

Building a Platform for Translational Research in Chronic Noncommunicable Diseases to Address Population Health

Lessons From NHLBI Supported CRONICAS in Peru

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ABSTRACT

The CRONICAS Centre of Excellence in Chronic Diseases, based at Universidad Peruana Cayetano Heredia, was created in 2009 with support from the U.S. National Heart, Lung, and Blood Institute (NHLBI). The vision of CRONICAS is to build a globally recognized center of excellence conducting quality and innovative research and generating high-impact evidence for health. The center's identity is embedded in its core values: generosity, innovation, integrity, and quality. This review has been structured to describe the development of the CRONICAS Centre, with a focus on highlighting the ongoing translational research projects and capacity-building strategies. The CRONICAS Centre of Excellence is not a risk-averse organization: it benefits from past experiences, including past mistakes, and improves upon them and thus challenges traditional research approaches. This ethos and environment are key to fostering innovation in research.

Established in 2009 in Lima, Peru, the CRONICAS Centre of Excellence in Chronic Diseases is based at Universidad Peruana Cayetano Heredia and was founded to close the research and capacity-building gap in relation to noncommunicable diseases (NCDs). In Peru, the field of NCDs is still nascent in nearly all of its constituencies, from research to training to policy intervention. The CRONICAS Centre of Excellence serves as a collaborative research platform for NCDs and signals an example of a Peruvian-based, internationally funded, and horizontally led group conducting relevant research in various fronts, as described in this report.

The CRONICAS Centre's mission dictates our "commitment to train young researchers and collaborate with local and international institutions. Our motivation is to improve population health through high quality research." Our vision is that "by 2024 CRONICAS will be a globally recognized Centre of Excellence, conducting quality and innovative research and generating high-impact evidence for health."

The center was established with support from the NHLBI, part of the U.S. National Institutes of Health. Within 5 years of its inception, the center has demonstrated that it is a recognized research-oriented and capacity-building group, both in the Peruvian and international contexts. It operates under its core values of generosity, innovation, integrity and quality and brings together a

multidisciplinary team from diverse backgrounds such as anthropology, communication, economy, medicine, nutrition, psychology, biostatistics, epidemiology, and public health.

The CRONICAS Centre of Excellence was built on the foundations of an established research-driven environment fostered within Universidad Peruana Cayetano Heredia. The consortium with Johns Hopkins University, one of many at Universidad Peruana Cayetano Heredia, provided a leveraging platform to conduct large-scale NCD-related population-based surveys. This collaboration enabled cross-fertilization among public health, clinical medicine, and epidemiology and was able to nurture long-term visions for a highly productive research and training platform. Another initiative that created awareness about the importance of broadening the scope of research in low- and middle-income countries was the Global Health Peru Program [1,2], funded by the Fogarty International Center. These initiatives, paired with solid international collaborations and partnerships, contributed to the creation of a critical mass aware of the major challenges facing global health. This capacity, based in Peru, was able to foster talent under a unique and exquisite academic environment within Universidad Peruana Cayetano Heredia.

Having an established center of excellence within Peru that operates under a "locally based yet globally competitive" approach, without sacrificing quality, signals a clear

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message to future researchers. Peru is developing and expanding its critical mass for conducting research, and in addition to decades of efforts in infectious diseases research and long-standing collaborative consortia, NCDs appear today as an attractive option for the development of younger generations of researchers and highly qualified professionals.

INFORMING GLOBAL HEALTH AND IMPLEMENTATION SCIENCE

Currently, there is no NCD surveillance system in Peru, making accurate monitoring of the 9 global NCD targets impossible [3,4]. At the national level, hypertension prevalence is 21% [4] and that of diabetes 4.5% [5], and NCDs are estimated to account for 66% of total deaths [4]. However, mortality profiles are heterogeneous throughout the country [6]. Peru's diverse geography combined with varying levels of urbanization and access to services accounts for the different stages of the epidemiological transition in different populations [7].

