DEVELOPING NATIONAL CAREX PROJECTS IN LATIN AMERICA & THE CARIBBEAN

Technical Guide (Annex) to the Workshop Proceedings:
Building Capacity For CAREX Projects In Latin America And The Caribbean
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Por el control del cáncer

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ACRONYMS AND ABBREVIATIONS USED

CAREX	CARcinogen EXposure
CWED	Canadian Workplace Exposure Database
EU	European Union
FINJEM	Finnish Job Exposure Matrix
FIOH	Finnish Institute of Occupational Health
IARC	International Agency for Research on Cancer
ILO	International Labour Organization
ISIC	International Standard Industrial Classification of All Economic Activities
KTE	Knowledge Translation and Exchange
LAC	Latin America and the Caribbean
NCD	Non-Communicable Diseases
PAHO	Pan American Health Organization
Pr(E)	Proportion Exposed
UN	United Nations
WHO	World Health Organization

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This work is dedicated in fond memory to the late Dr. Timo Partanen.

He provided scientific leadership on the adaptation of the CAREX model in Costa Rica, representing the first time that the CAREX approach was used outside of Europe. His visionary goal – that the CAREX methodology be more widely adapted so as to produce occupational carcinogen exposure estimates for the region of the Americas, and in particular for Latin America and the Caribbean – was inspirational in bringing this project to fruition.

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INTRODUCTION

Non-communicable diseases (NCDs) are the leading cause of morbidity and mortality in the Americas. These illnesses are responsible for substantial health and economic burdens; in the year 2012, non-communicable diseases accounted for approximately 73% of disability-adjusted life-years from all causes (1). Between 2006 and 2015 in Brazil alone, the cost of treatment and lost productivity due to five chronic diseases was an estimated $72 billion (2). Of the chronic health conditions that are prevalent in the Americas, cancer is among the leading causes of morbidity and mortality. Workplace exposures to known carcinogens are a cause of cancer, among other known and potential risk factors.

The 2004 Global Burden of Disease Study, conducted by the World Health Organization (WHO), found that occupational injury and disease contributed to approximately 15% of the total burden of disease (3). The subsequent 2010 Global Burden of Disease Study analyzed a cluster of carcinogens and demonstrated the proportion of premature deaths due to occupational hazards, loss of years of healthy life, and disability due to occupational diseases. This analysis highlighted the effects of asbestos, silica, environmental tobacco smoke, and diesel fumes (4). The WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020 (5) and the Global Monitoring Framework for NCDs established 9 targets and 25 indicators aiming to attain a 25% reduction in premature mortality from NCDs by 2025 (6).

Since 2008, the Pan American Health Organization (PAHO) has been raising awareness of occupational cancer and encouraging the prevention of occupational cancer as part of national cancer and workers' health policies in Latin America and the Caribbean (LAC). Occupational exposures to carcinogens are preventable, and PAHO has encouraged the identification of these substances and exposed working populations by promoting the development of job exposure matrices for occupational carcinogens. This approach can generate urgently needed knowledge of population-level exposure to carcinogens in workplaces. Policymakers in LAC will find this information useful for the prevention of occupational cancer and identifying high-risk populations, while researchers will be able to draw upon this data for monitoring exposures over time, studying the causes of occupational cancer, and calculating more refined estimates of the burden of occupational cancer in LAC and globally. For these reasons, PAHO has adopted the International Information System on Occupational CARcinogen EXposures (CAREX) methodology – created in collaboration with the International Agency for Research on Cancer (IARC) (7) – with the vision of a regional CAREX for LAC.

OBJECTIVE

The aim of this technical guide is to provide step-by-step instructions for establishing a national CAREX project. The definition and basic principles of CAREX are described for context, while examples and summarized results from existing CAREX projects, primarily in LAC and Canada, demonstrate how the methodology can be adapted to different settings. Researchers, occupational hygienists, and exposure assessment specialists will find this guide particularly useful, though it may be used by other groups as well. This guide (and the resources cited throughout) is designed to be practical and, once implemented, to lead to a national CAREX project that is tailored to the labour force of the country.

ORIGINS AND BASIC PRINCIPLES OF CAREX

Little is known about the prevalence and impact of work-related exposures on cancer development in LAC even though approximately one third of adult life is spent at work, not including commuting time and work outside of official work hours (8). What are the different cancer-causing agents that workers in this region encounter on the job? How many men and women are exposed to these agents, and where do they work? The answers to these and other related questions are essential for identifying high-risk occupations and industries and taking action to prevent the occupational causes of cancer. The CAREX model offers answers and a way forward.

CAREX is a framework for carcinogen exposure surveillance in a population. Its original design was conceived in the early 1990s by scientists at the Finnish Institute of Occupational Health (FIOH), who created the Finnish job-exposure matrix (FINJEM). The manifold objectives of this exercise were:

1. For occupational epidemiology: to create an instrument for exposure assessment of very large epidemiologic studies using general population-based registers;
2. For hazard control: to collect and computerize the relevant exposure data in Finland for general exposure assessment purposes;
3. For risk assessment: to provide the exposure component for the quantitative risk assessment at a national level; and,
4. For hazard surveillance: to summarize and chart the state and long-term development of the exposure panorama in Finland (9).

At the request of the European Union (EU), the project was further developed by an international group of experts from 15 countries that made up the EU as part of the “Europe Against Cancer” program. This group used the CAREX approach to estimate the proportion of workers occupationally exposed to 139 established and suspected carcinogens that had been evaluated by IARC as of 1990 to 1993. National labour force data, which covered 55 industries using an international classification scheme, were combined with measured and descriptive exposure data. The resulting estimates showed that overall, about 32 million workers (23% of those employed) in the EU were exposed to occupational carcinogens, with an average of 1.3 exposures per exposed worker (7). The database has been specifically amended for wood dust (WOODEX) with exposure level estimates for 25 EU member states (10). Although some shortcomings were noted by the authors – such as discord when adjusting default exposure estimates to the national context in several countries – the systematic nature, wide coverage, and ease of use of the CAREX model proved to be a valuable endeavor for producing initial exposure estimates with opportunities for further refinement.

