Acute Pesticide Poisonings in Nicaragua: Underreporting, Incidence and Determinants

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"Lo que ocurra con la tierra
recaerá sobre los hijos de la tierra.
El hombre no tejió el tejido de la vida,
El es simplemente uno de sus hilos.
Todo lo que hiciere al tejido,
lo hará a sí mismo."

Carta del Jefe Seattle al
Presidente de Estados Unidos, 1855

"If facts are the seeds that later
produce knowledge and wisdom,
then the emotions and the impressions
of the senses are the fertile soil
in which the seeds must grow."

Rachel Carson (1907-1964)

ABSTRACT

Background: Acute pesticide poisonings (APP) are a public health problem in Nicaragua. The quality and coverage of APP´s register, the real incidence of APP, the main determinants, the economic cost of treating cases and the effectiveness of educational intervention are not well known.

Aim: The overall aim was to investigate the acute health impact of pesticide use and to discuss the possible effectiveness of preventive measures in Nicaragua. The specific aims were to calculate the proportion of APP cases officially registered, to estimate one year cumulative incidence of APP cases among population 15 years and older, to identify the main determinants related to APP among pesticide sprayers and to evaluate the impact of an integrated pest management (IPM) training intervention.

Methods: For studies 1, 2, and 3, data concerning pesticide exposure and health effects were assessed in a nationally representative survey of 3169 persons 15 years and older in year 2000. For study 1, to estimate the proportion of underreporting of APP cases, the cases reported at the official surveillance system were cross matched with the cases reported through the survey. In study 2, based on self reported cases we estimated the one year incidence rate and the number of expected cases of APP in the country. In study 3, after regression analysis, the main determinants for APP among agricultural sprayers were identified. Study 4 assessed the impact of a 2 years IPM training to reduce economic costs and acute adverse health effects among 1200 basic grain farmers comparing the group of trained farmers and a group of "control" farmers who did not receive training.

Results: Less than 5% of medically treated APP cases were reported to the official register. The one year APP incidence among general population was 2.3% (95%CI 1.7-2.8). The rate was higher among men, rural population and agricultural workers. More than 66,000 cases were estimated to occur yearly. The national incidence rate of APP among sprayers was extremely high, 8.3% (95% CI 5.8-10.8) and more than 34,000 cases were estimated to occur among pesticide sprayers, and representing 52% of all APP's estimated in year 2000. Although most of the cases were minor and moderate, the poisonings caused near 340,000 disability days. The causal agents for APP in 95% of cases were WHO Class I-II pesticides. The main determinants of APP among sprayers were: backpack pump leakage and incomplete or no use of personal protective equipment. Seventy seven percent of cases were caused by pesticides proposed to be banned or restricted in Central America. The IPM training prevented acute health effects and maintained productivity: after two years of training, the trained farmers used fewer pesticides, spent less money on pest control, made higher net returns, and suffered less exposure to cholinesterase-inhibiting pesticides compared to farmers who did not receive IPM training.

Conclusion: Underreport figures leads to an erroneous interpretation of acute pesticide health effects. There is a high APP incidence rate in the general population, but it is four times higher among sprayers, causing important loss of or productivity and important economic costs. IPM interventions were successful in prevent the occurrence of APP cases and economic losses. Traditional prevention and control measures are insufficient and structural changes, including pesticides banning and restriction, and change to IPM agriculture models, are needed to transform the underlying determinants.

Key words: pesticide poisonings, surveillance system, underreport, incidence, economic costs, determinants, integrated pest management

RESUMEN (ABSTRACT IN SPANISH)

Antecedentes: Las intoxicaciones agudas por plaguicidas (IAP) son un problema de salud pública en Nicaragua. La calidad y cobertura del registro, la incidencia real, los principales determinantes, el costo económico del tratamiento de los casos y la efectividad de intervenciones educativas no son bien conocidas.

Objetivo: El objetivo general fue investigar el efecto en salud del uso de plaguicidas y la efectividad de medidas preventivas. Los objetivos específicos fueron calcular la proporción de IAPs registradas, estimar la incidencia acumulada anual de IAPs en mayores de 15 años, identificar los principales determinantes de IAPs entre fumigadores y el impacto de las capacitaciones en manejo integrado de plagas (MIP).

Métodos: Para los estudios 1, 2, and 3, se analizaron datos relacionados con exposición a plaguicidas durante el año 2000 y los efectos a la salud relacionados provenientes de una encuesta nacional representativa de 3169 personas mayores de 15 años. En el estudio 1, para la estimación del subregistro de IAPs, se cruzaron los casos reportados oficialmente con casos reportados por la encuesta. En el estudio 2, la incidencia anual y el número de IAPs estimados, se basó en los casos auto reportados por los encuestados y su extrapolación a las poblaciones nacionales. En el estudio 3, después del análisis de regresión logística a variables de exposición, se identificaron los principales determinantes para IAPs entre fumigadores agrícolas. El estudio 4 analizó el impacto de 2 años de capacitación en MIP para reducir los costos económicos y los efectos adversos a la salud en 1200 agricultores de escasos recursos, comparando a los agricultores capacitados con los no capacitados.

Resultados: El registro de IAPs atendidas fue menor del 5%. La incidencia anual de IAPs fue de 2.3% (IC95% 1.7-2.8) en población general, siendo más alta entre hombres, pobladores rurales y agricultores fumigadores. Más de 66,000 casos podrían ocurrir anualmente. La incidencia anual nacional entre fumigadores fue de 8.3% (IC95% 5.8-10.8), estimándose más de 34,000 casos, representando el 52% del total nacional. Pese a que la mayoría de los casos fueron menores y moderados, las IAPs causaron cerca de 340,000 días laborales perdidos. En 95% de casos, los agentes causales fueron plaguicidas clase I y II de la OMS. Los principales determinantes fueron: el derrame de plaguicidas de la bomba de mochila y el uso incompleto o no uso de equipos de protección personal. El 77% de los casos fueron causados por plaguicidas propuestos a prohibir o restringir en América Central. La capacitación en MIP previno efectos agudos a la salud sin reducir la productividad: después de 2 años de capacitación los agricultores capacitados usaron menos plaguicidas, gastaron menos dinero en controlar plagas, tuvieron un retorno neto mayor y sufrieron de menos exposición a plaguicidas inhibidores de la colinesterasa cuando se compararon con los agricultores que no recibieron capacitación en MIP.

Conclusion: El subregistro de las IAPs conduce a interpretaciones erróneas de los efectos agudos de los plaguicidas. La tasa de incidencia de IAPs es alta en la población general, siendo cuatro veces mayor entre los fumigadores, causando muchos días de discapacidad y pérdidas económicas directas. Las intervenciones en MIP previnieron exitosamente la ocurrencia de casos agudos y las pérdidas económicas. Las medidas tradicionales de prevención y control de IAPs son insuficientes y se requieren cambios estructurales, incluyendo prohibición y restricción de plaguicidas, así como cambio a modelos agrícolas basados en MIP para transformar los determinantes subyacentes.

Palabras claves: intoxicaciones por plaguicidas, sistemas de vigilancia, subregistro, incidencia, costos económicos, determinantes, manejo integrado de plagas.

LIST OF PUBLICATIONS

This thesis is based on the following studies, which will be referred to by their Roman numerals I-IV.

I. **Corriols M**, Marín J, Berroteran J, Lozano LM, Lundberg I, Thörn A (2008) The Nicaraguan Pesticide Poisoning Register: constant underreporting. Int J Health Serv. 38(4):773-87

II. **Corriols M,** Marín J, Berroteran J, Lozano LM, Lundberg. (2009) Incidence of acute pesticide poisonings in Nicaragua: a public health concern. Occup Environ Med. 66(3):205-10. Epub 2008 Nov 21.

III. **Corriols M**, Marin J, Berroteran J, Lozano LM, Aragon A, Lundberg I. Acute pesticide poisonings among Nicaraguan sprayers. Submitted

IV. Hruska A, **Corriols M**. (2002) The impact of training in integrated pest management among Nicaraguan maize farmers: Increased net returns and reduced health risk. Int J Occup Environ Health. 8(3):191-200

CONTENTS

LIST OF ABBREVIATIONS

APP	Acute pesticide poisoning
BCN	Central Bank of Nicaragua
CA	Central America
CI	Confidence Interval
DBCP	Dibromochloropropane
DDD, DDE	DDT metabolites
DDT	1,1,1-Tricloro-2,2-bis(4-clorofenil)-etano
FAO	Food and Agricultural Organization
GDP	Gross domestic product
HAS	Hectares
HB	Hemoglobin
IFCS	Intergovernmental Forum on Chemical Safety
INIDE	National Institute of Statistics and Census
IPM	Integrated Pest Management
IPCS	International Program on Chemical Safety
IUPAC	International Union of Pure and Applied Chemistry
MAGFOR	Ministry of Agriculture and Forestry.
MINSA/MOH	Ministerio de Salud de Nicaragua /Ministry of Health
PND	National Development Plan
PPE	Personal Protective Equipment
RESSCAD	Central American and Dominican Republic Ministries of Health Meeting
OC	Organochlorine
OP	Organophosphate
OPIDP	Organophosphate-induced delayed polyneuropathy
PAHO	Pan American Health Organization
PLAGSALUD	Proyecto Aspectos Ocupacionales y Ambientales de la Exposición a Plaguicidas en CA
PROMAP	Programa de Manejo de Plaguicidas
RR	Relative risk
RUP	Restricted use pesticide
SPU	Safe pesticide use
US	United States
WHO	World Health Organization

1 INTRODUCTION

Pesticide exposure is growing and represents an important occupational and public health problem (WHO, 1992). The largest group at risk of adverse health effects is agricultural workers but through environmental and accidental exposure, the general population also is exposed (Jeyaratnam, 1990). WHO estimations of acute pesticide poisonings and deaths due to these could not reflect reality. Unfortunately, the true size of the pesticide health problem is not known owing to difficulties in registering intoxications, particularly in developing countries, where health facilities in poor communities fail to diagnose cases and deaths due to pesticide poisonings (Wesseling et al., 1997). Such is the situation in Latin America. However, in the last decade, a number of studies in South and Central America have made important contributions to improving knowledge about the magnitude of the problem (Henao et al., 1993; Campos and Finkelman, 1998; Diaz and Lamoth, 1998; PAHO, 2000a; Galvao et al., 2002; PAHO, 2003; Chelala, 2004; Faria et al., 2005). Furthermore, a recent evaluation of the acute pesticide poisonings surveillance system showed a progressive increase of the incidence of poisonings as well as of the associated mortality and lethality. This has occurred in close relation to the increase of imports of pesticides (Arbelaez and Henao, 2002).

Even when active epidemiological surveillance is implemented, the figures registered are much lower than estimates based on self reports (Cole et al., 1988; London and Bailire, 2001; Osorio, 2002; Calvert et al., 2004). In more developed surveillance systems like in California, available data still do not take into account those exposed persons that, having become ill, did not visit a physician or call a poison centre, as well as cases of non-agricultural occupational exposures (Maddy et al., 1990).

We have not found studies that analyzed the pesticide poisoning incidence among the general populations (including non medically treated pesticide poisonings) in Central America and other developing countries. Official figures only report partially the cases that received medical care at health facilities. After years of institutional strengthening of the surveillance systems, only 7000 cases were reported in the Central American Region in 2000 (Murray et al., 2002) and they represented, according to PAHO estimations, between 1 and 20% of expected cases (PAHO, 2002; Arbelaez and Henao, 2004).

2 BACKGROUND

2.1 PESTICIDES IN DEVELOPING COUNTRIES

Pesticides are chemical substances used worldwide in agriculture and public health for the control of pests. While their benefits are well known, knowledge about adverse effects of pesticide exposure on human health used to be limited (Jeyaratnam, 1985; WHO, 1990). Today, however, the literature on health effects from exposure to pesticides is increasing rapidly (Clapp et al., 2008, Andersen et al., 2008).