Most cardiovascular diseases and their risk factors have socioeconomic patterns. In this vein, Peru's geographical scenario, with within-country variations in disease burden and disparity in health care delivery, adds complexities to the understanding of NCDs in low- and middle-income countries. These context-specific differences could help explain how cardiovascular diseases appear, coexist, and progress toward long-term complications and deaths. They also introduce additional considerations for NCD research programs in Peru.

This review has been structured to describe the development of the CRONICAS Centre. It highlights ongoing translational research projects the center has undertaken in an effort to achieve its mission. This review is intended not to present project-specific findings but to sensitize readers to eagerly anticipate the results of ongoing projects relevant to the country and the Latin American region. The reason for this is 2-fold. First, most research on NCDs has been conducted in high-income countries, but the need for research in low- and middle-income countries has been recognized [8]. Second, by understanding these research questions and its scope, we will be better positioned to address unanswered questions in the realms of post-clinical translational research and implementation science, much needed to advance global health and health inequities in general.

ONGOING TRANSLATIONAL RESEARCH PROJECTS

Late stage (T3 and T4) translational research is defined as “investigations that seek to establish in real world settings the effectiveness of proven efficacious interventions, including ensuring the appropriate adoption and implementation of such interventions with sustainable investment models.” T4 translational research ensures that evidence-based interventions are broadly applied and accessible to those who need them most, with a strong

emphasis on dissemination and implementation in real world settings [9,10].

In this section, we describe different initiatives directly related to late-stage translational research being conducted by our center, within Peru (Figure 1) and internationally (Figure 2). We initiate characterizing the epidemiological burden that serves as the basis to propose research interventions. We then present multicountry studies working under the same or similar study protocols, followed by specific examples of translational research in different spheres (i.e., interventions with expected impacts at the population level, the community level, and the individual clinical level). Studies focusing on health care organization and delivering evidence-based health care are also reviewed, using them as examples for assessing what works in real-world settings.

Characterizing the epidemiological context

Our center is extremely aware of the need to investigate what works in real-world settings. Peru is a country that hosts desert coastal, Andean mountainous, and rainforest Amazonian ecological niches, adding complexity to human-environment-disease interactions. In keeping with this, our center launched 2 population-based studies to characterize, in more detail, cardiovascular and pulmonary risk factor profiles in different geographical regions (Table 1). This was conducted initially in rural and urban populations with a particular emphasis on the effects of migration (PERU MIGRANT Study) (Table 2), and then in low- and high-altitude settings to further advance our understanding of rates of progression to disease in different environments (CRONICAS Cohort Study) (Table 3).

Multicountry studies

Through the UnitedHealth Group/NHLBI Centers of Excellence Network [27,28], our group has actively participated in designing and conducting pragmatic clinical trials with a direct focus on prevention and implementation. Together with teams from Argentina, Guatemala, and the United States, we explored the use of mobile technology (mHealth) to prevent the progression of pre-hypertension in urban settings, capitalizing on the commonalities of the Spanish language across countries and the potential of mHealth to deploy elements of preventative health (ClinicalTrials.gov identifier NCT01295216). Similarly, together with teams from Kenya, Nepal, and the United States, we worked on a feasibility intervention trial of 2 types of improved cookstoves (ClinicalTrials.gov identifier NCT01686867) to ascertain practical approaches to increasing its uptake and usage [29].