The CAREX system has since been applied by several countries outside of the EU, each with its own variation of the basic exposure estimation model. Nowadays CAREX is understood as a valuable resource with many applications in research and cancer prevention.

METHODS FOR ESTABLISHING A CAREX PROJECT

This technical guide describes 3 steps:

1. Establish priority occupational carcinogens
2. Identify the working population
3. Determine prevalence of exposure values

For each step, the general approach is described along with specific examples of how the methods have been used and modified in countries with CAREX projects. Some additional considerations are also described in order to encourage thinking around specific issues in LAC countries.

1 ESTABLISH PRIORITY OCCUPATIONAL CARCINOGENS

GENERAL APPROACH

The goal of a national CAREX project is to generate estimates of the number of workers exposed to known and suspected carcinogens. The first step is to identify priority carcinogens for your country. In general, carcinogens included in a CAREX project are selected based on:

• The strength of evidence of causing cancer in humans; and,

• The potential for exposure in the population of interest.

Feasibility is also an important factor, especially for substances not considered previously.

IARC routinely evaluates agents that are believed to cause cancer based on a combination of human, animal, and mechanistic studies. Evidence from all three types of studies are carefully weighed by teams of international scientists who voluntarily serve on IARC Working Groups to determine if agents are known (Group 1), probable (Group 2A), possible (2B), not classifiable (Group 3), or not probable (Group 4) carcinogens. These agents include occupational exposures. Therefore, IARC evaluations are a useful starting point for obtaining a list of known, probable, and possible occupational carcinogens by cancer site. Greater emphasis can be put on known and probable carcinogens since there is stronger and more consistent evidence compared to possible carcinogens. Agents assessed by IARC as not classifiable or not

probable carcinogens can be excluded from CAREX projects since these data are weak[1].

The selection of priority carcinogens can inform several aspects of occupational cancer research, surveillance, and prevention (11). These aspects should be considered early on in a project:

- Further research, e.g. for burden of occupational cancer studies; exposure assessment for occupational cancer epidemiologic and surveillance studies; identifying research priorities; risk assessment; etc.
- The identification of high-risk groups
- Priority setting for prevention-related activities (12)
- Surveillance of exposure trends over time
- Assessments of the impact of changing regulations

The two other parts of the general CAREX methodology – identifying the working population and determining prevalence of exposure values — are also directly related to research, surveillance, and prevention. For instance, knowledge of the working population can help to bring the focus on potentially highly exposed industries and occupations. The third component of CAREX, estimating the prevalence of exposure, is a particularly useful part of exposure assessment in burden studies.

1 If there are particular reasons for including a substance that IARC has not classified as a known or potential carcinogen (e.g. a substance of concern for other reasons such as respiratory or skin disease, or an exposure of unique concern for your country), then the principles described in this appendix also apply. The CAREX methods will still work well for these substances.

PRIORITY OCCUPATIONAL CARCINOGENS DIFFER ACROSS LAC

Occupational exposures vary between regions and countries based on their economic/industrial composition, workforce participation rates, public health policy interests, and other factors. For instance, regions with mining as a major industry might entail occupational exposure to crystalline silica, asbestos, radon, diesel engine exhaust, and other mining-related exposures. Countries with substantial agricultural activity may be concerned about workers' exposure to pesticides, solar ultraviolet radiation, diesel engine exhaust, and arsenic. Even so, pesticide exposures can differ between countries due to heterogeneous legislation, crop types, and pest management approaches. For example, pentachlorophenol was not included in the CAREX project in Costa Rica, since this substance has been banned in Costa Rica (13), but it was included in CAREX Canada since it continues to be used as a wood preservative (14). Persistent organic pollutants, including dioxin (2,3,7,8-tetrachlorodibenzo-para-dioxin) and the pesticide DDT, might also be banned in some countries and not in others. Sometimes, countries with similar industrial and workforce compositions can adapt priorities from one another. It may be helpful to prioritize carcinogens by industry, e.g. exposures to wood dust, solar radiation, diesel engine exhaust, etc. in the construction sector.

Newly recognized carcinogens are determined on a regular basis and should be considered when establishing priority carcinogens for a CAREX project. Shiftwork involving circadian disruption, for example, was not evaluated by IARC at the time of the EU and Central American CAREX projects. However, in 2007, IARC classified this exposure as a probable (Group 2A) carcinogen for breast cancer. The Canadian CAREX project subsequently included shiftwork given this evidence of carcinogenicity and the large proportion of night and rotating shift workers in Canada. Thinking carefully about what known and potential cancer-causing agents make sense to include in a specific country is an important and preliminary task for researchers. The most recent list of IARC occupational carcinogens (monographs.iarc.fr/ENG/Classification/index.php) should be consulted to select relevant carcinogenic exposures for the national working population.

IDENTIFYING PRIORITY OCCUPATIONAL CARCINOGENS WHEN THERE ARE DATA GAPS

There are sparse data about workplace hazards in Central America (15) and in other parts of LAC, but researchers are encouraged to think about how to address these data gaps for both long-standing occupational carcinogen exposures and recently recognized carcinogens. One example of the latter is ambient air pollution, which was classified by IARC as a known (Group 1) human carcinogen (16). Outdoor air pollution exposure (in general and among outdoor workers) in low- and middle-income countries is reportedly higher than standards by the WHO, Europe, and the United States. However, there are few studies with good quality exposure data and even fewer that are focused on workers' exposure (17). This is not necessarily a limitation. Outdoor air pollution can still be considered for inclusion in CAREX projects in LAC by making use of other sources of exposure data, such as international networks of pollution monitors, measurements taken as part of epidemiological studies, and imputation capabilities with land-use regression models. Other sources of data may readily exist in LAC. This example shows that estimates of the number of workers exposed can be developed even in the absence of traditional exposure measurement data for workers.