The adverse health effects are more common in less developed countries because of weak regulation, low hazard awareness of users, inadequate use of personal protective equipment, lack of proper care during application and use of highly toxic pesticides. Accidental and intentional poisonings have been studied more thoroughly than the occupational ones through hospital and toxicological center reports (Leveridge, 1998; Calvert et al., 2004; Nagami et al., 2005; Martins et al., 2006; Tagwireyi et al., 2006; Bochner, 2007; Rajasuriar et al., 2007). In developing countries, reported occupational and non-intentional causes vary from 10 to 50% (WHO, 2004). Many studies reported the health effects of pesticide exposure in the America´s Region (Henao et al., 1993), in Central America (Henao et al., 1993; Wesseling et al., 1997) and in specific countries: United States (Bell et al., 2006), Guatemala (Campos and Finkelman, 1998), El Salvador (Jenkins, 2003), Nicaragua (Cole et al., 1988; Mc Connell et al., 1993, Amador, 1993; Miranda, 2003; Aragon, 2005; Blanco, 2008), Costa Rica (Leveridge 1998; Wesseling et al., 1993, Wesseling, 1997, Wesseling et al., 2001a), Panama (Diaz and Lamonth, 1998), Bolivia (Jors et al., 2006), Ecuador (Cole et al., 2002) and Brasil (Faria et al., 2005; Martins et al., 2006).

About 7.5% of agricultural workers in Sri Lanka, 7.3% in Malaysia (Jeyaratnam et al., 1987), 4.5% in Costa Rica (Wesseling et al., 1993) and 2.2% in Brazil (Faria et al., 2005) have been estimated to be intoxicated in one year. In Vietnam, about 31% of farmers reported one episode compatible with acute pesticide poisoning during one year (Murphy et al., 2002). In Indonesia, 21% of pesticide spraying operations resulted in three or more neurobehavioral, respiratory, and intestinal signs or symptoms (Kishi et al., 1995). In United States, 7% of the cohort of licensed restricted-use pesticide applicators for whom health care visit data were available reported one or more pesticide-related health care visits (Alavanja et al., 1998). Only a small proportion of cases sought medical care, suggesting that pesticide poisoning surveillance data may seriously underreport the frequency of such events (Bell et al., 2006).

2.2 PESTICIDE EXPOSURE AND EFFECTS IN NICARAGUA

Pesticide use in Nicaragua has been mainly associated to agricultural production, but public health and domestic pest control is also relevant. As summarized in Table 1, since 1950, its use has been associated to environmental, agricultural and health problems, affecting mainly rural population. This situation is comprehensively analyzed by Murray (1994). The country's principal traditional export for three decades (1950-1980) was cotton. Cotton crop was associated to a high pesticide use, up to 28-35 times a season (Sweezy et al., 1986), provoking a vicious circle which increased pest resistance, and non sustainable production, evolving in a huge ecological crisis. The negative impact of massive pesticide use in cotton crop extended to other crops, such as sugar cane, bananas and coffee, due to the negative impact on beneficial pests, which increased the need to

apply more pesticides. Since the 60´s decade, pesticides have been used not only for export crops but also for small farmer's basic grain subsistence production. Moreover, pesticide multinationals introduced in the national market products which were prohibited, severely restricted or not registered in developed countries and for which there was scarce health or environment information available to the national regulatory authorities.

Table 1 Main characteristics of pesticide use in Nicaragua 1950-2000

Decades	Main characteristic of pesticide use in Nicaragua
50´s	Latifund model. Experiments with organochlorine pesticides in the country. DDT was widely used to control cotton crops (3000 has).
60´s 70´s	Cotton crop increased to 150,000 has (The country was in the first 24 world cotton producers). Cotton boom increased rich-poor gap. 50% reduction of basic grain cultivated area. GDP, poverty and malnutrition increased Millionaire loans to buy pesticides for cotton and basic grain crops Central American Market approved insecticide formulation plant (HERCASA), main toxaphen provider for CA and US. Companies established marketing networks and promoted their products through agricultural students, technicians and extensionists. Growing concern about pest's resistance. Change of pests' patterns and destruction of beneficial pests. Increased environmental, health and economic costs. First pesticides prohibited: aldrin, leptofos and DBCP.
80's	Social inequity caused social changes in Central America. Nicaraguan Revolution: agrarian reform, land and subsidies to poor peasants, increased access to pesticides. Donation of toxic products from other countries. DDT used in public health campaigns. Second pesticides prohibitions: dieldrin, endrin, lindano, dibromuro de etilo, 2,4-5 T and chlordimeform
90´s	Return to neoliberal economic model and reversal of agrarian reform. New agricultural model based on crop diversification. Reduction of agricultural subsidies and opening of new international markets. Free trade agreements. Definition of pesticide residue limits for exports. Self-regulation of the international cooperation for development. Third prohibitions: Pesticides´ dirty dozen. Advances in approval and adherence to international instruments. Mega projects for pesticide management (PROMAP/World Bank, PLAGSALUD/PAHO) generated evidence about environmental and health impact, and helped to improve legal framework and sector policies. Workers´ denounces and demands for pesticides chronic effects.
00's	RESSCAD recommended to ban or to restrict the new dirty dozen of pesticides in CA. New projects to comply with International Environmental Agreements (Stockholm Convention, Rotterdam Convention and Montreal Protocol) Increased demands from cane workers affected by DBCP Limited improvement of environment and health policies and strategies.

In the 1980's, under the revolutionary period, the country implemented social reforms, redistributed agricultural land to small farmers and provided universal health coverage. In the same decade, different factors determined the change of the agricultural pattern in the country: the drop of price for agricultural products, the war and the occurrence of natural disasters. Regardless of these influences, during the last twenty years, agricultural activity remained as the main economic source for the country (Murray 1994). The cotton crop´s areas reduced from 220,000 hectares to less than 3,000, and were replaced by traditional crops, mainly coffee, sugar cane, bananas, tobacco, beans, and more recently for nontraditional crops as black beans, peanuts, sesame and vegetables.

In 2000, Nicaragua, held a gross domestic product (GDP) of $2.4 billion and a per capita income of $466, and was the second-poorest country in the Western Hemisphere, depending largely upon agriculture, the main economic pillar (BCN, 2001). Since 1998, strengthening agricultural competitiveness based on export growth has been a key element of the country's development strategy (PND, 2001). Even though agricultural products provide one third of the GDP and employment and two-thirds of the nation's exports, the agricultural sector works with obsolete technology (BCN, 2001). In the year 2000 the country had 2,746,000 hectares of cropland and cultivated nearly one million, 70% with basic grain crops (MAGFOR, 2001).

More than one third of the population currently works in agriculture. The agricultural workers, one third of them small producers, earned an average of US$119 per month and were the lowest paid workers of all economic sectors (BCN, 2001). Besides their situation of poverty, pesticide use poses health and environmental risks affecting their quality of life and constraining the country`s productivity. This occupational risk is not being properly addressed by governmental programs and policies, and is resulting in alarming health effects.

2.2.1.1 Environmental effects

Since 1993, several studies were developed documenting the negative effects of pesticide misuse: environmental pollution due to chlorinated hydrocarbons in coastal lagoons of the pacific coast (Carvalho et al., 1999), river basins, coastal lagoons and old cotton fields. High concentrations of pesticides have been detected in river waters and sediments. DDT, DDD, DDE compounds and toxaphene are the most frequent organochlorine residues found in the water and sediment samples, while endrin, aldrin, dieldrin and lindane are mainly found in the waters of rivers and wells (Castilho et al., 2000). Despite the ban on the use of toxaphene and DDT, their residues continue entering the coastal lagoons due to erosion of, and leaching from, agriculture soils (Carvalho et al., 2002). Toxaphene is expected to remain in the coastal ecosystem and consumption of seafood may expose the population to unacceptably high intake of it (Carvalho et al., 2003). Due to the importance of toxaphene persistence its degradation process has been recently studied (Lacayo et al., 2006).

The first evidences of organochlorines (OC) residues in blood plasma were reported in 1993 (Rugama et al., 1993). Other studies also reported the presence of OC pesticide residues in cows´s milk (Zapata et al., 1996), human milk (Romero et al., 2000) and its effects in perinatal metabolism (Dorea et al., 2001). The persistent DDT metabolite pp'-DDE, was present in all samples of blood serum, adipose tissue, and breast milk.

Higher levels of pest's resistance to pesticides were found to those frequently used, mainly pyrethroides (Perez et al., 2000, Rueda and Shelton, 2003). Insecticide resistance in *Ae. Aegypti*, the dengue virus vector, was also reported as a serious problem facing control operations (Rodriguez et al., 2007). Very little is known about pesticide use among cattle workers. There is only a recent study that found misuse of insecticides for the treatment of cattle pests (Villarino et al., 2003).

2.2.1.2 Acute effects

The first evidence of APP in Nicaragua was reported by the Food and Agricultural Organization (1972), estimating nearly 3,000 yearly cases in the 60´s. The incidence rate was estimated in 176 cases/100,000 habitants, eight times higher compared to the US APP rate, a country which applied 25% of world´s pesticides. Pesticide poisoning was recognized as a major public health problem in Nicaragua in the Sixties-Eighties decades (Sweezy et al., 1986).

In 1987, 19% of crop duster aviation mechanics reported an APP episode in the previous year, related to some risk factors: less than one year in job and paradoxically, change work clothes less often than daily. Previous training (26%) did not seem to prevent APP (Mc Connell et al., 1990). Following to this study, an intervention study in the same area implemented changes in airstrip technology, and presented the paradox of the failure of closed system pesticide mixing which increased the hazard of protective technology when it was inappropriately applied. While a beneficial effect of training was shown, the availability of PPE had no influence on the prevention of cholinesterase reduction (Mc Connell et al., 1992).

Corresponding with the social reforms previously mentioned, in the region most exposed to pesticides, in the middles 80´s, an APP surveillance system began to register pesticide poisonings and deaths. Between 25 and 100 APP were reported monthly in a 630,000 population. The two peaks in frequency observed corresponded to the cultivation of maize and cotton. This incipient surveillance system was able to identify the occurrence of the first APP epidemic reported in the country. In 1987, the use of RUP carbofuran and methamidophos caused one of the main epidemic outbreaks reported in scientific literature (548 APP, mostly affecting small maize farmers). The main contributors to the epidemic were unsafe working conditions (manual application of pesticides and use of backpack sprayers), hazardous formulation of carbofuran, and agricultural subsidies that promote pesticide use (Mc Connell and Hruska., 1993).

In 1989, a study of agricultural cooperatives in the most exposed region in the country showed a 25% of incidence of APP among farmers (Keifer et al., 1996). Local studies estimated that 10% of exposed agricultural workers were intoxicated every year (Corriols and Rivas, 1992), and that at least 50% of farmers have been poisoned at least once in their lives (Castillo and Manzanares, 1993). In addition to occupational exposure, pesticides were used as method of para suicide in 19.1% of the attempts and represented a significant health problem among young people in Nicaragua (Caldera et al., 2004).

As seen in Figure 2, officially reported cases of APP at the national level increased from 322 in 1990 (MINSA, 1991) to 1651 in 2000 (MINSA, 2001). This improvement of the register of cases was possible due to the institutional strengthening of the surveillance system granted by international cooperation from CARE Nicaragua and PAHO. Even

though in 2000 the reported figure was five times greater than in 1990, a continuous underreport was masking the real situation.
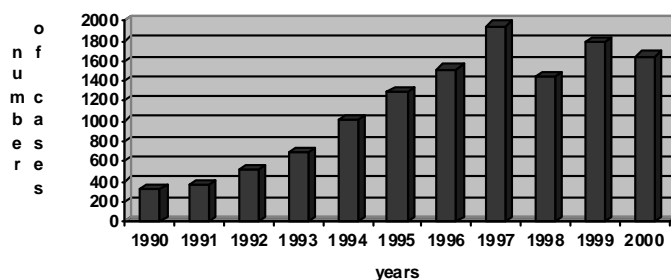

Figure 1. Acute pesticide poisonings cases, Nicaragua 1990-2000

Source: Ministry of Health. Pesticide Program Surveillance System

2.2.1.3   Chronic effects

The first study related to chronic effects was developed in Leon, between 1986 and 1988. This retrospective study of agricultural workers who had been admitted to hospital for occupationally related OP intoxication found that poisoned workers, tested two years after an episode of APP, did much worse than the control group on all neuropsychological subtests when compared with a matched control group. Their findings emphasized the importance of prevention of even single episodes of organophosphate poisoning (Rosenstock et al., 1991).

