel—an issue for building the human resource base.[38] Furthermore, physicians fear prescribing opioids for pain relief because of strict and unwieldy regulations. Another barrier is the lack of adequate training in medical schools, which leaves physicians unprepared to prescribe opioids appropriately.[38]

Recent policy changes will help improve stewardship capacity. In 2014 the Ministry of Health established an office to improve access to palliative care and pain control and is developing a national program to guide future work. The ministry also published the norms for implementation of existing legislation and developed new inter-institutional guidelines for effective implementation of the law.[40,41] The Federal Commission for the Protection against Sanitary Risks has put systems in place for safe and effective management of pain medications that include electronic prescription.[42]

While effective health system stewardship is a necessary base for successful improvement of

EXHIBIT 1

Barriers In Mexico To Access To Palliative Care, Pain Control, And End-Of-Life Care, By Health System Function, 2013

Health system function	Barriers
Stewardship	Absence of a national program or plan Weak and restrictive regulatory frameworks, especially for opioids, through the Comisión Federal para la Protección contra Riesgos Sanitarios No designated area or staff in the Ministry of Health or other guiding health entities Absence of a system for monitoring, evaluation, and accountability
Financing	Little financial coverage in Seguro Popular Ill defined for social security—broad package with little specificity and limited access
Delivery	Few pain control centers; concentrated in large cities Supply and distribution chains incomplete
Resource generation	Scarcity of qualified personnel Fear of prescribing pain medication among providers Not included in medical school curricula Absence of publications and research

SOURCE Authors' analysis.

access, it is not sufficient. Implementation of palliative care and pain management is now the major challenge. Developing a human resource base connected to a high-quality supply chain and adequate financing will require substantial work. Training curricula on palliative care are being designed and tested for both medical students and practicing primary care physicians and nurses. Researchers are beginning to study the topic, and international seminars have been held to discuss the latest evidence and help strengthen policy making. Still, this is only one step toward developing an effective monitoring and accountability framework to track and guide progress in implementing the laws and norms that are now in place spanning federal, state, and local provision of care.

The diagonal, health system–strengthening solutions that are now in place will support breast cancer patients as well as many others in need of palliative care in Mexico. By systematically tracing each health system function, the diagonal framework has been an important tool from which to develop integrated responses to meet the needs of all patients. Civil society—both national and global—working with physician groups, legislators, and the public sector has used the diagonal framework to work jointly and push forward advances. This same framework can serve as a tool for developing the next stages of implementation and accountability to improve access to pain control and palliative care in Mexico.

Conclusion

Health policy makers are continually challenged by trade-offs in making decisions on which diseases to invest in, which population groups to first target with interventions, and the extent of financial protection that can be offered in health coverage. Effective universal health coverage provides a new vision for more comprehensively realizing the right to health care in the context of the rising burden of chronic disease. A diagonal approach presents an opportunity to develop systemic responses for diseases such as breast cancer and to design integrated services for every stage of the chronic disease continuum. The diagonal approach counters a traditional zero-sum perspective where investing in one disease or stage of care has to come at the cost of neglecting another.

Management of chronic illness requires an integrated, diagonal strategy that considers each phase of the care continuum and each health system function. In the case study of Mexico, we illustrated this for palliative care, but a similar strategic analysis is required for each stage of disease, as well as across each health system function. The policy maker is thus challenged to design a set of health system responses as part of a long-term process that includes the patient and the disease or condition as a whole to manage the implications of chronicity.

The diagonal approach counters a traditional zero-sum perspective where investing in one disease comes at the cost of neglecting another.

There are wide-ranging options for progressive realization of effective universal health coverage by tracing population health needs and health system capacities across the care continuum to identify potential synergies for improving health access and services. Opportunities for implementing diagonal strategies should be exploited, and existing platforms should be harnessed to provide comprehensive care to individuals across their life course and across the disease care continuum. In low- and middle-income countries, integrated service delivery and monitoring and evaluation systems that cover a wide range of chronic diseases, including noncommunicable diseases, can be built on existing platforms that are expanded incrementally. For example, platforms for HIV and TB, which have been established through significant investments, can be expanded to cover noncommunicable diseases.[43]

The lack of data, monitoring, and accountability frameworks constitute key limiting factors for implementing an effective universal health coverage approach for the growing challenge of noncommunicable disease and chronic illness. Recent publications on universal health coverage and financial protection point to a data blind spot with regard to noncommunicable diseases.[1] Developing data and indicators that account for benefits across diseases and stages of the care continuum is challenging yet essential for moving universal health coverage forward in all countries. Furthermore, rigorous evaluation of the benefits and costs of the diagonal approach has never been done and should be considered

explicitly in monitoring and accountability endeavors.