Recognizing the large burden of hypertension and stroke, the family-oriented provision of care, and the low-resource and geographically isolated health system infrastructures [30], we are collaborating with China to address the impact of stroke on patients and their caregivers. This interest has expanded to taking advantage of Peru's

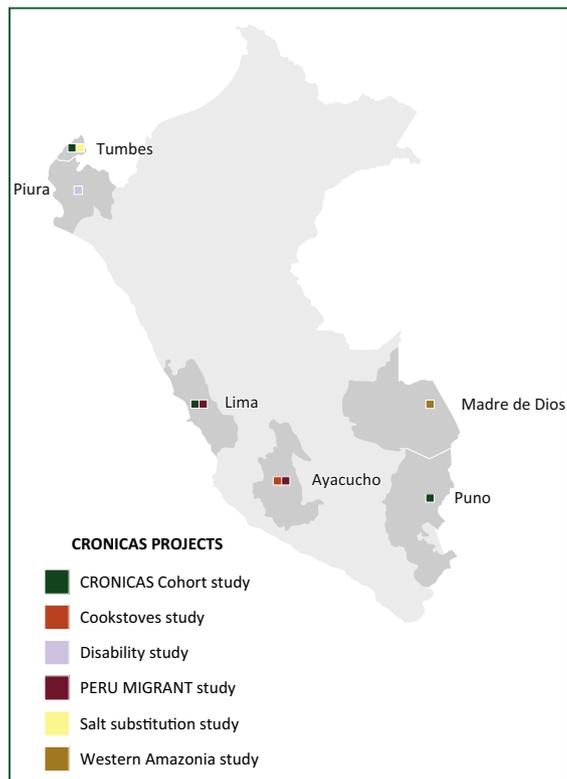


FIGURE 1. Study sites of ongoing projects in Peru.

national disability survey to explore the epidemiological profiles of disability in Peru. We found that approximately 1.6 million Peruvians have at least 1 disability, 40% require assistance in daily living activities, and informal caregiving is very common. In addition, together with colleagues from Tanzania and United Kingdom, including disability advocacy groups, we are working closely to understand the extent to which persons with disabilities are included in social protection systems.

Finally, together with colleagues from Brazil, the United Kingdom and the United States, we are investigating the

association between chronic diseases and mental health, with an emphasis on depression. This is being conducted as part of the Latin America Treatment & Innovation Network in Mental Health, which is part of a wider international network of collaborators that supports regional hubs for research, capacity building, and knowledge sharing.

Population level

Our experience with coordinating and completing large population-based epidemiological studies enabled us to move rapidly into other research design ventures, such as stepped-wedge trials. Our group leads one of the projects in the hypertension program of the Global Alliance for Chronic Diseases [31]. This project focuses on using social marketing strategies to promote and implement a low-sodium, high-potassium salt substitute campaign aimed at achieving population-wide reductions in blood pressure at the community level (ClinicalTrials.gov identifier NCT01960972) [32].

Community level

The center has engaged in several community-level undertakings. For instance, we created links with youth groups through a communication program, the *multiplicadores jóvenes* (young multipliers) [33]. In this program, high school students were given the opportunity to learn basic concepts of communication and access media resources, including video, photography, and radio. They then developed their own messages for health campaigns. Interestingly, they created a much different approach to health promotion, in visual terms, than expected (<http://pic.twitter.com/HCikSzmBwy>), highlighting the importance of including this community in the development of interventions.

In another community-level project, we introduced marketing techniques into poor urban settlements by capitalizing on community kitchens to deliver healthy diets to low-income families in Peru [34]. In slum settings, where a meal is sold for PEN 1.5 soles (USD \$0.52, GBP £0.32), we introduced sales of complementary salads and

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FIGURE 2. Global map of network collaborations.

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TABLE 1. Research study sites, CRONICAS Cohort Study

Setting	Degree of Urbanization	Use of Biomass Fuels	Outdoor Air Pollution	Altitude
Lima	Highly urbanized	Rare	High	Sea level
Tumbes	Semiurban	Highly prevalent	Low	Sea level
Puno, urban	Urban	Rare	Low	3,825 m above sea level
Puno, rural	Rural	Highly prevalent	Low	3,825 m above sea level

Source: CRONICAS Cohort Study protocol [11].

fresh fruit. By challenging assumptions that poor people are not willing or not interested in eating healthy foods, this project's aim to address whether accessibility to fresh products in poor communities can be improved and under what circumstances. Price, food preparation time, amenability to storage, product availability, and quality control arose as important factors. Since the completion of the pilot phase of this work, a total of 8 community kitchens have continued to prepare and offer salads and fruit options as part of their menus.