Following the evaluation of chronic effects of organophosphate APP, another study found that over one fourth of agricultural workers had abnormal vibrotactile thresholds, suggesting that previously reported cases of organophosphate-induced delayed polyneuropathy (OPIDP) represented the worst sequel of exposure (Mc Connell et al., 1994; Mc Connell et al., 1999a.).

Other studies demonstrated that residents of communities living near sprayed fields were significantly more likely to complain of one or more acute and/or chronic symptoms, showing strong association between exposure to aerial pesticides and symptoms (Keifer et al., 1996). In the same region, subclinical health effects of environmental pesticide contamination were found in 35% of exposed children who had abnormally low cholinesterase levels (Mc Connell et al., 1999b).

Another study reported respiratory symptoms, spirometry and chronic occupational paraquat exposure among 134 workers. Nail damage was the most frequent symptom reported (58%), followed by skin rash or burn (53%), paraquat splashed in the eyes (42%) and epistaxis (25%); and a high prevalence of respiratory symptoms (i.e dyspnea and episodic wheezing) associated with exposure (Castro et al., 1997).

In the following years, continuous evidence was generated about peripheral neuropathy: Grip and pinch strength were impaired among all OP-poisoned subjects (Miranda et al., 2002a); threshold impairment as a consequence of severe intentional poisonings with

neuropathic OPs (Miranda et al 2002b.; Miranda et al 2003); persistent, mainly motor, impairment of the peripheral nervous system two years after OP poisoning, possibly due to remaining OPIDP (Miranda et al., 2004); visuomotor performance and possibly short-term verbal memory affected after severe acute OP poisoning (Delgado et al., 2004).

2.2.1.4 Exposure assessment

More recently, pesticide research in Nicaragua has been developed on methods for pesticide exposure assessment. Urinary levels of chlorpyrifos applicators and their families (Dowling et al., 2005) and saliva biomonitoring of diazinon in plantation workers (Lu et al., 2006) were measured initially. The biological monitoring of pesticide exposures among applicators and their children had shown that proximity to spraying and spray mixture preparation in homes were important exposure factors to diazinon. Workers and children were also exposed to chlorpyrifos through contact with impregnated bags used in banana production (Rodriguez et al., 2006).

Several studies have been evaluating dermal exposure. Aragon et al (2004) had studied the reliability of a visual scoring system with fluorescent tracers to assess dermal pesticide exposure and its modification for developing countries (Aragon et al., 2006). Blanco et al (2005) showed that a combination of observation and visual scoring techniques can provide valuable information on determinants of pesticide exposure and proposed an approach for developing countries (Blanco et al., 2008). More specifically, insecticide residues on hands were assessed and modeled with video observations of determinants of exposure (Lopez et al., 2009).

2.3 THE NICARAGUAN PESTICIDE POISONING REGISTER

In 1979, the National Unified Health System in Nicaragua included APP cases in its list of mandatory reportable diseases. Despite this, reporting of APP was rare through the early 1980s. Regulations and measures to enforce compliance did not exist. The reporting of information was not linked to any action on the part of the health sector. While some information could be obtained from hospital registers, the country did not have an official register for APP until registration of cases began in 1983 in the western region, Leon and Chinandega departments (Cole et al., 1988). By 1990, the register was extended to four other departments in the Pacific region (Masaya, Granada, Carazo, and Rivas). Finally, in 1995, the Ministry of Health created a national program (MINSA, 1995), which made APP case reporting compulsory on a national, standardized registration form. From 1995 to 2002, APP surveillance strengthened in Nicaragua and other Central American countries with international cooperation and support (Murray et al., 2002).

The official register of acute pesticide poisonings is based, since 1995, on a compulsory notification of all cases. According to the surveillance system's definition, a case of APP is any case in which a person develops the clinical manifestations of poisoning within 24 hours of being exposed to one or more pesticides by any route of exposure (dermatologic, respiratory, digestive, or other). Doctors and nurses who provide health care to patients in health centers, clinics, or hospitals must report such cases.

The required written forms include information on the patient's sex, age, address, occupation, condition of exposure, type of pesticide, diagnosis, treatment, and source of the information. These forms are collected by epidemiological surveillance officers at the

health care facility level, who analyze the information and perform outbreak control activities. At the end of the day, the officers report the number and main characteristics of the cases by telephone to the surveillance system at the municipal level. The municipal level then sends this information to the departmental level, and the departmental level to the national level. The written forms from health care facilities are sent to the municipal level monthly and from there to the pesticide program at the departmental level. Departmental epidemiologists transfer the information to a computerized database, analyze the information, and develop activities for prevention and control of pesticide exposure. All 17 departmental surveillance systems send their information to the national pesticide surveillance program database. At the national level, the information is compiled, analyzed, and distributed with the aim of generating input for the development of better health policies, legislation, and preventive programs. The national level defines the pesticide program norm to be implemented throughout the country.

It was evident that APPs were a severe health problem in Nicaragua. Despite this, the official figures represented a substantial underestimation of the real incidence. In 1988, a self report study of 633 workers at 25 agricultural cooperatives found that only 8 of the 23 subjects self reported as poisoned were found in the MOH register. Considering that 65% estimate underreporting to the registry, 6,700 (95% CI 4,100-18,000) systemic poisonings were estimated to occur in that region (Keifer et al., 1996). In 1995, a health units underreport study in eight departments found 45% of underreporting of APP cases who attended public health centers and hospitals (Corriols, 1995).

2.4   THE ECONOMIC COST OF PESTICIDE POISONING

Despite the great direct and indirect costs, agricultural producers depend heavily on pesticides in their attempts to avoid lost crops owing to pest attacks. The farmer, however, in his immediate short-term economic calculations of cost and benefit only has to consider the direct costs of purchasing and applying the pesticides. The indirect, long-term costs (health effects, environmental degradation etc.) are paid by the families and the public health and environmental sectors.

Pimentel calculated the external costs of pesticide use in the United States in 1981 at $8,123 billion (Pimentel et al., 1991). This was approximately the value of market of pesticides, meaning that for $1 spent on buying pesticides, society pays another $1. Few studies have been done to evaluate economic costs of pesticide use in Nicaragua. In 1993, Vaughan, calculated the costs of negative consequences of pesticide use in Nicaragua at $450,084,181, in contrast to a benefit reported by the agriculture of $89.000.000 in the same year. The relation between the amount spent on buying pesticides and the external costs in Nicaragua was 1: 10 (Vaughan, 1993).

Recently, the willingness-to-pay (WTP) approach was used to assess the health effects of chemical pesticides among Nicaraguan vegetable farmers. The farmers' valuation of health measured by their WTP for low-toxicity pesticides showed that farmers are willing to spend an additional amount of about 28% of current pesticide expenditure to avoid health risks (Garming and Waibel, 2009).

2.5 THE DETERMINANTS OF PESTICIDE EXPOSURE

There is growing evidence demonstrating the relationship between specific determinants and the occurrence of APP cases. Some studied determinants, mostly in agricultural settings are: socio-demographic (Van der Hoek and Konradsen, 2005), dermal exposure (Marquart et al., 2003), safe pesticide use and personal protective equipment use (Schenker et al, 2002; Cameron et al., 2006; McFarlane et al., 2008), knowledge, attitudes and practices (Strong et al., 2008; Flocks et al., 2007; Rao et al., 2006) risk perception, (Ibitayo, 2006; Austin et al., 2001), spraying risks (Kishi et al., 1995; van Wendel de Joode et al., 1996), training (Liebman et al., 2007), health promotion (Janhong et al., 2005, Buranatrevedh and Sweatriskul, 2005), violations of worker safety laws (Reeves and Schafer, 2003), legislation (Roberts et al., 2003; Calvert and Higgins, 2009), pesticides registry control (Gunnell et al., 2007), pesticides banning and financial incentives (Rautiainen et al., 2008), and gender (London et al., 2002a; Reed, 2006). Pesticide exposure and effects were also studied as an issue of ethical concerns, human rights and environmental justice (London and Kisting, 2002b; London, 2003)

In Nicaragua, the main factors associated to APPs had been historically determined. In the early 1900´s, after the liberal revolution with President Zelaya, agriculture was the base for the country´s development scheme. In the following decades, agriculture shifted from the traditional self subsistence´s crops to non- traditional agricultural exports. Even though the cotton crop was linked with the first pesticide use crisis, the substitution for other similar chemically dependent non- traditional crops aggravated the problem. Since the decade of the 1950´s, this development strategy relied on intensive pesticide use for pest control (Meyrat, 1992). In the international context, pesticides and fertilizers were considered as the key factors of modernization. Paradoxically, pesticide use led to a non sustainable model, causing dependence, chemical contamination of the environment and pesticide related illnesses. Murray (1994) attributed the persistence, and even growing, of the problem to the efforts to resolve it through alternative pest-control and safe use strategies, both parts of the traditional development paradigm which maximizes short-term growth opposed to environmental and socioeconomic sustainability.

Considering a broader framework of social determinants on health, we identified the following determinants for pesticide exposure and effects:

At economic level, the country participation in the international market is a key determinant of the development model based on export crops. The negative influence of international pesticide industries on weak national pesticides registries allows the register of highly toxic substances, often not registered in the country that exports it. Due to economic interests, chemical and agricultural industries do not withdraw dangerous pesticides voluntarily despite the growing evidence about chronic and acute effects. (Murray, 1984; Forget, 1991; Wesselinge et al., 2001b; Murray, 2002)

At the level of policy and regulatory framework, there is a permissive pesticide register for highly toxic substances and lack of compliance of current pesticide legislation, including the recommendations of the International Code of Conduct on the Distribution and Use of Pesticides of the Food and Agriculture Organization (FAO 1990; Wesseling et al., 2005). This situation continues despite the fact that Central American countries agreed in 2000 to

ban or to restrict twelve of these more toxic pesticides (PAHO, 2000b; Wesseling et al., 2005).

At environmental, agriculture and health sector levels, there is a lack of sustainable agricultural policies, insufficient promotion of IPM and organic agriculture (Weinger 1992), inadequate monitoring of pesticides' environmental and health effects, and deficient use of the evidence about adverse effects (Wesseling et al., 2005).

At the working environment level, many authors have reported unsafe conditions of pesticide application (Blanco et al., 2005), inadequacy of protective devices and environmental factors (Aragon et al., 2001; Aragon et al., 2006). This situation is aggravated by the extensive use of very hazardous pesticides, despite the growing documentation of acute pesticide poisonings during several decades and recently. Dermal exposure to pesticides is one of the most important factors associated with the low use of PPE and lack of appropriate training.(Aragon et al., 2001; Blanco et al., 2005; Aragon et al., 2006).

The individual factors are also important. Poverty and cultural factors are associated to dangerous work practices (Aragon et al., 2001). Knowledge, attitudes and practices regarding pesticide use are key determinants at this level.

2.6 THE NEED TO DEVELOP ALTERNATIVES

Strategies to reduce the exposure to pesticides are needed within the agricultural process. Alternative ways of pest control must be adopted, for example, integrated pest management and organic agriculture. Although there have been positive experiences, such alternatives are performed in Nicaragua only on a very small scale (less than 4% of agricultural producers).

In the 80´s decade, some interventions to reduce risks were implemented (McConnell et al., 1990) and sometimes, as the closed mixing system for air dust, they were ineffective or showed paradoxical effects (Mc Connell et al., 1992).