There is an immense opportunity and a pressing need to better chart the next generation of health reforms in the face of the growing burden of noncommunicable disease, chronic illness, and disability. Diagonal strategies should be considered and rigorously evaluated as high-potential tools for health system strengthening in the post-2015 development agenda and as a route to exploit the many linkages that exist between health and other social sectors, as well as economic growth and human development. Diagonal frameworks offer the opportunity to implement person-centered, instead of disease-specific, approaches that consider the needs and the potential of individuals throughout their lives and in the myriad ways in which they can contribute to families, communities, economies, and societies. ■

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NOTES

1 World Health Organization, World Bank. Tracking universal health coverage: first global monitoring report. Geneva: WHO; 2015 Jun.
2 World Health Organization. Health financing for universal health coverage. What is universal coverage? [Internet]. Geneva: WHO; [cited 2015 Aug 11]. Available from: http://www.who.int/health_financing/universal_coverage_definition/en/
3 Frenk J, Bobadilla JL, Sepúlveda J, Cervantes ML. Health transition in middle-income countries: new challenges for health care. Health Policy Plan. 1989;4(1):29–39.
4 Knaul FM, Alleyne G, Piot P, Atun R, Gralow JR, Neal C, et al. Health system strengthening and cancer: a diagonal response to the challenge of chronicity. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, editors. Closing the cancer divide: an equity imperative. Cambridge (MA): Harvard Global Equity Initiative; 2012. p. 95–122.
5 World Health Organization. The world health report 2000—health systems: improving performance. Geneva: WHO; 2000.
6 Langer A, Meleis A, Knaul FM, Atun R, Aran M, Arreola-Ornelas H, et al. Women and health: the key for sustainable development. Lancet. 2015 Jun 4. [Epub ahead of print].
7 World Health Organization. The world health report 2010: health systems financing: the path to universal coverage. Geneva: WHO; 2010.
8 World Health Organization. Global status report on noncommunicable diseases 2014. Geneva: WHO; 2014.
9 Alleyne G, Binagwaho A, Haines A, Jahan S, Nugent R, Rojhani A, et al. Embedding non-communicable diseases in the post-2015 development agenda. Lancet. 2013;381(9866):566–74.
10 Frenk J. Leading the way towards universal health coverage: a call to action. Lancet. 2015;385(9975):1352–8.
11 World Health Organization. Innovative care for chronic conditions: building blocks for action. Geneva: WHO; 2002.
12 Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2197–223.
13 Institute of Medicine. From cancer patient to cancer survivor: lost in transition. Washington (DC): IOM; 2005 Nov.
14 Knaul FM, González-Pier E, Gómez-Dantés O, García-Junco D, Arreola-Ornelas H, Barraza-Lloréns M, et al. The quest for universal health coverage: achieving social protection for all in Mexico. Lancet. 2012;380(9849):1259–79.
15 World Health Organization Maximizing Positive Synergies Collaborative Group, Samb B, Evans T, Dybul M, Atun R, Moatti JP, et al. An assessment of interactions between global health initiatives and country health systems. Lancet. 2009;373(9681):2137–69.
16 Frenk J. Bridging the divide: global lessons from evidence-based health policy in Mexico. Lancet. 2006;368(9539):954–61.
17 Sepúlveda J, Bustreo F, Tapia R, Rivera J, Lozano R, Oláiz G, et al. Improvement of child survival in Mexico: the diagonal approach. Lancet. 2006;386(9551):2017–27.
18 International Agency for Research on Cancer. GLOBOCAN 2012: estimated cancer incidence, mortality, and prevalence worldwide in 2012 [Internet]. Lyon (France): IARC; [cited 2015 Aug 17]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
19 Knaul FM, Adami H-O, Adebamowo C, Arreola-Ornelas H, Berger AJ, Bhadelia A, et al. The global cancer divide: an equity imperative. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, editors. Closing the cancer divide: an equity imperative. Cambridge (MA): Harvard Global Equity Initiative; 2012. p. 29–70.
20 Knaul FM, Bhadelia A, Arreola-Ornelas H, Dos-Santos-Silva I, Rodin D, Atun R, et al. Women's reproductive health in transition: the overlapping challenge of breast and cervical cancer. Cancer Control [serial on the Internet]. 2014 Jun [cited 2015 Aug 17]. Available from: http://www.cancercontrol.info/cc2014/knaul/
21 Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): a population-based study. Lancet Oncol. 2012;13(8):790–801.
22 Knaul FM, Bhadelia A, Gralow J, Arreola-Ornelas H, Langer A, Frenk J. Meeting the emerging challenge of breast and cervical cancer in low- and middle-income countries. Int J Gynaecol Obstet. 2012;119(Supp 1):S85–8.
23 Lozano R, Knaul FM, Gómez Dantés H, Arreola-Ornelas H, Méndez O. Tendencias en la mortalidad por cáncer de mama en México, 1979–2006. Observatorio de la Salud. Documento de trabajo. Mexico City: Competitividad y Salud, Fundación Mexicana para la Salud; 2008.
24 Knaul FM, Nigenda G, Lozano R, Arreola-Ornelas H, Langer A, Frenk J. Breast cancer in Mexico: a pressing priority. Reprod Health Matters. 2008;16(32):113–23.
25 Knaul FM, Frenk J. Health insurance in Mexico: achieving universal coverage through structural reform. Health Aff (Millwood). 2005;24(6):1467–76.
26 Knaul FM, Arreola-Ornelas H, Méndez-Carniado O, Bryson-Cahn C, Barofsky J, Maguire R, et al. Evidence is good for your health system: policy reform to remedy catastrophic and impoverishing health spending in Mexico. Lancet. 2006;368(9549):1828–41.
27 Shulman LN, Willett W, Sievers A, Knaul FM. Breast cancer in developing countries: opportunities for