ENGAGING FIELD EXPERTS

Because of the vast gap in exposure measurements in LAC, researchers working on CAREX projects are encouraged to involve field experts as much as possible. Field experts are persons knowledgeable from the industry or the economic sector under study, capable of identifying sources of exposure, and providing input on the potential for exposure to occupational carcinogens in the country. They can include worker and employer representatives, occupational or industrial hygienists, scientists, government officials, and others. In the early stages of the project, field experts have been very useful. They may even be able to identify exposure data sources and data-rich substances (e.g. crystalline silica in Brazil). Input from field experts has played an important role in CAREX projects in the EU, Canada, Central America, Colombia, and Peru. Representatives from different countries with similar industrial compositions may also collaborate to compare and share their lists of priority occupational carcinogens.

EXAMPLES

Different countries have taken variations of this general approach to selecting priority carcinogens. For CAREX Canada, the process was data-driven and involved expert assessment. All occupational agents evaluated by IARC as known, probable, and possible human carcinogens were selected as the initial agents of interest. These agents were further assessed for inclusion based on 3 criteria: a. likely to be present in Canadian workplaces in the year 2006, with an estimated minimum of 10,000 workers exposed; b. evidence of toxic effects, including carcinogenicity (IARC known [Group 1] carcinogens were given higher priority than probable [Group 2A] and possible [Group 2B] carcinogens); and c. feasibility of assessing exposure based on available data. Exposures to individual agents that were likely to occur together were grouped; this was the case for polycyclic aromatic hydrocarbons and antineoplastic agents. In the end, the CAREX Canada project included 44 known and suspected occupational carcinogens (11). The Canadian Workplace Exposure Database (CWED), a repository of occupational exposure measurement data from across Canada, was also used to identify the potential for exposure in specific industries and occupations, and was subsequently used to estimate levels of exposure for data-rich agents (11).

In Costa Rica, Nicaragua, and Panama, the list of included agents in the European CAREX was consulted and refined, and commonly used pesticides (regardless of their carcinogenic classifications) were added since they were relevant to the working population in these countries. In Costa Rica, where the project was called "TICAREX", 27 carcinogens and 7 groups of pesticides were included (13, 18). These pesticides were selected with input from a diverse group of field experts. Other exposures of importance in TICAREX were diesel engine exhaust, solar ultraviolet radiation, and polycyclic aromatic hydrocarbons. Nicaragua's CAREX project encompassed 35 substances, and

Panama's included 31 agents (19). Field experts were consulted as well, resulting in slightly different lists of included carcinogens in each of these 3 Central American countries.

In Colombia, researchers built the first job exposure matrix (JEM) by selecting carcinogens that met three criteria: 1) those included by IARC as a causal agent for any of the 10 cancer sites selected to have potential occupational exposures (larynx, lung, pleura, liver, kidney, bladder, prostate, colon and rectum, hematopoietic system and lymphoid system); 2) those registered in the EU-CAREX and related to occupational exposures, adding hepatitis B virus, hepatitis C virus, human immunodeficiency virus, and aflatoxins; and, 3) the feasibility of being present in Colombian workplaces between 1970 and 2006. For the third criteria, field experts played a fundamental role, and finally 61 agents were selected (20). These agents were included in the National Plan for the Prevention of Cancer 2012-2021 and prioritized asbestos, silica, benzene, inorganic lead compounds, and ionizing radiation (21). This JEM built with a group of hygienists served as the basis for building the CAREX project, which included all carcinogens published by 18 European countries, and others considered relevant were added by field experts in Colombia. A total of 86 agents classified by IARC as known (Group 1) or suspected (Groups 2A and 2B) carcinogens were included in the Colombian CAREX project. The priority carcinogens were similar for Peru, where they compared data from the EU, the Central American countries, Colombia, and Canada. In addition to the aforementioned agents, the Peruvian CAREX project included eight pesticides and two radiation exposures. The key carcinogens for the country were solar radiation, diesel fumes, lead, silica, polycyclic aromatic hydrocarbons, asbestos, and benzene. Exposure to cigarette smoke and hexavalent chromium were also important.

2 IDENTIFY THE WORKING POPULATION

GENERAL APPROACH

Labour force information is essential for determining where people work and the number of workers in the national population. Labour force data can have various levels of detail, ranging from summarizing the number of workers in broad industry sectors to including employment numbers by different occupations in specific industry groups. There may also be demographic information about the working population, such as sex and state/province of residence. In most cases, labour force information is available through the national census, national statistics departments/offices/institutes, or a country's labour, economic, or social security ministry.

In order for exposures to be assessed for different workers, the working population must be classified into different groups, usually by industry and/or occupation.

There are many different types of schemes available to systematically classify the industries and occupations of the labour force. CAREX does not prescribe or endorse a specific scheme. However, the United Nations' (UN) International Standard Industrial Classification of All Economic Activities (ISIC) Revision 3 (1990) (22) or Revision 4 (2008) (23) can be considered if either of these schemes have been adopted by the country. Industry and occupation data are usually classified using a hierarchical coding scheme that is current and relevant to the population under investigation. Researchers are encouraged to use classification schemes that are suitable and available in the local language for the country. In most cases, these will be industry codes (and occupation codes where available) that are commonly used in LAC.

EXAMPLES

Labour force data in the European CAREX were mainly sourced from the Organization for Economic Cooperation and Development. The number of employed people was calculated from the mean number of employed people between 1990 and 1993. National statistics in individual EU countries were used if available and experts were sought to correct and complete the data if needed. The project aimed to include all people employed in each industry by covering salaried workers, self-employed workers, working family members, and part-time workers. The UN ISIC Revision 2 (1968) was used to classify industry information at a detailed level (the three digit level); for some non-manufacturing sectors, broader groups (one or two digit codes) were used. An international classification scheme was appropriate given the heterogeneity of industries in the EU, leading to a total of 55 industrial groups (7).