Individual clinical level: shared-decision making

In collaboration with the Mayo Clinic's Knowledge and Evaluation Unit and Conocimiento y Evidencia, a group of young investigators focused on the implementation of evidence-based practice at Universidad Peruana Cayetano Heredia, CRONICAS pioneered a study of patient-centered care for patients with chronic conditions in Peru.

This team first studied the context in which clinicians and patients interact and the likelihood that clinicians would invite patients to take part in decision making [35]. We also sought to understand the context of consultations in the public and private sector and the extent to which noise, lack of privacy, interruptions by health care personnel, and interruptions through the clinicians' phones impaired the ability of patients and clinicians to engage [36].

More recently, this collaborative partnership has begun to explore the notion of minimally disruptive medicine in Peru [37], which refers to the attainment of patient goals

while maintaining the smallest possible health care footprint. This notion has important implications for health care delivery, which includes determining the patient's available capacity that can be mobilized to access, use, and enact care, as well as the work load necessary to achieve patient outcomes. The patient's capacity results from the physical and mental health, financial health, social capital, literacy, and resilience, among other factors, and permits connections to be made among social determinants of health and clinical medicine. This concept of imposing the smallest possible health care footprint could revolutionize the patient-centered care of individuals with chronic conditions.

Health care organization

Our group, together with collaborators based in Switzerland, was asked to conduct a pilot study of a tool developed by the World Health Organization to identify barriers in accessing NCD care and medicines [38]. This tool approaches the health system for the conditions of interest at 3 different levels: 1) the macro-level, which includes policies, funding allocation, and pricing and distribution of medicines, related to the conditions of interest; 2) the meso-level, which is the organization of the health care system, including referral paths; and 3) the micro-level, which is at the point of care, including patients and human resources [39,40]. The work in Peru was focused on diabetes and hypertension, and builds on the rapid assessment protocol developed for insulin access [41].

TABLE 2. PERU MIGRANT Study

Urbanization, in historical terms, is a fairly recent phenomenon: in 1975, only 27% of people in low- and middle-income countries lived in urban areas, but by 2000, the proportion was 40%. Projections suggest that by 2030, low- and middle-income countries will be 56% urban [12]. Rapid urbanization, including rural-to-urban within-country migration, will certainly have a significant impact on the profile of risk factors for NCDs, patterns of risk exposures, and potential outcomes [13].

The cardiovascular, metabolic, and inflammatory risk factor profiles of rural, urban, and rural-urban Andean immigrants were explored to demonstrate that uniform risk profiles are not the norm and are influenced by the age at which migration occurs [14]. This study, funded by the Wellcome Trust, also demonstrated that using glycosylated hemoglobin for the diagnosis of diabetes, per recent recommendations, would triple its prevalence compared with fasting glucose [15], possibly explained by discrepancies between hemoglobin-glucose in low- versus high-altitude settings. Data generated by this study have demonstrated important health burdens among immigrant population and socioeconomically deprived groups in terms of mental health and social capital [16], physical activity [17], and acculturation [18], as well as awareness, treatment, and control gaps in hypertension and diabetes [19]. Among broader impacts of these findings, the PERU MIGRANT study is among the very few studies that have contributed Andean population data in the analyses of global trends [20,21], avoiding the task of data imputation on the region. At the local level, it highlights challenging scenarios for local within-country health prioritization in terms of NCDs [22].

TABLE 3. CRONICAS Cohort Study

Understanding the effects of rapid urbanization is one of the grand challenges concerning chronic NCDs [23]. Peru offers a unique opportunity to assess the impact of geographical variation on NCDs, hence the rationale for the CRONICAS Cohort Study [11]. Importantly, the comprehensive data generated by this cohort across a diversity of scenarios will, in turn, provide important advances for public health and for the field of NCDs in low- and middle-income countries.