improved survival. J Oncol. 2010;595167. [Epub 2010 Dec 29].
28 Gralow JR, Krakauer E, Anderson BO, Ilbawi A, Porter P, Gospodarowicz M, et al. Core elements for provision of cancer care and control in low and middle income countries. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, editors. Closing the cancer divide: an equity imperative. Cambridge (MA): Harvard Global Equity Initiative; 2012. p. 123–65.
29 Instituto Nacional de Salud Publica. La Encuesta Nacional de Salud y Nutrición 2012. Cuernavaca: INSP; 2012.
30 Knaul FM, Arreola-Ornelas H, Velázquez E, Dorantes J, Méndez O, Ávila-Burgos L. El costo de la atención medica del cáncer mamario: el caso del Instituto Mexicano del Seguro Social. Salud Pública Méx. 2009;51(Suppl 2):s286–95.
31 Chávarri-Guerra Y, Villarreal-Garza C, Liedke PE, Knaul FM, Mohar A, Finkelstein DM, et al. Breast cancer in Mexico: a growing challenge to health and the health system. Lancet Oncol. 2012;13(8):e335–43.
32 Keating NL, Kouri EM, Arreola-Ornelas H, Méndez O, Valladares LM, Knaul FM. Evaluation of breast cancer knowledge among health promoters in Mexico before and after focused training. Oncologist. 2014;19(10):1091–9.
33 International Narcotics Control Board. Report of the International Narcotics Control Board for 2014. New York (NY): United Nations; 2014.
34 Treat the Pain. Interactive map [Internet]. New York (NY): American Cancer Society; [cited 2015 Aug 19]. Available from: http://www.treatthepain.org/StatPlanet.html
35 Knaul FM, Farmer PE, Bhadelia A, Berman P, Horton R. Closing the divide: the Harvard Global Equity Initiative–*Lancet* Commission on Global Access to Pain Control and Palliative Care. Lancet. 2015;pii: S0140–6736(15)60289–6. [Epub ahead of print].
36 Steedman MR, Hughes-Hallett T, Knaul FM, Knuth A, Shamieh O, Darzi A. Innovation can improve and expand aspects of end-of-life care in low- and middle-income countries. Health Aff (Millwood). 2014;33(9):1612–9.
37 Seya MJ, Gelders SF, Achara OU, Milani B, Scholten WK. A first comparison between the consumption of and the need for opioid analgesics at country, regional, and global levels. J Pain Palliat Care Pharmacother. 2011;25(1):6–18.
38 Human Rights Watch. Care when there is no cure: ensuring the right to palliative care in Mexico. New York (NY): Human Rights Watch; 2014 Oct. p. 122.
39 Cossío-Díaz JR, González-Salas JFF, Kershenobich-Stalnikowitz D, Goslinga-Remírez L, Montes de Oca-Arboleya R, Torres-Morán LE, et al. Regulación de los cuidados paliativos y muerte asistida. Gac Méd Méx. 2015;151:119–30.
40 Consejo de Salubridad General. Diario oficial, tercera seccion [Internet]. Mexico City: Secretaria de Gobernación, Government of Mexico; 2014 Dec 26 [cited 2015 Aug 11]. Available from: http://www.csg.gob.mx/descargas/pdfs/2015/Acuerdo_CSG_esquema_cuidados_paliativos.pdf
41 Secretaria de Governacion. Diario oficial de la federacion. Norma Oficial Mexicana NOM-011-SSA3-2014, Criterios para la atención de enfermos en situación terminal a través de cuidados [Internet]. Mexico City: Government of Mexico and Ministry of Health; 2014 Sep 12 [cited 2015 Aug 11]. Available from: http://www.dof.gob.mx/nota_detalle.php?codigo=5375019&fecha=09/12/2014
42 Human Rights Watch. Mexico: breakthrough for pain treatment. Modernized system for prescribing strong medicines [Internet]. New York (NY): Human Rights Watch; 2015 Jun 15 [cited 2015 Aug 11]. Available from: https://www.hrw.org/news/2015/06/15/mexico-breakthrough-pain-treatment
43 Atun R, Jaffar S, Nishtar S, Knaul FM, Barreto ML, Nyirenda M, et al. Improving responsiveness of health systems to non-communicable diseases. Lancet. 2013;381(9867):690–7.