National censuses have been used in CAREX projects in Central America and Canada as data sources for the working population. TICAREX in Costa Rica used workforce data that were available from the 2000 national census. This included employed and self-employed persons, as well as working family members older than 12 years. Information about sex was also obtained so that exposures could be assessed separately for men and women. This approach covered the informal sector and young workers in exposure estimates, which is an important consideration in many countries that have large proportions of informal and young workers. In all, 55 industrial sectors were included at broad levels (two and three digits) using the UN ISIC Revision 2 (1968) (13).

In Nicaragua, employment data from the 2005 census were ascertained to obtain industry- and sex-specific numbers of the economically active population. CAREX in Panama used the 2000 census to collect this information. These countries were able to capture the formal and informal workforce in this manner. Workforce numbers were then classified into 44 industries using the same scheme as in the EU and Costa Rica, and were also stratified by sex.

In Canada, the CAREX project obtained numbers of people employed by industry, occupation, province, and sex from the 2006 national census for those aged 15 years and over. Industries were coded in detail using the North American Industry Classification Scheme (2002) and occupations were coded using the National Occupational Classification for Statistics (2006). This led to exposure being considered for 307 detailed industries and 520 detailed occupations. In Colombia, CAREX researchers applied the UN ISIC Revision 3 (adapted for Colombia) to the 55 economic groups that were included in the European CAREX. The national census was not used to enumerate the working population;

instead, the working population was limited to those workers who were affiliated with the national social security system in 2012. This meant that the resulting CAREX estimates represented the formal sector and excluded workers without social security (i.e. informal workers) (24). On the contrary, in Peru, general census data were used, which captured both formal and informal workers. It was important to include informal workers in the Peruvian CAREX given the significant proportion of informal workers in the country (25). Researchers in Peru used the UN ISIC Revision 4 classification scheme and applied it to the 55 industry groups used in the CAREX matrix with the exposure data of all CAREX projects aforementioned that was built for comparison purposes.

3 DETERMINE PREVALENCE OF EXPOSURE VALUES

GENERAL APPROACH

Prevalence of exposure is obtained from linking/multiplying proportion exposed (Pr(E)) values with working population data obtained in step 2.

Pr(E) values can be determined in a variety of ways. To inform Pr(E) values, measurement data from occupational hygiene samples/assessments are a useful source of information and should be used when available. However, in many countries there are little or no measurement information, and the quality of available measurement data may be unclear. In this case, default Pr(E) values can be used or adapted. LAC countries can review Pr(E) values from the Finnish/EU, Central American, other LAC countries and Canadian CAREX projects to determine if they are relevant to the specific country's context. Canadian CAREX Pr(E) values can be made available at a wide variety of levels of detail to accommodate different coding schemes and detail of population (i.e. census) data. These values can be adapted as needed, typically with the input of field experts who can advise on the proportion of workers likely to be exposed by industry/economic sector and any other variables available (e.g. occupation, sex). Canadian Pr(E) values may be particularly useful for carcinogens not previously included in the EU CAREX, such as shiftwork. Pr(E) values from the EU CAREX project are older but some may still be applicable to LAC, in particular for economies that are similar to the EU when its CAREX was designed in the 1990s. However, countries in LAC are encouraged to adapt (rather than directly apply) Pr(E) values used in other previous CAREX projects, or to establish their own Pr(E) values de novo.

Previously existing Pr(E) values may not be available in the coding structure of your country and time will need to be devoted to translating Pr(E) values from another country or level of detail into one that works for your country. Many concordance/correspondence tables for different classification systems do exist for these translations and should be consulted. However, these are normally created for economic purposes, and all translations should be reviewed by industrial hygienists for clarity when occupational exposure assessment is the purpose. Whatever methods are used, they should be clearly documented in detail along with the decision-making process for establishing Pr(E) values.

It is also important to consider the current industrial and occupational composition of the working population, which may differ from the distribution of workers in the past. Latin America in particular is an extremely heterogeneous and urbanized region with respect to its industrial and occupational makeup. For example, in Latin America, the working population is generally moving away from agriculture and towards industry and services (15), a factor that would need to be considered in determining or adopting Pr(E) values. In the Caribbean, the major economic activities are relatively more limited than in Latin America, which could result in using different Pr(E) values than those used in Latin America.

EXAMPLES

All Latin American CAREX projects carried out until now relied significantly on previously developed Pr(E) values and field expert judgment since there was a lack of exposure measurement data in these countries. Costa Rica's adaptation of the European CAREX involved modifying default Pr(E) values for certain substances, including cadmium and cadmium compounds, ionizing radiation, lead and lead compounds, and asbestos. Default Pr(E) values were also changed for radon and strong inorganic mists containing sulfuric acid. Occupational exposure to diesel engine exhaust and solar radiation were redefined given the high levels of workplace exposure to these carcinogens in Costa Rica, causing notable increases in the default European Pr(E) values for the most affected Costa Rican industries.

Additionally, Costa Rica developed exposure estimates for seven groups of pesticides. Pesticides were not included in the European CAREX projects and so this effort by Costa Rica represented a relevant and important advancement of the CAREX approach. Minimum and maximum Pr(E) values for pesticides were based on national academic databanks and field expert judgment of the number of workers per hectare in farms of various crops, proportions of farms using pesticides by crop, data on aerial spraying, and numbers of workers in road maintenance (13). Minimum, maximum, and point estimates were also generated for agents with high uncertainty. Creating a range based on minimum and maximum values is a good approach in the development of CAREX projects because it helps to convey the confidence with which the estimates are presented. Ranges can similarly be produced for other (non-pesticide) carcinogens as well.