Adoption of alternative or non-chemical control on a large scale will be acceptable for farmers and governments only if their economic feasibility is comparable with the chemically based pest control system. Therefore, there is an urgent need to perform studies to reveal the costs of the pesticide use, including the health and environmental effects, as well as whether or not these alternative forms for pest control are effective and efficient. Such studies could serve as a basis for politicians and decision makers in defining realistic and sustainable development policies to reduce the adverse health and environmental effects of agricultural pest control in Nicaragua. Several studies developed in other countries reinforce the need to implement integrated approaches (Wesseling et al., 2001b; Kishi, 2002; Kesavachandran et al., 2009; Weinberg, 2009; Mancini, 2009).

By putting into practice a sustainable approach, the country shows a positive trend to reduce the heavy use of pesticides in public health campaigns, implementing alternatives for domestic vector control (Kroeger et al., 1999) and for malaria control (Garfield, 1999). More efficient alternatives for Chagas disease vector (Acevedo et al., 2000) and dengue virus vector control (Hammond et al, 2007) has been reported.

3 OBJECTIVES

3.1 GENERAL OBJECTIVE

To investigate the health and economic impact of pesticide use and to discuss the possible effectiveness of structural preventive measures in Nicaragua.

3.2 SPECIFIC OBJECTIVES

a) To estimate the underreporting of APP in Nicaragua in the year 2000. (Study I)

b) To estimate the one year cumulative incidence of cases of APP among Nicaraguan population older than fifteen years in the year 2000. (Study II)

c) To examine the incidence, severity and main determinants related to acute pesticide poisonings (APP) among Nicaraguan pesticide sprayers in the year 2000. (Study III)

d) To assess the impact of farmers training in pesticide alternatives (integrated pest management) on agricultural, economic and health indicators (Study IV).

4 METHODS

4.1 STUDY AREA AND POPULATION

4.1.1 Study I, II, and III

In cooperation with the Nicaraguan National Institute of Statistics and Census, we collected a representative multistage sample of the entire Nicaraguan population aged 15 years and older. In the first stage, a random sample was drawn from each of the 17 national departments. The sample size for each department corresponded to the proportion of the national population living in that department. In the second stage, each department was divided into census segments and random samples chosen as in the first step. In the third step, homes were selected randomly within each segment as in the preceding steps. An individual who met inclusion criteria (age, ability to answer the questionnaire) was selected in each house from the group of eligible household members present when visited. We planned interviews with 3430 individuals and completed 3169, representing 92% of selected individuals. Part of the South Atlantic region (less than 4% of the national population) did not participate in the survey due to adverse weather conditions. The survey was conducted in November 2001 and the questionnaire asked for details about pesticide exposure and effects that occurred from January 1 to December 31, 2000.

In addition, for Study I, the total number of APP cases older than 15 years registered at the Ministry of Health surveillance system in 2000, consisting of 1384 APP cases was used as a secondary source of information.

For study III, as seen in Fig 1, we analyzed a subsample of 469 sprayers who were the most exposed group in the whole sample.

Figure 1: Distribution of sub sample of sprayers from the national survey   n=1369
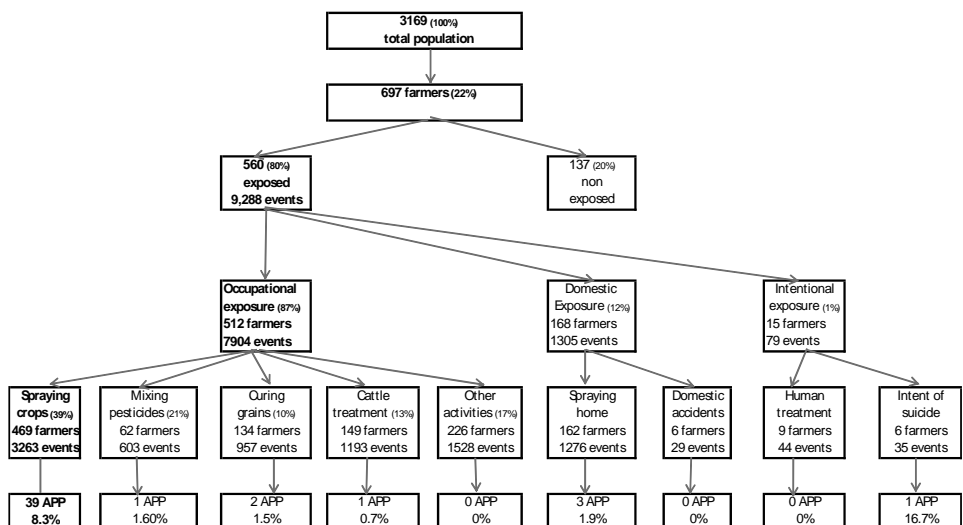
4.1.2 Study IV

In 1990, seven communities were chosen in the Departments of Chinandega and León, the most exposed region to pesticides in the country. These communities were chosen based on their high concentration of basic grain production under cooperative administration, high levels of pesticide use, high levels of reported pesticide poisoning and willingness to participate in the program. Fifty-five cooperatives were identified in the seven communities, with 1200 members and 60 agricultural promoters (promoters are trained farmers that volunteered to carry out demonstration plots and exercises on their farms, and to train neighboring farmers).

Eleven percent of the examined workers were promoters (intensively trained), 54% were non-promoter project cooperative members (trained), and the remaining 35% were members of control cooperatives (did not receive training). In the second year of the project the control cooperatives were offered to participate in the training and became trained cooperative members.

4.2   INTERVIEW QUESTIONNAIRE

4.2.1   Studies I, II, and III

A questionnaire designed to reveal pesticide exposure and its acute health effects was validated in a pilot survey performed in a sample of 600 inhabitants from rural and urban areas of Nicaragua (Corriols et al., 1999). The questionnaire was adjusted following the pilot survey. We confirmed that the questionnaire's questions were clearly understood by respondents and that we were obtaining appropriate information regarding pesticide exposure and health effects.

Detailed information was collected on socio-demographic and economics characteristics (sex, age, area of residence, occupation, income, level of education, employment and occupation), exposure assessment in the year 2000 (pest control activities, pesticide contact, frequency and duration of pesticide exposure, previous training, use of personal protective equipment, unsafe pesticide handling and application practices), health effects (presence of signs and symptoms in 2000, knowledge of the definition of acute pesticide poisoning, self-reported pesticide poisoning in lifetime and in 2000, name of pesticide causing the acute poisoning, activity related to acute pesticide poisoning, type of attention received), and health and economic consequences (number of days lost because of disability, cost of health care).

Symptoms related to cholinesterase inhibiting pesticides, pyrethrins, herbicides, fumigants and other pesticide exposure were included in the questionnaire. These symptoms were: headache, blurred vision, salivation, dizziness, nausea, vomiting, dyspnoea, muscle cramps (tremor and muscle twitching), asthma, fatigue, itchiness, skin lesions (irritation, rash, erosion, blistering), nail lesions (damage, lost), eye injuries, lack of concentration, muscle weakness and depression. The respondent also could report any other symptom that they had experienced even though it was not listed.

In addition, for study I, the APP compulsory case report form was used. We had access to the national pesticide program electronic data file to obtain all the cases older than 15 years registered in year 2000.

4.2.2   Study IV- Intervention register

This is an intervention study that compares three different groups of farmers, with different levels of exposure to IPM (Integrated Pest Management) training. Data on agricultural practices, pesticide use, pesticide expenditures, crop yields, and net returns were obtained during 1990-1991 and collected via a field book.

4.3   DATA COLLECTION

4.3.1   Studies I, II, and III

The gathering of data was carried out carefully by a trained group of health personnel under the close supervision of the research team. Local health workers responsible for the Pesticide Control Program administered by the Ministry of Health were trained as interviewers by the research team. The interviews took place in the interviewees' homes. The participants were informed about the purpose of the study and gave verbal consent to participation. A field supervisor reviewed the quality of the data gathered and entered them in a database for analysis. The data were collected during November 2001.

Two sources of information for acute pesticide poisonings will be used in this study: the National surveillance system of the Ministry of Health and a self report survey applied at the community level (by multiphase sampling). The surveillance system is supposed to capture all the pesticide poisonings that occur in the country and are attended in a public health unit. Nurses and doctors at different levels of the Ministry of Health fill out a specific questionnaire which is then reported through the surveillance system. The study used the information gathered at national level in 2001 and included variables related to pesticide exposure and acute pesticide poisonings in 2000.

4.3.2   Study IV

The intervention groups (farmers and promoters) were trained in IPM techniques by 13 agricultural extensionists (extensionists are agricultural technicians that provide technical assistance to the farmers) in a rural development program. The intervention consisted of training farmers with simple IPM techniques to reduce the use of pesticides on maize through an agricultural extension method. The techniques taught during the first year of training (1990) consisted principally of the management of two principal maize pests, the fall armyworm and the corn leafhopper. The first steps in managing pests are the correct identification of the pests, the relation of the pests to crop damage and yields, an understanding of insect ecology, including natural enemies, and the entering of fields to scout pest presence and estimate population levels.

In addition to the trained farmers (producers and promoters), a group of 'control' farmers was monitored. They were matched based on geographic zones, areas of planted crops planted, and type of crops grown with the trained farmers. They did not receive training during the intervention.

Data on pesticide use, including product used, date of application, dosage, and costs, and data on crop yields were collected via the field notebooks that farmers kept with the help of the extensionists.

Cholinesterase levels were measured between January and November, 1991. The Cholinesterase Testmate Kit (EQM Research, Cincinnati, Ohio) was used to measure erythrocyte cholinesterase in blood samples.

To determine the normal range for our population we used values from 378 unexposed Nicaraguan agricultural workers from January through May 1991. In addition, we used pre exposure values from a representative group of farmers (9 promoters, 28 intervention cooperative members and 24 control cooperative members) before the agricultural cycle began, when the farmers had not manipulated pesticides. Post exposure tests were performed on161 workers who had manipulated organophosphates in the preceding 30 days.

4.4 EXPOSURE AND SELF-REPORT CASE DEFINITION

4.4.1 Studies I, II and III

Exposure and health effects (signs, symptoms and acute pesticide poisonings) were self-reported. The participants were specifically asked if they were exposed to pesticides in 2000 (January 1st - December 31) and if after that exposure they had suffered signs, symptoms, and considered themselves to have been poisoned.

Acute pesticide exposure was defined as contact between a pesticide agent and a person occurring over a short time period, generally less than a day. For this study, a self-reported case of acute pesticide poisoning was defined as a person who considered himself to have suffered an acute pesticide poisoning event in 2000 as a consequence of a reported acute exposure to one or more pesticides at any dose and by any route (dermatological, respiratory, digestive or other), and who developed any clinical manifestation of poisoning related to the reported pesticide in the first 24 hours after the exposure.

An acute pesticide poisoning case was self-reported but was confirmed by the researchers. Each self-reported case had to provide a plausible description of pesticide exposure that had occurred in the 24 hours immediately preceding the reported health effect. These reported effects were reviewed by toxicologists who established the relationship between them and the pesticide reported. The presence of a known toxic syndrome or at least three symptoms or one physical sign compatible with the reported pesticide exposure was considered as an acute pesticide poisoning case.

4.4.2 Study IV

Unexposed: farmers that had not applied pesticides in the preceding 30 days.

Exposed: farmers exposed to pesticides in the last 30 days.

Pre exposure cholinesterase values: farmers' values before the agricultural cycle began, (January through May 1991) when the farmers had not manipulated pesticides.

Post exposure cholinesterase values: farmers' values during the agricultural cycle when they had manipulated organophosphates in the preceding 30 days.

Low cholinesterase level: Twenty percent below the "normal" or "pre exposure" value was considered a depressed level, indicating significant exposure to cholinesterase-depressing pesticides.