The CRONICAS Cohort Study has 2 main aims. First, the effects of variation in geographical settings on both cardiovascular and chronic pulmonary disease are evaluated using a longitudinal design. Second, being aware of the reliance on biomass fuels, a feature that distinguishes low- from high-income countries, we are also looking into the longitudinal evaluation of lung function across different settings [24]. Exposure to by-products of biomass fuel combustion is considered the most important risk factor for chronic obstructive pulmonary disease after cigarette smoking [25].

The CRONICAS Cohort Study, a joint effort between Universidad Peruana Cayetano Heredia and Johns Hopkins University, is funded by the NHLBI and has been implemented at different population sites with varying degrees of urbanization, air pollution, and altitude features (Table 1). The choice of these populations provides the opportunity to study the potential effects of geographical location and other risk factors unique to low- and middle-income countries. For example, our group has characterized differences in household environmental exposures between urban and rural settings [24] and reported a link between chronic exposure to biomass fuel and increased carotid artery intima-media thickness [26].

Mental health has also been part of our explorations of what works in real-world settings. Working within the health system and advocating for the incorporation of mental health services into the routine practice of primary health care is a big step toward integrated care [42]. This route addresses the existing gap in mental health treatment caused by insufficient specialized human resources [43] and the high prevalence of comorbid mental health conditions with both infectious and chronic NCDs [44,45]. Allillanchu (meaning “Hello, how are you” in Quechua language), a currently ongoing project at CRONICAS, aims to integrate mental health screening practices into primary health care services, specifically for people at increased risk for depression, such as pregnant women and patients with tuberculosis, diabetes, human immunodeficiency virus infection or acquired immune deficiency syndrome, and hypertension. By combining the training of non-specialized health providers with the use of mHealth technology, specifically a screening application and a text message delivery system to remind and motivate patients to seek mental health care, we expect to achieve early detection, opportune referral, and access to treatment for patients with depression [46].

Delivering evidence-based health care

Evidence-based clinical practice and translation of findings from clinical trials into everyday practice [47] is a pending agenda in Peru. Hypertension and stroke are 2 important areas in which therapeutic interventions have already demonstrated efficacy, but the major unresolved challenge rests on the adoption and implementation of those strategies. In the case of hypertension, only 50% of patients are aware of their conditions, and of those who are aware, only 40% adhere to treatment [48]. Stroke is a common complication of hypertension, and its presence marks a significant patient burden [49]. This is compounded by ongoing human resource deficiencies and the absence of stroke care units to provide comprehensive

care and rehabilitation services. Recognizing the need to implement practical solutions, our group is working toward a school for the caregivers of patients with stroke focusing on rehabilitation therapy, control of cardiovascular risk factors, recognition of the signs of stroke, and adherence to medications. This initiative is complemented by our participation in a multicountry study in the Latin American region aimed at achieving adherence to evidence-based stroke management strategies [50] within the first 48 h of the onset of stroke and at discharge from the hospital.

CAPACITY BUILDING AND AVOIDING A SILO MENTALITY

Capacity building is a key aspect of our center’s development. This is achieved through a number of initiatives, including supported fellowships, hands-on engagement of students through the different aspects of research, and the attraction of PhD graduates.

Also, our group believes in the advantages of linking diverse areas of expertise as a means to move forward in conducting research. Hence, it is vital that every single team member from the CRONICAS Centre, from junior to senior levels, step out of their silos and work together to maximize the returns of innovative research. For example, some of these interdisciplinary interactions include linking infectious disease and child health with NCDs, hypoxia and human adaptation to high altitude and its effects on chronic diseases, individual-environment ecosystems, and human vulnerability related to climate change.