In Nicaragua and Panama, industry- and sex-specific Pr(E) values from Costa Rica, stratified by job activity and sex, served as the starting default estimates. These were modified or completely reconstructed by

25 governmental, union, industrial hygiene, employer, and academic experts in each country. The approximate frequencies of people exposed to pesticides in Panama were calculated on the basis of average number of men and women in agriculture per sprayed cultivated land area (19).

Peruvian researchers built a table that compared exposure estimates from 18 European countries (average of EU 1990-1993); Costa Rica, Guatemala, Nicaragua, and Panama (average of Central America 2002-2010); Colombia (2008-2013); their own initial results using ISIC V2 (2015); and the silica job exposure matrix estimates from Brazil, Chile and Peru (2012). Estimations distributed by sex and economic sector were assessed by 67 field experts from 42 different institutions, and were later refined in 8 additional workshops with more specific field experts by economic sector.

CAREX Canada generated Pr(E) values for likely exposure by combining information from several primary resources (when available) and by using expert assessment and agreement by a minimum of two occupational hygienists. Primary resources included Pr(E) values from the U.S. National Occupational Exposure Survey (NOES) and European CAREX studies, published studies, Canadian-specific information on exposure from government and other reports, and exposure measurement data in the CWED. Some agents had unique data sources while others had particular assessment challenges (e.g. asbestos, shiftwork, radon, diesel engine exhaust) (11). Occupational hygienists evaluated and used data from the primary resources to develop Pr(E) values, by industry and occupation, for each of the 44 carcinogens included in the project. All methods and estimates were externally reviewed by a scientific advisory committee of research and practice professionals in occupational hygiene and epidemiology (11). Pr(E) values were then linked to census 2006 data to calculate the prevalence (number) of workers exposed by agent.

It is important to note that even in the EU, there was generally a lack of exposure measurement data and therefore, an indirect exposure estimation approach was taken by calculating Pr(E) values using data from Finland, the United States, and an average of both Finland and the United States. Expert judgment was sought for which of these three estimates was considered to be the most valid; this valid estimate was set as the default Pr(E) value (usually the average value). Potentially low levels of exposure were flagged in order to identify exposures that were close to the background level. Industrial classifications from both countries were converted to the scheme used in the EU CAREX project.

ESTIMATING EXPOSURE BY LEVEL, SEX, AND/OR REGION

CAREX projects can vary with respect to the amount of detail of exposure estimates. It may be possible to build upon exposure prevalence estimates by generating information about different levels of exposure (e.g. high/low or high/medium/low), sex, and/or region (i.e. state/province). CAREX Canada hygienists also recorded qualitative markers of certainty (high/low) for each Pr(E) that was developed. Generally, detailed exposure estimates are possible for data-rich carcinogens. Substances with little or no exposure information are not well suited for detailed estimates. For most agents included in the CAREX Canada project, there were not enough data to estimate exposure levels. However, sufficient exposure measurement data were available in the CWED for 18 agents, e.g. benzene, trichloroethylene, wood dust, etc. Exposure level estimates (high/medium/low) were calculated for these 18 carcinogens. The definitions of "high", "medium", and "low" levels were pre-defined with respect to the number of individual samples in the CWED and the percentage of samples with an exposure concentration higher than the threshold value based on occupational exposure limits in Canadian jurisdictions. The numbers of workers exposed at each level of exposure was calculated by similarly linking Pr(E) values to the national 2006 census.

CAREX projects in Central America generated exposure estimates by sex and included informal workers, which represented an important advancement of the CAREX methodology for the LAC context. There are few informal workers in Canada, but detailed information in the 2006 Canadian census enabled researchers to estimate exposure by sex and specific industries, occupations, provinces, as well as for level of exposure where possible.

Researchers in Colombia analyzed data from 18 European countries and categorized the source of estimation used by each country: Finland, EU, average of Finland and the EU (PROM), or from own country (PROP). Exposed workers were distributed by industrial sector in absolute figures and then converted to percentages exposed by dividing by the exposed workers by the total number of workers in each industry assessed. Results were reviewed by an expert group of occupational hygienists who used national occupational health and safety guidelines to classify "exposed" workers as those with values equal to or greater than 50% of the ACGIH threshold limit value (qualitatively, "medium" or higher). These experts thought that estimates would differ for formal and informal sectors, and that there were not enough data to produce exposure estimates by sex. A second analysis was made with field experts from industry, occupational hygiene associations, occupational health and safety groups, company advisors, and union representatives, who made final recommendations about the estimates. The major occupational carcinogens identified were solar radiation, silica, diesel fumes, formaldehyde and benzene. Exposure to other agents such as wood dust, inorganic acids mist, asbestos, and polycyclic aromatic hydrocarbons were also reported in several economic activities.

Even though measurement data are usually not available for many carcinogenic agents, qualitative information can be used in addition or as an alternative to any measurement data. Assessment by industrial hygienists and other experts has been used to classify exposures as high, medium, and low based on pre-determined criteria in previous CAREX projects. This is a distinct improvement over the prevalence estimates and should be considered when possible.

ADDITIONAL CONSIDERATIONS FOR LAC

CAREX is essentially a model for estimating where and how many workers are exposed to known and suspected occupational carcinogens. Collectively, the three aforementioned components (selection of carcinogens, labour force information, exposure data) have been used to estimate the numbers of people exposed to carcinogens in workplaces. Some CAREX projects have been able to estimate occupational carcinogen exposure by province/state, industry/occupation, sex, exposure level, or a combination of these strata. The examples of how CAREX has been adapted and established in several countries demonstrate that it is a robust framework for exposure estimation with practical applications in research and policy.

There are multiple opportunities to expand upon this core information depending on the availability of data and resources. Below are some additional considerations for those developing CAREX projects.