4.5 DATA ANALYSIS

4.5.1 Studies I, II, and III

For studies I, II, and III, specific information was obtained about the cases who self reported poisoning. The self-reported cases were analyzed by sex, age, occupation, area of residence, type of exposure, type of poisoning, specific pesticide and severity. The cases were also classified as intentional (intending suicide) and non-intentional (occupational and accidental). We used the WHO poisoning severity score that classifies cases by severity of symptoms, and also analyzed, the number of work days lost due to illness and the location where health care was received (no attention, self-medication at home, health centre and hospital). This allowed us to relate the clinical manifestations of poisonings with the therapeutic behavior of patients and their families and the impact on workers' productivity.

For study I, in 2001, one year after information was sent from the local to the national level through the reporting procedure, we analyzed the national pesticide surveillance program database for APP case matches between our questionnaire data and the registry data. We estimated the level of underreporting based on the percentage of self-reported cases that matched with the registry. We also reviewed the Ministry of Health evaluation reports on the pesticide program surveillance system in 2000.

For study II, the 1-year cumulative incidence rates in the entire cohort and in different subgroups (age, sex, occupation, area of residence, educational level and type of poisoning) were calculated. Based on estimated figures of the Nicaraguan population in 2000, we applied these specific rates to calculate the number of individuals in each subgroup and in the entire population who had experienced an episode of acute pesticide poisoning. The 95% confidence limits for these estimations were determined. The data analysis was carried out using SPSS v 13.

For study III, the number of acute pesticide intoxications among sprayers in Nicaragua during the year 2000 was estimated based on the incidence rate of APP among sprayers (obtained from the number of sprayers and the self reported cases among them during the year 2000 obtained from the sample), and the estimated population of sprayers (obtained from multiplying the proportion of agricultural workers that had participated in spraying activities in 2000 and the estimated population of agricultural workers older than 15 years in Nicaragua. To estimate the number of APP cases among sprayers we multiplied the incidence rate among sprayers and the number of estimated sprayers in the country. The 95% confidence interval was calculated for both the APP incidence rate among sprayers and the estimation of sprayer´s population. The confidence interval for the estimation of number of sprayers poisoned was calculated by multiplying both lower and upper limits of the sprayers´ incidence rate by the lower and upper limits of the sprayer´s population. This wide interval reflects the uncertainties based on estimates that involved two estimations.

For study III, the WHO (2004) poisoning severity score was used to classify cases by severity of symptoms, and, in addition, by the number of work days lost due to illness and the place where health attention was received (no attention, self medication at home, health centre and hospital).

For study III, an univariate analysis was calculated to analyze the associations between potential determinant variables (general categories were substance and product characteristics, tasks done by the worker, process techniques and equipment, exposure control measures, worker characteristics and habits) and the occurrence of APP. Variables

were excluded from the multivariate analysis since they were neither significant in the univariate analysis (p<0.05) nor associated with odds ratios less than 0.8 or more than 1.2 in the univariate analysis. Seven variables (age, cleaning pump nozzle by mouth, backpack pump leakage, training before pesticide use, having eaten while applying without washing hands, preparing the mix of pesticides and incomplete use of PPE) were examined in unconditional logistic regression analyses with odds ratios as the indicator of effect. The crude and adjusted (adjusted for all seven other variables) odds ratios with 95% confidence limits were calculated. The data analysis was carried out using SPSS version 16.

4.5.2 Study IV

Descriptive statistics on crop yields, pesticide use, pesticide expenditures and net returns to pesticide use were calculated and comparison between the three groups of farmers was done. From these data the economic return of each group of farmers was calculated.

To analyze the cholinesterase levels, we compared pre and post exposure levels among the three groups of farmers. To construct the normal range for our population we used values from 378 unexposed Nicaraguan agricultural workers from January through May 1991, obtaining a mean value of 33.19 iu/gr/hb (SD = 4.1, normal range 26.5–39.9). For a small group of farmers we compared pre and post exposure values.

5 RESULTS

5.1 STUDY I

This study estimated the level of underreporting of APP in the pesticide surveillance system in Nicaragua in the year 2000. Data concerning pesticide exposure and health effects were assessed in a nationally representative cross sectional survey of 3169 persons 15 years and older. More than half of the respondents (52.6%) said they were exposed to pesticides in 2000. As seen in Figure 1, we found 72 cases of self-reported poisoning in 2000. The analysis of treatment-seeking behavior showed that self-medication was the most common response to the event (48%), followed by visit to a public health unit (23%), staying at home without medication (22%), and seeking care from private providers (7%). Responses to questionnaires revealed 22 cases of APP that sought medical attention in the sample. In 2000 we found 1369 cases of APP in the official register. Only one of the 22 cases, less than 5%, that sought medical attention was reported to the national register (Figure 2). We estimated that nearly 30,000 pesticides poisonings received medical treatment and they were not reported.

Figure 2 Treatment-seeking behavior and reporting of cases
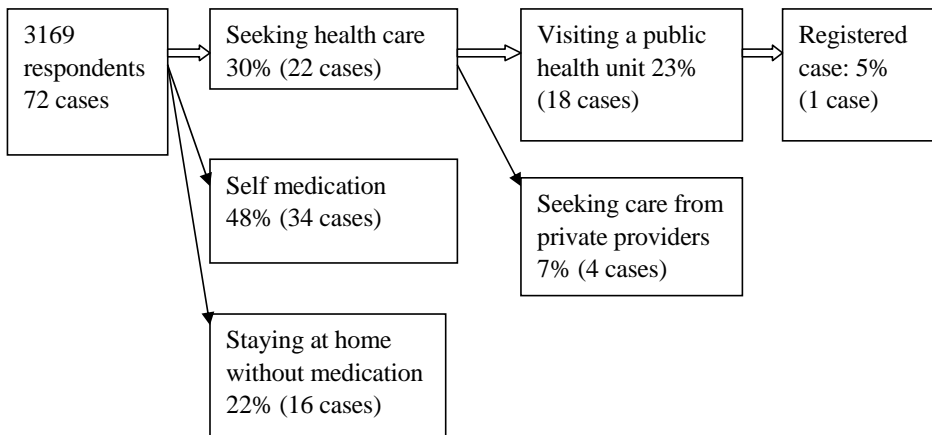
As seen in Table 1, most of the cases that searched for medical care were moderate and severe, and caused more than 3 days of absence from work. Most of these cases were agricultural workers spraying organophosphate pesticides, mostly Class-Ia-Ib (WHO, 2005). For 68% of cases, the out of pocket costs for the attention of one APP episode represented a mean of $41, almost equivalent to one month of salary. In the official figures, the non-occupational cases of APP registered in 2000 represented 62 percent of all registered cases (45% intentional and 17% domestic accidents), contrasting with the 9.6 percent found in our sample (2.8% and 6.8%, respectively). Occupational cases represent only 38 percent of the official figures but 91 percent of the cases reported in our sample. On the type of pesticides, the two more toxic pesticides, aluminum phosphide and paraquat, which are associated with intentional poisonings, appeared more often in the official registry figures than in our sample (19% and 10% for paraquat, 13% and 4% for aluminum phosphide, respectively).

Table 1   Medically treated self reported APP cases by severity in survey respondents in 2000 (n=3 169)

Score	Description of signs and symptoms	Days absent from work	Place of treatment	Self reported cases No.	%
1= minor	Mild, transient and spontaneous resolving signs or symptoms	<2	Health center	2	10
2= moderate	Pronounced or prolonged symptoms or signs	3-7	Health center Hospital	10	45
3= severe	Severe or life-threatening symptoms or signs	> 8	Hospital	10	45
Total				22	100

Note: Severity score modified by authors from WHO poisoning severity score (WHO, 2004)

5.2   STUDY II

Among the 3 169 survey respondents, we identified 72 persons who self reported one episode of acute pesticide poisoning. Of these, 90% were related to occupational exposure, 7% to domestic exposure and 3% to intentional exposure. The one year cumulative incidence rate/100 individuals of acute pesticide poisonings was 2.3 (CI 1.7-2.8) in the entire population of Nicaragua in 2000. This corresponds to 66 113 cases (CI 95% 51 017 – 81 210). As seen in Table 2, the cumulative incidence rate was high among males in rural areas, particularly among farmers, agricultural workers and cattle workers.

Table 2   Incidence and expected cases of acute pesticide poisonings in Nicaragua in 2000   n=3169

n	Number of respondents	Number of self-reported cases	Incidence of APP/100 individuals (95% CI)	National population > 15 years old in 2000	Number of expected APP cases (95% CI)
n	3169	72	2.3 (1.7 to 2.8)	2 909 911	66 113 (51 017 to 81 210)
Sex					
Female	1646	13	0.79 (0.36 to 1.2)	1 485 850	11 735 (5381 to 18 089)
Male	1523	59	3.9 (2.9 to 4.8)	1 424 061	55 167 (41 366 to 68 969)
Residence					
Urban	1866	26	1.4 (0.86 to 1.9)	1 600 451	22 300 (13 788 to 30 812)
Rural	1303	46	3.5 (2.5 to 4.5)	1 309 460	46 228 (33 107 to 59 349)
Occupation					
Farmers, agricultural and cattle workers	697	47	6.7 (4.9 to 8.6)	650,000	43 831 (31 730 to 55 932)
		25	1.0 (0.62 to 1.4)	2 259,911	22 855 (13 941 to 31 769)
Other	2472				
Education					
< 7 years	2088	59	2.8 (2.1 to 3.5)	1 920 541	53 775 (48 206 to 64 722)
>/ 7 years	1081	13	1.2 (0.55 to 1.8)	989 370	11 872 (5 442 to 18 303)

APP, acute pesticide poisoning.

26

5.3 STUDY III

We analyzed a subsample of 469 agricultural sprayers among whom 39 acute pesticide poisonings had occurred in 2000. As seen in Table 3, the incidence rate of APP was 8.3 (95% CI 5.8-10.8) per 100 individuals exposed in year 2000. The APP incidence rate seemed to be higher among men, younger than 30 years, urban residents, less educated and labourers, but the difference was significant only for the age group variable.

Table 3 Demographic and socioeconomic characteristics of the sprayers sample, pesticide exposure and APP incidence. n=469

Variable	Number of sprayers	Number of APP cases	Incidence rate per 100 individuals exposed	Relative risk (95% CI)
n	469	39	8.3 (5.8-10.8)	
Sex				
Male	432	37	8.6 (5.9-11.2)	1.58 (0.4-6.3)
Female	37	2	5.4 (1.9-12.7)	
Age group				
15-29	119	16	13.4 (7.3-19.6)	2.05 (1.12-3.74)
>30	350	23	6.6 (4.0-9.2)	
Education				
< 7 years	377	33	8.7 (5.9-11.6)	1.34 (0.58-3.11)
>/ 7 years	87	6	6.9 (1.6-12.2)	
Occupation				
Farmer land owners	352	25	7.1 (4.4-9.8)	0.59 (0.32-1.10)
Agricultural laborers	117	14	12 (6.1-17.8)	

5.3.1 Estimated cases among sprayers

In 2000, 34 149 cases were estimated (95% CI 23 764 - 44 533) to occur among pesticide sprayers in the country, representing 52% of all APP's estimated in Nicaragua in that year. Although most of the cases were minor and moderate the poisonings caused an estimated 338 070 (95%CI 235 265 – 440 876) disability days and a direct wages loss of $1 379 600 (95%CI 960 070 – 1 799 131).

5.3.2 Pesticide exposure in the 24 hours previous to the poisoning

The use of Class Ia-Ib (WHO, 2005) pesticides (parathion-methyl, terbufos, methamidophos, methomyl, and dichlorvos) in the previous 24 hours to the occurrence of an APP was reported as causal agent in 67% of cases. By far, methamidophos was the most frequently reported pesticide causing 44% of all cases. Twenty eight percent of cases were caused by Class II pesticides (chlorpyrifos, deltamethrine, cypermetrine, paraquat, copper sulfate and endosulfan) and only 5% of cases were caused by Class III pesticides (malathion).

Most cases were caused by pesticides (parathion-methyl, terbufos, methamidophos, methomyl, chlorpyrifos, paraquat and endosulfan) proposed to ban or to restrict in Central American by the RESSCAD (PAHO, 2000b).