SUMMARY

All the initiatives and ongoing projects described are or have been possible thanks to the confluence of common interest from international funding agencies (see the disclosure statement for a list of all funding sources), local institutions, and international collaborators in high-income

countries. This confluence, primarily concentrated around capacity building, has generated, supported, and promoted a unique environment in which research can flourish. The research conducted at the CRONICAS Centre of Excellence is highly collaborative and interdisciplinary. This provides a foundation to address and engage in translational research—research with strong emphasis on dissemination and implementation in real world settings—by combining mixed methods, sound study designs, and both qualitative and quantitative research questions.

The core research group is funded entirely through research grants, so grant writing consumes a sizable portion of our efforts, and it is key to anticipate future periods of uncertainty. A part of our strategy for growth and sustainability relies on expanding the components of our research portfolio exemplified by the flagship projects described in this report. However, this is particularly challenging because as new research focuses and approaches arise, we are placed in a constant search for balance and equilibrium among the quest for growth, risk aversion, and the possibility of spreading ourselves too thin. Regardless, overall the center is not a risk-averse organization: it benefits from past experiences, including past mistakes, improves on them, and challenges traditional research approaches. This ethos and environment are key to fostering innovation in research. In so doing, the center contributes to the advancement of global health and reduction of health disparities, by actively bringing the unique perspective of professionals based in low- and middle-income settings.

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REFERENCES

- Garcia P, Armstrong R, Zaman MH. Models of education in medicine, public health, and engineering. *Science* 2014;345:1281–3.
- Villafuerte-Galvez J, Curioso WH. Teaching global health at the frontlines. A multidisciplinary course in Peru presents basic concepts to students. *PLoS Med* 2007;4:e130.
- World Health Organization. Noncommunicable Diseases Country Profile 2011—WHO Global Report. Geneva, Switzerland: World Health Organization; 2011.
- World Health Organization. Noncommunicable Diseases Country Profiles 2014. Geneva, Switzerland: World Health Organization; 2014.
- International Diabetes Federation. IDF Diabetes Atlas. 6th ed. Brussels, Belgium: International Diabetes Federation; 2013.
- PAHO-Peru. Health in Americas—2007 Edition. Washington, DC: PAHO; 2007.
- Goldstein J, Jacoby E, del Aguila R, et al. Poverty is a predictor of non-communicable disease among adults in Peruvian cities. *Prev Med* 2005;41:800–6.
- Ebrahim S, Pearce N, Smeeth L, et al. Tackling non-communicable diseases in low- and middle-income countries: is the evidence from high-income countries all we need? *PLoS Med* 2013;10:e1001377.
- National Institutes of Health. Biennial Report of Director, National Institutes of Health, Fiscal Years 2010 & 2011. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services 2012. Available at: http://report.nih.gov/biennialreport/chapter2/NIH_Postclinical_Translational_Research.html. Accessed August 15, 2014.
- Caravedo MA, Painschab MS, Davila-Roman VG, et al. Lack of association between chronic exposure to biomass fuel smoke and markers of right ventricular pressure overload at high altitude. *Am Heart J* 2014;168:731–8.
- Miranda JJ, Bernabe-Ortiz A, Smeeth L, et al. Addressing geographical variation in the progression of non-communicable diseases in Peru: the CRONICAS Cohort Study protocol. *BMJ Open* 2012;2:e000610.
- United Nations Centre for Human Settlements. Cities in a Globalizing World: Global Report on Human Settlements 2001. London: Earthscan Publications; 2001.
- Batty GD, Victora CG, Lawlor DA. Establishing family-based life course studies in low- and middle-income countries. In: Lawlor DA, Mishra GD, editors. *Family Matters: Designing, Analysing and Understanding Family Based Studies in Life Course Epidemiology*. Oxford, United Kingdom: Oxford University Press; 2009. p. 129–50.
- Miranda JJ, Gilman RH, Smeeth L. Differences in cardiovascular risk factors in rural, urban and rural-to-urban migrants in Peru. *Heart* 2011;97:787–96.
- Miranda JJ, Bernabe-Ortiz A, Stanojevic S, et al. A1C as a diagnostic criteria for diabetes in low- and middle-income settings: evidence from Peru. *PLoS ONE* 2011;6:e18069.
- Loret de Mola C, Stanojevic S, Ruiz P, et al. The effect of rural-to-urban migration on social capital and common mental disorders: PERU MIGRANT study. *Soc Psychiatry Psychiatr Epidemiol* 2012;47:967–73.
- Masterson Creber RM, Smeeth L, Gilman RH, et al. Physical activity and cardiovascular risk factors among rural and urban groups and rural-to-urban migrants in Peru: a cross-sectional study. *Rev Panam Salud Publica* 2010;28:1–8.
- Bernabe-Ortiz A, Gilman RH, Smeeth L, et al. Migration surrogates and their association with obesity among within-country migrants. *Obesity (Silver Spring)* 2010;18:2199–203.
- Lerner AG, Bernabe-Ortiz A, Gilman RH, et al. The “rule of halves” does not apply in Peru: awareness, treatment, and control of hypertension and diabetes in rural, urban, and rural-to-urban migrants. *Crit Pathways Cardiol* 2013;12:53–8.
- Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011; 377:568–77.

21. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet* 2011;378:31–40.
22. Miranda JJ, Wells JC, Smeeth L. [Transitions in context: findings related to rural-to-urban migration and chronic non-communicable diseases in Peru]. *Rev Per Med Exp Salud Publica* 2012;29:366–72.
23. Daar AS, Singer PA, Persad DL, et al. Grand challenges in chronic non-communicable diseases. *Nature* 2007;450:494–6.
24. Pollard SL, Williams DL, Breyse PN, et al. A cross-sectional study of determinants of indoor environmental exposures in households with and without chronic exposure to biomass fuel smoke. *Environ Health* 2014;13:21.
25. Torres-Duque C, Maldonado D, Perez-Padilla R, et al. Biomass fuels and respiratory diseases: a review of the evidence. *Proc Am Thorac Soc* 2008;5:577–90.
26. Painschab MS, Davila-Roman VG, Gilman RH, et al. Chronic exposure to biomass fuel is associated with increased carotid artery intima-media thickness and a higher prevalence of atherosclerotic plaque. *Heart* 2013;99:984–91.
27. Nabel EG, Stevens S, Smith R. Combating chronic disease in developing countries. *Lancet* 2009;373:2004–6.
28. UnitedHealth Group/National Heart, Lung, and Blood Institute Centres of Excellence. A global research network for non-communicable diseases. *Lancet* 2014;383:1446–7.
29. Klasen E, Miranda J, Khatry S, et al. Feasibility intervention trial of two types of improved cookstoves in three resource-limited settings: study protocol for a randomized controlled trial. *Trials* 2013; 14:327.
30. Valle GA, Poterico JA, Quispe R. [Informal caregivers of patients with cerebrovascular diseases]. *Rev Peru Med Exp Salud Publica* 2014;31: 169–80.
31. Project 11: Launching a Salt Substitute to Reduce Blood Pressure at the Population Level. London: Global Alliance for Chronic Diseases 2012. Available at: <http://www.gacd.org/projects/current-projects/hypertension/project-pages/project11>. Accessed August 15, 2014.
32. Bernabe-Ortiz A, Diez-Canseco F, Gilman RH, et al. Launching a salt substitute to reduce blood pressure at the population level: a cluster randomized stepped wedge trial in Peru. *Trials* 2014; 15:93.
33. Farchi S, Molino N, Giorgi Rossi P, et al. Defining a common set of indicators to monitor road accidents in the European Union. *BMC Public Health* 2006;6:183.
34. International Development Research Center. Delivering Healthy Diets to Low-Income Families Through Community Kitchens in Peru 2014. Available at: http://www.idrc.ca/EN/Themes/Science_Policy/Pages/ProjectDetails.aspx?ProjectNumber=106887. Accessed July 31, 2014.
35. Zevallos-Palacios C, Quispe R, Mongilardi N, et al. [Patients' participation in clinical decision making as a strategy to protect their rights]. *Rev Peru Med Exp Salud Publica* 2013;30:363–4.
36. Mongilardi N, Montori V, Riveros A, et al. Clinicians' involvement of patients in decision making. A video based comparison of their behavior in public vs. private practice. *PLoS One* 2013;8:e58085.