EXPOSURE MEASUREMENT DATA

Exposure measurement data may be available and can be used in CAREX projects. Measurement data may have been collected for various reasons. Some measurements may have been taken by regulatory agencies as a part of legal requirements; by industry for self-monitoring; by scientists for research purposes; and/or by other groups for international databases. For example, in Canada, the CWED (26) is a part of CAREX Canada that contains measurement data on exposure to some, but not all, carcinogens included in the CAREX Canada project. The CWED brings together data using a variety of sources primarily from two of Canada's largest provinces (British Columbia and Ontario). The CWED has been used to identify the potential for exposure in particular industries and occupations, as well as to create exposure level estimates for data-rich priority carcinogens.

It is important to note that exposure measurements may not reflect the industries with higher exposure since measurement data are often not collected in a systematic and comprehensive way, resulting in gaps in coverage of certain industries and occupations. This occurs in Canada as well as other countries. For instance, in Colombia, asbestos exposure has been assessed in many industries since the 1990s. The first national study on asbestos exposure in Colombia was carried out between 1989 and 1992, and measurements were collected for occupational exposure to asbestos in textile, friction material, and fibre-cement industries (27). More recent studies were carried out in heavy vehicle brake repair shops in Bogota as part of a study of asbestos exposure and respiratory health among workers in these shops (28). A separate study measured asbestos exposure among transmission mechanics in auto repair shops in Bogota (29). There are many more workers in other industries and occupations who are exposed to asbestos in Colombia, but their exposures may not have been sampled and published studies are sparse. Information from historical sampling studies may be used as they can be applicable to modern working contexts. However, there is no national asbestos exposure surveillance program or worker registry in Colombia (and in most LAC countries and Canada). The results of single exposure studies are a step in the right direction and can contribute to population-based exposure estimates.

In Central America, researchers have established methods for monitoring pesticide use that primarily involve quantitative indicators (i.e. kilograms of active ingredient) of imported pesticides (30). While this is a good indicator of trends of pesticide use, it does not actually measure workers' exposure. SALTRA, a regional program for workers' health and sustainable development in Central America, was launched in 2003 with a component of occupational carcinogen exposure surveillance (31). Data from this program can be explored as a potential source of exposure information. Involving field experts in the early stages of a CAREX project will increase the likelihood of identifying potential exposure information and can help with obtaining access to measurement data.

OCCUPATIONAL EXPOSURE TO MULTIPLE CARCINOGENS

The term "exposure" does not refer to the number of times in the year that may be in contact with the agent but the qualitative occurrence of worker exposure to a carcinogen (i.e. exposed or not exposed). CAREX estimates the number of workers exposed to a given agent; however, in many economic activities, workers are exposed to more than one carcinogen at the same time or in their working lifetime. If all exposures of an economic activity are added together, the same workers can be counted several times, resulting in an overestimation of the population exposed by economic activity. For this reason, in the case of exposures to multiple agents, exposure modulating factors are needed to convert these exposures to a single worker. In the EU CAREX project, industry-specific factors were developed from the Finnish data to convert the number of exposures to the number of exposed workers, and thus avoid re-counting workers exposed to multiple carcinogens.

INFORMAL WORKERS

According to the International Labour Organization (ILO), the informal economy is usually associated with poor employment conditions and poverty. ILO clearly defines informal work[2] and informal employment[3], with the former more relevant than the latter in LAC. Statistics on the informal economy (32) indicate that countries with proportions of informal employment greater than 60% at that time were Bolivia (75.1%), Ecuador (60.9%), El Salvador (66.4%), Honduras (73.9%), Nicaragua (65.7%), Paraguay (70.7%), and Peru (69.9%). That same year, the countries with proportions of people in the informal sector higher than 45% were Bolivia (52.1%), Colombia (52.2%), El Salvador (53.4%), Honduras (58.3%), Nicaragua (54.4%), and Peru (49%). The informal economy includes low-income groups, a high proportion of which live below the poverty line. Informal workers are excluded from social protection; while informal employees have a salary but are not protected from non-payment of wages, compulsory overtime or extra shifts, layoffs without notice or compensation, unsafe working conditions, and there is an absence of social benefits such as pensions, sick pay, workers' compensation, and health insurance (33). Informal workers amount to a substantial number of workers in LAC and are the majority of workers in certain countries. Although non-agricultural informal employment in LAC fell marginally from 50% in 2009 to 47.7% in 2012 (34), informality remains pervasive and disproportionally occurs in women, indigenous and migrant populations and it is inherent in child and bonded labour.

Informal workers typically perform dangerous tasks such as street vending, housekeeping, construction, fishing, agriculture, manufacturing, recycling, mining, maintenance, sex work, and so on. They live in a survival economy, belonging to very poor and vulnerable communities. They are most often self-employed, and sometimes work in small- and medium -size enterprises in low skilled and low wage jobs. Working conditions are mostly precarious, with long working hours under hazardous conditions and without any means of health and safety at work. As self-employed or owners of small businesses, they usually work in their own household, increasing hazardous exposures for themselves and their families. Hence, exposure prevalence trends are expected to be much higher, but less assessed, than exposures among formal workers.

TICAREX in Costa Rica and CAREX projects in Nicaragua and Panama included exposure estimates for informal workers. Of the 12,024 workers interviewed for the Central American Survey of Working Conditions and Health, 37% were reportedly self-employed, 8% of employees lacked a work contract, and 74% of the workforce was not covered by social security. These proportions were higher in Guatemala, Honduras and El Salvador compared to Costa Rica, Panama, and Nicaragua. Workers in the formal and informal economy also reported frequent or usual exposures to breathing chemicals (12-18%) and handling toxic substances (5-12%) (35). Some activities in the formal and informal sectors are very similar. A collaborative approach should be used to better identify and document carcinogenic exposures among informal workers. Involving stakeholders, such as non-governmental and advocacy organizations, could be of help.