5.3.3 Potential determinants of APP among sprayers

As seen in Table 4, in univariate analysis, "Backpack pump leakage", "No or incomplete use of personal protective equipment", and "Preparing the pesticide mix" appeared as significant determinants. After multivariate analysis, only "Backpack pump leakage", "No or incomplete use of personal protective equipment" were significant determinants.

Table 4   Main determinants of APP among sprayers (n=469)

Variable	Exposed % (n)	APP cases % (n)	OR crude (95% CI)	OR adjusted (95% CI)
Age <30 years	29 (137)	41 (16)	1.8 (0.9-3.6)	1.8 (0.9-3.5)
Cleaning pump nozzle by mouth	30 (143)	41(16)	1.7 (0.8-3.2)	1.1 (0.5-2.3)
Backpack pump leakage	47 (220)	77 (29)	3.6 (1.7-7.6)	3.5 (1.5-8.0)
Incomplete or no PPE Use	92 (429)	82(32)	2.7 (1.1-6.6)	3.3 (1.5-8.0)
Lack of training before pesticide use	75(351)	64(25)	1.8 (0.9-3.6)	1.6 (0.8-3.4)
Preparing pesticides mix	52 (242)	67(26)	2.0 (1.0-3.9)	1.2(0.6-2.6)
Eating while applying without washing hands	11 (50)	21 (7)	2.0 (0.8-4.7)	1.9 (0.7-4.8)

5.4   STUDY IV

Training had a highly significant effect on the number and dose of insecticide applications made during the production of the maize crop. Farmers with intensive and normal training applied 41% the number of applications of farmers without training. Farmers with intensive and normal training applied 22-35% of the chlorpyrifos and 43-102% of the methamidophos doses of farmers without training (Table 5).

Table 5   Effects of training on numbers of insecticide applications and average doses of chlorpyrifos and methamidophos   n=146

Training Group of Farmers	Average No. of Insecticide Applications to Maize Crop (n)	Average Dose (lt/ha) of Chlorpyriphos (n)	Average Dose (lt/ha) of Methamidophos (n)
Intensively trained	0.95 (57)	1.04 (17)	0.49 (6)
Trained	1.45 (70)	1.69 (26)	1.16 (13)
Not trained	2.32 (19)	4.79 (5)	1.14 (5)
p-value	< 0.0001	0.017	<0.001

Training (and the associated decrease in pesticide use) did not have a significant effect on maize yields. (Table 6) However, the training did have a significant effect on crop-production expenditures (purchased inputs). Farmers with intensive and normal training spent 70% to 75% of what farmers without training spent on crop production. The combination of the reduction of the expenditures on crop production and the similar yields resulted in training which had a significant effect on net returns from maize production. Farmers without training lost an average of $24/ha, while farmers receiving normal training had a net positive return of $12/ha and farmers receiving intensive training had a net positive return of $43/ha (Table 6).

Table 6   Effect of training on maize yields, production input costs and net returns   n=92

Training Group of Farmers (n)	Maize Yield (kg/ha)	Crop Production Input Expenditures (US$/ha)	Net Return (US$/ha)
Intensively trained (31)	1,690	205.49	43.33
Trained (50)	1,560	221.80	11.86
Not trained (11)	1,810	293.91	-24.04
p-value	n.s	<0.01	<0.05

The farmers who received the training (intensive and normal) showed no significant change in pre and post exposure cholinesterase levels (+1.6%) while farmers without training showed a significant decrease (–16.7%), indicating exposure to cholinesterase-inhibiting pesticides (Table 7). We analyzed the relative risk of having cholinesterase levels below the normal minimum value. There was a significant effect of training on the proportion of farmers who had cholinesterase activity below the 20% below normal threshold.

Table 7   Changes of cholinesterase levels of farmers with and without training during the pesticide spray season   n=92

Training group	Mean Cholinesterase Activity (IU/ g Hb)		Change (%)
	Pre-pesticide exposure	Post-Pesticide Exposure	
Farmers with training (intensive and normal	31.47	31.51	+1.6
Farmers without training	35.67	30.88	-16.7

Paired t-test, p=0.0009

Personal protective equipment (PPE) was used in a very incomplete manner. Less than 4% of farmers used complete PPE. Generally farmers used only one or two of the possible items of equipment (gloves, boots, masks, long-sleeved shirts, overalls). There was no significant difference in changes in cholinesterase levels between the farmers who used protective equipment, either individually or in combination, and the farmers who did not use the equipment.

Table 8.   Impact of use of protective equipment on cholinesterase levels   n=161

	Farmers who used equipment (n=161)	Mean cholinesterase activity (IU g/Hb)		p value
	%	Used equipment	Did not use any equipment	
Gloves	5.6	30.66	30.96	0.82
Boots	15.0	31.25	30.89	0.70
Overalls	3.7	30.25	30.97	0.68
Long-sleeved shirt	11.8	30.34	31.03	0.50
Mask	14.3	30.25	31.06	0.79

6 DISCUSSION

This thesis aims to evaluate the acute health impact of pesticide use in Nicaragua. To reach this purpose we demonstrated, in the first place, the huge underreporting of APP cases (95%), the number of cases medically treated and their direct costs ($41 per case). Secondly, we demonstrated that exposure to highly toxic pesticides is widespread in Nicaragua, especially among farm workers. We estimated there are approximately 66000 cases of APP annually, 90% of which are related to occupational exposure. In third, we identified in the most affected group of farmers, the sprayers (8.3 poisonings per 100 person years), the main determinants of APP which were backpack leaking pump and incomplete or no use of personal protective equipment. These inadequate precautions and conditions when applying Class Ia-Ib, II and other restricted pesticides in Central America were the main causes of APP. Around 34 000 cases of APP might have occurred among pesticide sprayers in Nicaragua in the year 2000, causing an estimated 340 000 disability days and $1.4 million of direct wage losses. Finally we demonstrated the positive impacts of IPM training reducing the dose and number of pesticide applications and increasing the yields obtained by trained farmers.

6.1 DATA COLLECTION

6.1.1 The participants selection

Studies I, II and III were based on a representative participant selection. In cooperation with the Nicaraguan National Institute of Statistics and Census, we collected a representative multistage sample of the entire Nicaraguan population aged 15 years and older. The sampling technique allowed us to obtain a representative sample of the whole country. Random sampling techniques ensured that there was very limited selection bias and had many advantages including convenience, economy and efficiency. The questionnaire was validated in a pilot survey. The non-response rate was low. The interviews were carried out by a trained group of technicians who were instructed not to influence respondents' answers. No benefits were involved in reporting poisoning.

Study IV was a non randomized intervention study where the participants were the agricultural cooperatives participating in the first year of an agricultural program. The control group was chosen from similar agricultural cooperatives that were incorporated in the second year of the program. Three categories of trained farmers were established allowing the comparison among farmers with different levels of knowledge and practices regarding IPM.

6.1.2 The methods selection

Studies I, II, and III were based on the same retrospective survey that explored pesticide exposure and the effects of that exposure on the population in the year before the survey. As subjects had to remember events that occurred 12–23 months previously, a memory bias is possible and is one possible weakness of this study. Each exposed participant provided a detailed description of the exposure and its effects; some could not recall the name of the pesticide involved. Pesticide exposure is so frequent among the Nicaraguan population that people easily characterized their exposure. They also remembered the specific pesticide they applied in the months before the survey.

The main concern regarding validity was the use of self reported data that could have underestimated or overestimated the incidence of toxic effects. However, the consistency

of reported exposure history, self-reported effects, days lost and out of pocket costs suggests poisonings were recalled accurately, especially the moderate and severe cases. Some of the reported cholinergic symptoms could have been caused by other factors such as heat stroke, while dermatological signs could also have been caused by trauma or infectious disease. Thus there is a possibility of over-reporting of symptoms. On the other hand, it is possible that some symptoms actually due to pesticides may have been attributed to heat stroke and not reported to the interviewers.

Even though 62% of exposed respondents reported they had experienced at least one sign or symptom after pesticide exposure, only 4% of them considered that they were poisoned after the pesticide exposure. Thus, the likelihood of minor cases being reported was lower than for moderate or severe cases. Therefore, our results probably underestimate the number of less severe cases. Our results are unlikely to overestimate the number of mild, moderate or severe cases. All self-reported cases were checked to confirm that they met the criteria for our case definition. Each case was carefully reviewed to ensure that the reported effects were in accordance with the signs and symptoms linked to the poisoning agent. All 72 self-reported cases had a consistent history of previous acute pesticide exposure and had at least three symptoms or one sign related to the reported pesticide exposure. Information on all self-reported intoxication cases were retained following review. Complete information on case description, including pesticide exposure, severity, health care location and private cost for moderate and severe cases is available in our previous publication.

The lack of a universally accepted definition of poisoning has been reported as a major difficulty when interpreting the findings of case reports. A recent definition proposed by Thundiyil et al (2008), the product of work conducted at the Intergovernmental Forum on Chemical Safety (IFCS), defines an acute pesticide poisoning as ''any illness or health effect resulting from suspected or confirmed exposure to a pesticide within 48 hrs. An acute pesticide poisoning case can be classified as probable, possible or unlikely/unknown''. According to this proposal, the case definition used in this study refered to ''probable cases'', where three criteria were met (exposure, health effect and causality). In our definition of probable case there was a plausible description of exposure reported by patient, there were one sign and/or three or more symptoms compatible with pesticide exposure and there was a temporal cause–effect relationship between exposure and health effect consistent with the known toxicology of the pesticide.

This study also proposes that the WHO poisoning severity classification (2004) should be complemented with other dimensions of severity, such as medical treatment levels and number of work days lost. In fact, we found that these two dimensions showed almost a complete overlap with the clinical severity categories. The two dimensions seem to be useful additions to the severity score in terms of evaluating socio-economic cost, including the substantial private economic cost experienced by those poisoned and their families.

Study IV was an intervention study designed to demonstrate the positive impact of IPM training evaluated by reducing exposure for the intervention group (trained farmers and agricultural promoters). The frequency of a related biomarker, in this case the levels of acetyl cholinesterase enzyme, was then compared to a control population (non trained farmers) to assess the magnitude of the response differential for the two levels of exposure.

The subjects receiving the intervention were similar to those in the comparison group. The two year follow-up and registration of all events in field books was a strength.

This study was the first to have used cholinesterase levels to directly quantify the reduction in exposure to organophosphate pesticides as a result of training farmers to better manage their pests and crops. This method was very attractive, in that individuals can be followed from their individual basal (no organophosphate exposure) levels to their post-exposure levels.

6.2   THE QUALITY OF THE APP REGISTER

Study 1 is the first study of APP underreporting at the national level in Nicaragua. A previous study, based on the same method of comparing self reported cases with the official register, in the most exposed region demonstrated a lower underreporting estimation of 65% (Keifer et al., 1996a). In 1995, another underreport study, based on multiple sources review at health units in eight departments of the country, found 45% of underreporting of APP cases who attended public health centers and hospitals (Corriols, 1995). Underreporting figures were also higher in other studies performed in Central American countries using different methodologies and sample frames (Corriols, 2002). Most epidemiological studies on APP in other countries are based on hospital and poison center data and are biased toward severe cases, whereas field studies indicate that occupational pesticide poisoning is typically associated with less severe symptoms (Lietchfield, 2005; Wesseling et al., 2001b).

The huge underreporting found in our survey means that the information generated by the national surveillance register downplays the scale of acute pesticide poisoning. The epidemiological profile of APP as reported in the surveillance system misinforms and does not contribute to the development of adequate prevention and control programs.

In the Nicaraguan pesticide poisoning register, occupational poisonings were underrepresented compared with intentional and domestic poisonings when the results of the national survey were used for comparison. The latter two types of poisoning were registered 16 and 2.5 times more often than occupational poisonings, respectively. The most toxic pesticides (which are associated with these non-occupational events), aluminum phosphide and paraquat, were also overrepresented in the official figures (two and three times higher) in comparison with our sample.