37. Zeballos-Palacios C, Morey-Vargas OL, Brito JP, et al. [Shared decision making and minimal disruptive medicine in the management of chronic diseases]. *Rev Peru Med Exp Salud Publica* 2014;31:111–7.
38. Beran D, Higuchi M. How to Investigate Access to Care for Chronic Noncommunicable Diseases in Low- and Middle-Income Countries. A Survey Manual Based on a Rapid Assessment Protocol. Draft for field testing, May 2012. London: International Insulin Foundation; 2012.
39. Beran D, Yudkin JS, de Courten M. Access to care for patients with insulin-requiring diabetes in developing countries: case studies of Mozambique and Zambia. *Diabetes Care* 2005;28:2136–40.
40. Beran D, Yudkin JS, de Courten M. Assessing health systems for type 1 diabetes in sub-Saharan Africa: developing a "Rapid Assessment Protocol for Insulin Access." *BMC Health Serv Res* 2006;6:17.
41. Beran D, Silva Matos C, Yudkin JS. The Diabetes UK Mozambique Twinning Programme. Results of improvements in diabetes care in Mozambique: a reassessment 6 years later using the Rapid Assessment Protocol for Insulin Access. *Diabet Med* 2010;27:855–61.
42. Diez-Canseco F, Ipince A, Toyama M, et al. [Integration of mental health and chronic non-communicable diseases in Peru: challenges and opportunities for primary care settings]. *Rev Peru Med Exp Salud Publica* 2014;31:131–6.
43. World Health Organization. Integrating Mental Health Into Primary Care. A Global Perspective. Geneva, Switzerland: World Health Organization; 2008.
44. Gilbody S, Whitty P, Grimshaw J, et al. Educational and organizational interventions to improve the management of depression in primary care: a systematic review. *JAMA* 2003;289:3145–51.
45. Thota AB, Sipe TA, Byard GJ, et al. Collaborative care to improve the management of depressive disorders: a community guide systematic review and meta-analysis. *Am J Prev Med* 2012;42:525–38.
46. Diez-Canseco F, Araya R, Ipince A, et al. Allillanchu: Integration of Mental Health into Quotidian Routine Practices of Primary Health Care Service 2014. Available at: http://figshare.com/articles/Allillanchu_Integration_of_Mental_Health_into_Quotidian_Routine_Practices_of_Primary_Health_Care_Services/1128652. Accessed August 15, 2014.
47. Woolf SH. The meaning of translational research and why it matters. *JAMA* 2008;299:211–3.
48. Carhuallanqui R, Diestra-Cabrera G, Tang-Herrera J, et al. Adherencia al tratamiento farmacológico en pacientes hipertensos atendidos en un hospital general. *Rev Med Hered* 2010;21:197–201.
49. Ferri CP, Schoenborn C, Kalra L, et al. Prevalence of stroke and related burden among older people living in Latin America, India and China. *J Neurol Neurosurg Psychiatry* 2011;82:1074–82.
50. Fonarow GC, Reeves MJ, Smith EE, et al. Characteristics, performance measures, and in-hospital outcomes of the first one million stroke and transient ischemic attack admissions in get with the guidelines-stroke. *Circ Cardiovasc Qual Outcomes* 2010;3:291–302.