The results of scientific studies of informal workers, although limited, can inform the selection of priority carcinogens and what Pr(E) levels to assign. Risks among informal recyclers and rag pickers in Latin America have been reported in peer-reviewed scientific literature published in English. In one study of informal recyclers in squatter communities in Paraguay, it was found that respirable dust exposure in 18 workers was substantially higher than levels at home or in another occupation in their neighbourhood (36). A separate study in Brazil documented occupational health risks and outcomes in informal recyclers, but no exposure measurement data were collected (37). In Colombia, there is a registry for research on informal workers that records their economic activities. Street vendors are ubiquitous in the region and while most studies of

2 Work in the informal sector refers to the total number of people in informal production units, which are characteristically unorganized; produce goods or services for sale or exchange; they lack official registries, are small in size, have unregistered workers, and do not keep worker records.

3 Informal employment refers to the total number of people whose main job is informal, and thus lacks basic social or legal protections, or social benefits. It can be found in the formal and informal sectors, and in domestic work.

their exposures have focused on noise and solar UV radiation, exposures to diesel and benzene are also important. Waste pickers and recyclers often handle and burn plastics involving exposure to dioxins and other harmful agents. Similarly, tire refurbishers are known to be exposed to carcinogens. Greater efforts are needed to fully address the work-related exposures and causes of ill health among informal workers.

National statistics about informal employment and work in the informal sector are available on the ILO website (38). The Information System and Labour Analysis of Latin America and the Caribbean (SIALC) collects, processes, organizes, disseminates and maintains records of social and labor information from LAC (39). These types of statistics alone may not capture the entire picture; informal workers can also be found in outsourcing, sub-contracting and third party work, clandestine or illegal work often related to child labour and slavery, migrant work within or between countries, and temporary work (e.g. via an employment agency). Self-employed, family business and informal migrant workers are more challenging to locate and quantify since they may not be included in national census data. Existing or planned surveys can help to enumerate this population of workers in the LAC countries.

The presence of informal work can vary substantially between countries in LAC. For example, in Cuba, there is no informal work because individuals can register themselves as self-employed according to a list of approved occupations by the Ministry of Labour and Social Security. Self-employed workers have social security benefits and can retire. Unionized co-operatives have been established for construction, mechanical work, and other labour. These groups can be hired by the government as needed. However, in the Caribbean, the British Factories Act of 1937 is still followed and only describes industrial workers. According to this definition, almost all workers in the Caribbean are informal because there are currently no industrial workers. These factors can be taken in to consideration for a national CAREX project.

ESTIMATING EXPOSURE TO ENVIRONMENTAL CARCINOGENS

The CAREX methodology is robust and can be adapted for environmental carcinogen exposure estimation. Many carcinogens that are found in the workplace are also found in the environment, e.g. pesticides, diesel engine exhaust, solar ultraviolet radiation, etc. CAREX Canada is the only project so far to have assessed the potential lifetime excess cancer risk due to environmental exposures, based on measured data for each substance and exposure pathway. This represented a very different approach compared to occupational exposure estimation. Innovation of the basic CAREX concept is important and encouraged in LAC.

DATA MANIPULATION TOOLS

There are different ways to display CAREX data. Tools that manipulate data allow knowledge users to aggregate exposure estimates based on their primary interests. For instance, eWORK is an online, interactive tool that has been developed for exploring CAREX Canada's occupational exposure estimates to known and suspected carcinogens: http://www.carexcanada.ca/en/eWORK/. A more detailed version of eWORK is available for desktop use. CAREX Canada has also developed a multi-platform data entry and display tool for internal use. This platform contains all census, exposure, and expert assessment data in one package, and also serves as the expert assessment tool for all data entry and manipulation.

KNOWLEDGE TRANSLATION AND EXCHANGE

Knowledge translation and exchange (KTE) is defined as a dynamic and iterative process that includes synthesis, dissemination, exchange, and ethically-sound application of knowledge to improve public health (40). It is of vital importance that all methodology and detailed decision-making during the course of a CAREX project is meticulously recorded. This is one of the main strengths of CAREX Canada; each line of data is stored and described for all exposures, and can be changed as new information becomes available.

CAREX estimates are valuable to many groups, including scientists, policy makers, workers, and employers. A transparent way of communicating this information is integral in each stage of a CAREX project. Websites have been established for the EU and Canadian CAREX projects (41, 42) to communicate knowledge in a centralized, publicly accessible way. Fact sheets, presentations at scientific and stakeholder meetings, peer-reviewed publications, and tools to enhance awareness and education about occupational carcinogen exposure and cancer prevention can be developed and used as standalone pieces or in addition to a website. CAREX Canada actively engages in KTE with several stakeholder groups in Canada, including First Nations groups, policy makers, and labour organizations.

In general, CAREX Canada works actively with groups to develop tailored KTE products that are useful for their organizations, as well as offer free hands-on and specialized training for users on how to use tools and interpret results. Some of the knowledge translation products that CAREX Canada has created are profiles for priority carcinogens, a regular media scan of occupational and environmental exposures ("Carcinogens in the News"), and interactive tools to explore and use CAREX data such as eWORK, eRISK, and the Emissions Mapping Project. In addition, CAREX Canada creates packages that summarize knowledge by requests for information on specific topics (e.g. mining industry, lung carcinogens).

Developing collaborations and partnerships are essential for applying knowledge. For example, CAREX Canada is working with the British Columbia workers' compensation board (WorkSafeBC) to co-develop exposure reduction resources, support strategic planning on target substances, and cross-link website resources. Since CAREX Canada was designed to amalgamate existing exposure data, it has naturally involved more interaction with government agencies, which are currently important collaborators, along with unions. CAREX Canada maintains updated statistics of website visitor numbers and other potential indicators of knowledge translation impact.