Even in more developed countries, studies show that only a small proportion of people with symptoms resulting from pesticide exposure sought medical care, suggesting a serious level of underreporting (Bell et al.; 2006, Mancini et al., 2005). The lack of awareness in the population about early symptoms of APP and people's treatment-seeking behavior are worrying. In our study, the majority of individuals who sought medical attention had moderate to severe poisoning as defined by data on absence from work, out-of-pocket expenses, and medical classification. This raises the question of how many individuals, especially in less severe cases, fail to seek medical attention after poisoning events. In contrast to the official figures, which show a higher proportion of accidental and intentional causes, it is evident that a substantial proportion of cases of agricultural worker poisonings that receive medical care are not being reported. This causes an important underestimation of a truly occupational health problem. The causes of this underreporting problem are multiple. Health regulations on compulsory disease reporting are not followed by public and private health providers.

6.3 THE NATIONAL INCIDENCE OF APP

Study 2 is the first study to estimate the real incidence of APP at the national level in Nicaragua. Previous studies were based on official figures representing only the cases attended at health units, and vary in range from early FAO´s estimations of 0.2% in the 60´s decade, to 25% in the most exposed groups in the 80´s. This study is the first one to estimate incidence rates for different sub groups in the country by sex, age, occupation, residence, education, severity and type of poisoning.

Previous studies of the incidence of acute pesticide poisonings provided information only on exposure and effects in the agricultural sector or estimated national figures from official health registries of cases that received medical care. More accurate estimates from such sources were not possible due to under-reporting. We believe that this is the first study which estimates a year-long cumulative incidence of pesticide poisoning in a national population, and which considers both medically treated and untreated acute pesticide poisoning cases. Our source of information was a national survey and most of the self-reported cases did not receive medical attention and were not registered.

Compared to data previously reported in the literature (Jeyaratnam et al., 1987; Wesseling et al., 1993; Alavanja et al., 1998; Solomon et al., 2000; Faria et al., 2005; Chitra et al., 2006), our study shows a high frequency of intoxications related to pesticide exposure. Also, compared to reports from the official register of the Pesticide Surveillance Program, our findings suggest a very much higher 1-year cumulative incidence. Based on that register, the PAHO found that Nicaragua had one of the highest incidence rates of acute pesticide poisoning in Central America, with over 35 cases per 100 000 in 2000 (Henao y Arbelaez, 2002). However, the 1-year cumulative year incidence rate/100 individuals calculated from our sample was 65 times higher than the official rate. The estimation of intended suicides and domestic accidents were three and 19 times higher than the reported figures, while the occupational figures were extremely high at 115 times the level of official figures.

6.4 THE MAIN DETERMINANTS OF APP AMONG SPRAYERS

Occupational exposure to pesticides in agricultural settings involves product distributors, transportation, retailers, mixers and loaders, applicators or sprayers, bystanders, and rural workers re-entering the fields shortly after treatment. The category of sprayers is broad: from bare hand applicators to sprayers who uses manual backpack pumps or motorized pumps. Usually, the studies evaluating agricultural exposure and effects do not disaggregate the analysis by specific tasks. Most of the APP cases are reported as occupational APP cases and the spraying activity usually entails the highest pesticide exposure among agricultural workers (Murphy et al., 2002; Kishi et al., 1995; van Wendel de Joode et al., 1996). Sprayers can be exposed during mixing and loading of a pesticide, during the application process, or afterwards. There are multiple potential routes of exposure, including topically (through the skin and eyes), or via inhalation or oral ingestion.

In this study we have found a higher annual incidence rate of APP among sprayers than among general farm workers population in Sri Lanka and Malaysia, Nicaragua, Costa Rica and Brazil, reinforcing the finding that the spraying activity is one of the most dangerous among agricultural activities (Jeyaratnam et al., 1987; Wesseling et al., 1993, Faria et al., 2005) .

Out of 22 studies reviewed we found three that studied pesticide health effects among sprayers (Murphy et al., 2002; Kishi et al., 1995, Wesseling et al., 1993) and 2 that studied only the sprayers' exposure (van Wendel de Joodel et al., 1996; Yassin et al., 2003). Most of the studies reported the occurrence of APP among farm workers, but the spraying activity was not studied separately.

Considering only the effects on the sprayers group, Kishi et al (1995) found in Indonesia that the number of spray operations per week, the use of hazardous pesticides, and skin and clothes being wetted with the spray solution were significantly and independently associated with the number of signs and symptoms. In Costa Rica, van Wendel de Joode et al (1996), found that the use of protective clothing did not effectively protect against dermal exposures. In Nicaragua, Blanco et al (2005) found that some working practices, spraying equipment and worksite related determinants explained 52, 33 and 25% of the exposure variability, respectively, while clothing and hygiene practices (wearing protective clothes and rinsing of hands) showed to be weaker determinants. Our study found that backpack pump leakage and incomplete use of PPE were stronger determinants. Still, we found that the use of hazardous pesticide was highly frequent and almost 7 out of 10 cases were caused by Class Ia-Ib pesticides.

6.5 THE ECONOMIC COSTS

According to the 2001 national economic survey, 45.8% of Nicaragua's population lives in poverty. Of them, 15.1 percent lives in extreme poverty (INIDE, 2002), taking the poverty line as an income of less than US$1 per day. Agricultural workers' monthly wage is less than $45. At the national level, the mean out-of-pocket costs for the poisoning were $40.4 for a single episode, meaning that the farmer had to spend almost one month's salary on medical care. Additionally, poisoned people reduced their productive time by about 10 days, which also reduced their income for the rest of the year. Most Nicaraguans, especially agricultural workers are not covered by social security and are not adequately covered by the Ministry of Health. It is evident that most of these individuals are paying high health and economic costs.

Nearly 34 000 cases of APP should have occurred among pesticide sprayers in Nicaragua in year 2000, causing an estimated 340 000 disability days and a direct loss of wages of around $1,4 million.

6.6 THE ALTERNATIVES

Study IV is the first study in Nicaragua to clearly show the health and economic benefits of providing training to resource-poor maize farmers in a series of steps to reduce dangerous pesticide use. Training during a two-year period resulted in decreased pesticide use, lower costs, greater economic returns, and reduced health risk. There is no evidence from this study, however, that the use of protective equipment reduced health risk.

Similar results of other farmer IPM training programs on pesticide use, yield, and net returns have been found. The FAO-sponsored Indonesian National IPM Program found pesticide use was reduced by 40–50% and average expenditure on pest management decreased about 50%, while yields were not changed, as a result of training in farmers' field schools (FAO, 1990).

6.7   CONCLUSIONS

The enormous underreporting demonstrated in this study results in a failure to promote the interest of authorities in resolving the problem of adverse pesticide health effects. The characterization of APP based only on the official figures without considering the underreported cases leads to a constant inability to interpret and report on pesticides' health effects. Right now, the public and policymakers are unaware of the magnitude of the problem among agricultural workers and erroneously think that non-occupational poisonings are the main problem. The quality of the register is closely linked to the quality of the health system. The results of this study on underreporting indirectly evaluate one dimension of the quality of Nicaragua's health system. The typical poisoned person is a male, rural, 40 year old agricultural worker, who is almost illiterate, and poor. He passes almost invisibly through the health system.

This study provides strong evidence that pesticide use in Nicaragua results in a very high cumulative incidence rate of acute pesticide poisonings in Nicaragua. Unlike previous reports on acute pesticide poisoning incidence, this study dealt with the general adult population. It demonstrated that a very substantial proportion of acute pesticide poisonings occurred in an urban population not involved in agricultural or cattle-breeding occupations. Therefore, pesticide poisoning in Nicaragua, rather than primarily being seen as an occupational health concern, should be considered an important general public health problem. Consequently, it is important that decision makers are fully informed about the magnitude of the pesticide poisoning public health problem in Nicaragua. They must be aware that nearly 66 000 cases of acute pesticide poisonings occur annually and that they should take action to control this problem. Even though our data are from the year 2000, there are no indications that the situation has since changed.

There is an extremely high incidence rate of acute pesticide poisoning among Nicaraguan sprayers, mostly related to two preventable determinants. We estimated that nearly 34 000 cases of APP occurred among sprayers in Nicaragua, representing half of all APP's estimated in Nicaragua in the year 2000. This caused an important loss of productivity in many subjects as well as important economic costs. We found two significant potential determinants of APP in sprayers in Nicaragua: backpack pump leakage and incomplete or no use of PPE. Most cases were caused by Class Ia-Ib/II pesticides.

There are proven alternatives to the heavy pesticide use for agricultural pest control in Nicaragua. IPM training is a highly effective intervention to reduce pesticide use, health effects and economic costs among small farmers. After two years of IPM training, the trained farmers used fewer pesticides, spent less money on pest control, made higher net returns, and suffered less exposure to cholinesterase-inhibiting pesticides than did farmers who did not receive IPM training. In addition, a comparison of cholinesterase levels of farmers who used personal protective equipment showed no reduction of exposure to organophosphate insecticides, compared with farmers who did not use the equipment.

6.8   FURTHER STEPS AND RESEARCH

In the last two decades, some positive impacts on the Nicaraguan pesticide regulation occurred based on information generated by the APP surveillance system. Therefore, the pesticide surveillance system must be reinforced improving registration routines, the analysis and interpretation of the data, health personnel training and participation of private providers. In order to provide valuable information for the design of better

policies aimed at reducing the current high exposures and harmful health effects, the poisoning surveillance register needs to be strengthened. The Ministry of Health of Nicaragua must improve registration routines and reduce organizational, logistical, and human reasons for underreporting. Private health providers must be incorporated into the epidemiological surveillance system and training activities. It is imperative to increase the quality of analysis, interpretation, and dissemination of information.

Acute pesticide poisonings should be considered not only as an occupational health concern but an important general public health problem. The decision makers should be informed and also take action to control this problem by introducing regulatory measures and promoting alternatives for pest control.

Given that other strategies to reduce health effects have proven ineffective, interventions should focus on restricting the use of highly toxic compounds and educating farmers on IPM. National policies are needed to effectively articulate agricultural pest control activities with environmental and occupational health. The main focus should be to diminish pesticide exposure and effects, without reducing the crops yields.

Regulatory and educational interventions are required to reduce risks and adverse health effects. In order to effectively prevent intoxications, regulatory control is necessary, emphasizing the banning or restricting of the Class Ia-Ib pesticides (WHO, 2005) and other dangerous pesticides. This recommendation was made at the XVI Meeting of Central American and Dominican Republic Health Sector Ministries (PAHO, 2000b) but it has being only partially implemented in Nicaragua.

Comprehensive programs to reduce risks among agricultural workers must be implemented, including alternatives to chemical pest control, such as IPM and organic agriculture. Changes in the agricultural production patterns are long term challenges, meanwhile, specific prevention strategies should be reinforced: training for proper use, replacement, maintenance and repair of back pack pumps; awareness campaigns about early symptoms of APP and adequate treatment-seeking behavior; evaluation and adjustment of current training methodologies for farmers; and reinforcement of legal requirements for employers to provide complete PPE and training to pesticide sprayers.

Finally, further studies to estimate the economic costs of poisonings for families and health sector institutions should be carried out. Any economic evaluation of pesticide use in developing countries must look very closely at the impact of current practices on health risk (including the cholinesterase measurement where OP are used) and the potential for reducing that risk through innovative pest-management tactics.

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8 REFERENCES

Acevedo F, Godoy E, Schofield CJ. (2000) Comparison of intervention strategies for control of Triatoma dimidiata in Nicaragua. Mem Inst Oswaldo Cruz. 95(6):867-71.

Alavanja MC, Sandler DP, McDonnell CJ et al. (1998) Factors associated with self-reported, pesticide-related visits to health care providers in the agricultural health study. Environ Health Perspect. 106:415-20.

Amador R (1993). Neurotoxic effects from organophosphate insecticide exposure in Nicaragua. Methodological and epidemiological studies. Licenciate Thesis. Karolinska Institute. Stockholm, Sweden.