Target audiences can be similarly identified in LAC and knowledge can be packaged in ways that help these groups advance workers' health and cancer prevention objectives. Unions and workers can drive changes in attitudes about exposure and prevention, promote awareness among policy-makers, and encourage the timely diagnosis and treatment of occupational cancer. Some interventions and recommendations could be easily implemented to reduce exposure immediately, such as wood dust exposure in small workshops or flexible shift scheduling in service, transportation, and other industries.

APPLICATIONS OF CAREX DATA

The examples of how CAREX has been adapted in Latin America and Canada demonstrate that it is a robust framework for population-based exposure estimation with practical applications in research and policy. In surveillance studies, CAREX data have been used to quickly and cheaply identify the substances, industries, and occupations where cancer risk may be elevated. Recent burden projects in the United Kingdom (43) and Canada (44) have leveraged CAREX data to assign exposure prevalence and level values separately to men and women in a variety of industry and occupations. In LAC, exposure estimates can be used to estimate the burden of occupational cancer in each country and for the region as a whole. National figures drawn from rigorous exposure estimates can substantially improve overall global burden of disease calculations and raise awareness of occupational exposures as an important, preventable cause of cancer. Furthermore, burden of occupational cancer studies can help inform policy-makers about allocating limited prevention resources to the most affected workers, selecting priorities for occupational hazard control, and aid scientists with quantitative risk assessment.

CAREX estimates can be used to assess changes in exposure over time and detect potential reasons why changes may have occurred. One example of this is how CAREX shows that benzene levels in two Canadian provinces (Ontario and British Columbia) have decreased over time, partly due to changes in the occupational exposure limit. Current CAREX estimates have been applied to historical labour force data to estimate how many people were exposed to carcinogens in the past. CAREX projects also provide the means to project future exposure in the working population.

Data produced from a CAREX project can have further applications in occupational cancer prevention policies. In Colombia, relevant occupational carcinogens have been identified and an occupational cancer prevention public policy has been established by the National Cancer Institute. An action plan has been designed for its implementation, and in addition to the country's CAREX project, an occupational cancer surveillance system (SIVECAO) has been established to identify cancers attributed to exposures to known carcinogenic agents of interest.

TOWARDS A REGIONAL CAREX FOR LAC

PAHO's commitment to achieve a regional CAREX has been included in the Action Plan for Workers' Health 2015-2025 (45), as part of efforts to control and prevent occupational cancer in LAC. The Ministries of Health committed to move this agenda forward as part of actions to control and decrease preventable deaths caused by NCDs, particularly from cancer.

PAHO together with the CAREX LAC steering committee will support the forging of partnerships between countries to share knowledge, resources, and drive innovation in CAREX methods; gaining access to labour force and occupational exposure measurement data; generating detailed CAREX estimates for priority occupational carcinogens in each country; and strengthening the training of industrial hygienists to help lead, sustain, and evolve CAREX in the future. Achieving these steps involves careful planning and resourcefulness, especially in countries where workers' health is not a public health priority or there are simply not enough people specialized in industrial hygiene.

There has been a long-standing effort to developing a region-wide CAREX for LAC, analogous in scope to CAREX in the EU. By 2019, PAHO is aiming for at least 50% of countries in LAC to have national CAREX projects and exposure estimates. In addition, it is hoped that these countries will issue pubic policies and regulations for controlling hazardous exposures to carcinogens at the workplace and assess the burden of occupational cancer. With a vision of a regional CAREX that covers all countries in LAC, exposure estimates can make a significant and much-needed contribution to occupational cancer research and informed decision-making for cancer prevention. As the second region in the world to widely adapt the CAREX methodology, this research has the potential to be a key driving force in improved carcinogen exposure surveillance, estimations of the human and economic burden of occupational cancer, and the prevention of occupational cancer in the LAC.

The CAREX LAC workshop held in Bogota in 2014 with representatives from 13 LAC countries demonstrated varying levels of interest, capacity, and progress in developing CAREX projects. Argentina, Venezuela, Grenada, and Cuba were in greatest need of partnerships, access to data, and stronger training of industrial hygienists. There are a number of ways to proceed despite constraints. For instance, the proximity of these countries to Central America and Colombia, where CAREX projects are the most developed in the region, can facilitate the exchange of knowledge, skills, and methods. Exposure estimates here could be used as a starting point for refinement by countries with limited capacity and resources. Job exposure matrices can be adapted or developed since it is costly to obtain exposure measurements. Threshold limit values may be used as cutoffs for exposure (yes/no and levels). If it is not possible to generate point estimates of numbers of workers exposed, a probabilistic approach could be used to produce interval estimates. Exposure in occupation or industry groups can be classified qualitatively and compared to measured levels elsewhere as a benchmark for prevention. CAREX researchers will also need to develop clear definitions of occupational exposure for agents such as solar radiation, for which exposure may occur both at work and in other settings.

Countries that already have exposure prevalence estimates can advance by further stratifying estimates by level of exposure, sex, state, informal/formal workers, and detailed industry/occupation. These countries currently are Colombia, Costa Rica, Nicaragua, and Panama. In the meantime, existing CAREX estimates from these countries can be made available online to stakeholders and the public. A tool to aid the use of data, similar to CAREX Canada's eWORK module, could be considered as part of knowledge translation, awareness raising, training, and capacity building involving government, employer, worker, and other groups. Burden of occupational cancer projects can likely be initiated in Colombia, Costa Rica, Nicaragua, and Panama, with other countries joining this effort as their CAREX results emerge.

Bilateral and multilateral cooperation is a cornerstone of this work. Not only will partnerships aid with the sharing of resources and methods, but they can also deal with specific issues, such as enumerating the migrant worker population in CAREX estimates. Methodological advancements can address complex phenomena like climate change, which has affected the intensity of solar radiation exposure in outdoor workers. All of the CAREX reports and databases from LAC countries are available and serve as an important reference of results from the collective CAREX LAC research groups. More broadly, a concerted effort by governments, scientists, and the private sector is needed to bring CAREX to life in the form of research, public policy, and the health and well-being of workers.

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