Andersen HR, Schmidt IM, Grandjean P, et al.(2008) Impaired reproductive development in sons of women occupationally exposed to pesticides during pregnancy. Environ Health Perspect. 116:566-572.

Aragón A, Aragón C, Thörn A. (2001) Pests, peasants, and pesticides on the Northern Nicaraguan Pacific Plain. Int J Occup Environ Health. 7(4):295-302.

Aragon A, Blanco L, Lopez L, Liden C, Nise G, Wesseling C. (2004) Reliability of a visual scoring system with fluorescent tracers to assess dermal pesticide exposure. Ann Occup Hyg. 48(7):601-6.

Aragon A. (2005). Dermal exposure to pesticides in Nicaragua. A qualitative and quantitative approach. Doctoral Thesis. Karolinska Institute. Stockholm, Sweden.

Aragón A, Blanco LE, Funez A, et al (2006). Assessment of dermal pesticide exposure with fluorescent tracer: a modification of a visual scoring system for developing countries. Ann Occup Hyg. 50(1):75-83. Epub 2005 Aug 26.

Arbelaez MP, Henao S. (2002) Situación epidemiológica de las intoxicaciones agudas por plaguicidas en el Istmo Centroamericano. OPS/OMS, DANIDA.Costa Rica.

Arbelaez M, Henao S. (2004) Vigilancia sanitaria de plaguicidas: experiencia de Plagsalud en Centroamérica. OPS/OMS. Washington DC.

Austin C, Arcury TA, Quandt SA, Preisser JS, Saavedra RM, Cabrera LF (2001) Training farmworkers about pesticide safety: issues of control. J Health Care Poor Underserved. 12(2):236-49.

Banco Central de Nicaragua, BCN. (2001) Memoria anual 2000. In http://www.bcn.gob.ni/publicaciones..

Blanco LE, Aragón A, Lundberg I, Lidén C, Wesseling C, Nise G. (2005) Determinants of dermal exposure among Nicaraguan subsistence farmers during pesticide applications with backpack sprayers. Ann Occup Hyg. 49(1):17-24.

Blanco L (2008). Dermal exposure determinants – a pesticide exposure assessment approach for developing countries. Doctoral Thesis. Karolinska Institute. Stockholm, Sweden.

Blanco LE, Aragón A, Lundberg I, Wesseling C, Nise G. (2008) The determinants of dermal exposure ranking method (DERM): a pesticide exposure assessment approach for developing countries. Ann Occup Hyg. 52(6):535-44

Bell EM, Sandler DP, Alavanja MC. (2006) High pesticide exposure events among farmers and spouses enrolled in the Agricultural Health Study. J Agric Saf Health. 12:101-116.

Bochner R. (2007) National Poisoning Information System - SINITOX and human intoxication by pesticides in Brazil. Cien Saude Colet. 12(1):73-89.

Buranatrevedh S, Sweatsriskul P. (2005) Model development for health promotion and control of agricultural occupational health hazards and accidents in Pathumthani, Thailand. Ind Health. 43(4):669-76.

Caldera T, Herrera A, Renberg ES, Kullgren G. (2004) Parasuicide in a low-income country: results from three-year hospital surveillance in Nicaragua. Scand J Public Health. 32(5):349-55.

Calvert GM, Plate DK, Das R et al. (2004) Acute occupational pesticide-related illness in the US, 1998-1999: surveillance findings from the SENSOR-pesticides program. Am J Ind Med. 45:14-23.

Calvert GM, Higgins SA.(2009) Using surveillance data to promote occupational health and safety policies and practice at the state level: A case study. Am J Ind Med. May 28. [Epub ahead of print]

Cameron L, Lalich N, Bauer S, et al.(2006) Occupational health survey of farm workers by camp health aides. J Agric Saf Health. 12(2):139-53.

Campos M, Finkelman J. (1998) Situación actual del uso y manejo de plaguicidas en Guatemala. OPS/OMS, Guatemala.

Carvalho FP, Montenegro-Guillen S, Villeneuve J, et al. (1999) Chlorinated hydrocarbons in coastal lagoons of the pacific coast of Nicaragua. Arch Environ Contam Toxicol. 36(2):132-9

Carvalho FP, Villeneuve JP, Cattini C, et al. (2002) Ecological risk assessment of pesticide residues in coastal lagoons of Nicaragua. J Environ Monit. 4(5):778-87.

Carvalho FP, Montenegro-Guillén S, Villeneuve JP, et al. (2003) Toxaphene residues from cotton fields in soils and in the coastal environment of Nicaragua.Chemosphere. 53(6):627-36

Castillo R, Manzanares M.(1993) Intoxicaciones Agudas por plaguicidas en Nindirí, Masaya en 1981-1991. Monografía UNAN. Managua, Nicaragua.

Castilho JA, Fenzl N, Guillen SM, Nascimento FS. (2000) Organochlorine and organophosphorus pesticide residues in the Atoya river basin, Chinandega, Nicaragua.: Environ Pollut. 110(3):523-33

Castro-Gutiérrez N, McConnell R, Andersson K, Pacheco-Antón F, Hogstedt C. (1997) Respiratory symptoms, spirometry and chronic occupational paraquat exposure. Scand J Work Environ Health. 23(6):421-7.

Chelala C. (2004) Un reto constante: los plaguicidas y su efecto sobre la salud y el medio ambiente. Washington DC: OPS.

Chitra G, Muraleedharan VR, Swaminathan T et al. (2006) Use of pesticides and its impact on Health of Farmers in South India. Int J Occup Environ Health. 12:228-233.

Clapp RW, Jacobs MM, Loechler EL. (2008) Environmental and occupational causes of cancer: new evidence 2005-2007. Rev Environ Health. 23:1-37.

Cole DC, McConnell R, Murray DL, Pacheco Antón F. (1988) Pesticide illness surveillance: the Nicaraguan experience. Bull Pan Am Health Organ. 22(2):119-32.

Cole DC, Carpio F, Leon N. (2000) Economic burden of illness from pesticide poisonings in highland Ecuador. Rev Panam Salud Publica. 8:196-201.

Corriols M., Rivas F. (1992) Evaluación del Componente de Salud del Programa Uso Seguro y Racional de Plaguicidas, II Región. Ministerio de Salud de Nicaragua y CARE Internacional. León, Nicaragua.

Corriols M. (1995) Subregistro de intoxicaciones agudas por plaguicidas en ocho departamentos de Nicaragua en 1994. Proyecto Plagsalud OPS. Serie Investigaciones # 1, Managua, Nicaragua.

Corriols M, Silva D, Rios F et al. (1999) Estudio piloto: Incidencia de intoxicaciones agudas por plaguicidas en dos municipios de Nicaragua. OPS-MINSA- PROMIPAC Nicaragua.

Corriols M. (2002) Incidence of acute pesticide poisonings in Centroamerica. Plagsalud project. Preliminary report, PAHO Nicaragua.

Corriols M, Marín J, Berroteran J, Lozano LM, Lundberg I, Thörn A. (2008) The Nicaraguan Pesticide Poisoning Register: constant underreporting. Int J Health Serv. 38(4):773-87.

Corriols M, Marín J, Berroteran J, Lozano LM, Lundberg I. (2009) Incidence of acute pesticide poisonings in Nicaragua: a public health concern. Occup Environ Med. 66(3):205-10. Epub 2008 Nov 21

Delgado E, McConnell R, Miranda J, et al. (2004) Central nervous system effects of acute organophosphate poisoning in a two-year follow-up. Scand J Work Environ Health. 30(5):362-70.

Díaz F, Lamoth L. (1998) Características ocupacionales y ambientales de los plaguicidas en Panamá. Proyecto Plagsalud. MASICA/HEP. Panamá.

Dorea JG, Cruz-Granja AC, Lacayo-Romero ML, Cuadra-Leal J. (2001) Perinatal metabolism of dichlorodiphenyldichloroethylene in Nicaraguan mothers. Environ Res. 86(3):229-37

Dowling KC, Blanco LE, Martínez I, Aragón A, Bernard CE, Krieger RI. (2005) Urinary 3,5,6-trichloro-2-pyridinol levels of chlorpyrifos in Nicaraguan applicators and small farm families. Bull Environ Contam Toxicol. 74(2):380-7.

Eddleston M, Karaliedda L, Buckley N et al. (2002) Pesticide poisoning in the developing world- a minimum pesticides list. Lancet. 360:1163-67.

Faria NM, Facchini LA, Fassa AG et al. (2005) Rural work and pesticide poisoning. Cad Saude Publica. 21:1298–1308.

Flocks J, Monaghan P, Albrecht S, Bahena A. (2007) Florida farmworkers' perceptions and lay knowledge of occupational pesticides. J Community Health. 32(3):181-94.

Food and Agriculture Organization of the United Nations. (1990) Guidelines for personal protection when working with pesticides in tropical climate. Rome.

Food and Agriculture Organization of the United Nations. (1990) Farmers and experts. The Indonesian National IPM Program. Indonesia, Jakarta.

Food and Agriculture Organization of the United Nations. (1992) The International Code of Conduct on the Distribution and Use of Pesticides. In http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/en/

Forget G. (1991) Pesticides and the Third World. J Toxicol Environ Health. 32:11-31

Galvao LA et al. (2002) Plaguicidas y salud en el istmo centroamericano. División de Salud y Ambiente. Programa de Calidad Ambiental, OPS/OMS. Washington.

Garfield R. (1999) Malaria control in Nicaragua: social and political influences on disease transmission and control activities. Lancet. 31;354 (9176):414-8

Garming H, Waibel H. (2009) Pesticides and farmer health in Nicaragua: a willingness-to-pay approach to evaluation. Eur J Health Econ. 10(2):125-33.

Gunnell D, Fernando R, Hewagama M, Priyangika WD, Konradsen F, Eddleston M. (2007) The impact of pesticide regulations on suicide in Sri Lanka. Int J Epidemiol. 36(6):1235-42. Epub 2007 Aug 27.

Hammond SN, Gordon AL, Lugo Edel C, et al. (2007) Characterization of Aedes aegypti (Diptera: Culcidae) production sites in urban Nicaragua. J Med Entomol.44(5):851-60

Henao S, Finkelman J, Albert L et al. (1993) Pesticides and health in the Americas. Washington, DC. Pan American Health Organization, Division of Health and Environment, Environmental Series Number 12.

Henao S, Arbelaez MP. (2002) Epidemiological situation of acute pesticide poisoning in the Central American Isthmus, 1992-2000. Pan American Health Organization (PAHO) –Plagsalud. Epidemiol Bull. 23:5-9.

Hruska A, Corriols M. (2002) The impact of training in integrated pest management among Nicaraguan maize farmers: Increased net returns and reduced health risk. Int J Occup Environ Health. 8:191-200

Ibitayo OO. (2006) Egyptian farmers' attitudes and behaviors regarding agricultural pesticides: implications for pesticide risk communication. Risk Anal. 26(4):989-95

INEC-CELADE (2001) Nicaragua: Estimaciones y proyecciones de población nacional 1950-2050. Managua, Nicaragua.

Janhong K, Lohachit C, Butraporn P, Pansuwan P. (2005) Health promotion program for the safe use of pesticides in Thai farmers. Southeast Asian J Trop Med Public Health. 36 Suppl 4:258-61

Jenkins J. (2003) Plaguicidas y Salud en El Salvador: Aproximación a la problemática. San Salvador, El Salvador: OPS/OMS.

Jeyaratnam, J. (1985) Health problems in pesticide usage in the Third Word. Brit J Indus Med. 42:505-506

Jeyaratnam J, Lun KC, Phoon WO. (1987) Survey of acute pesticide poisoning among agricultural workers in four Asian countries. Bull World Health Organ, 65:521-527

Jeyaratnam J. (1990) Acute pesticide poisoning: a major global health problem. World Health Stat Q. 43:139-44.

Jors E, Cervantes R, Condarco G, et al. (2006) Occupational pesticide intoxications among farmers in Bolivia: a cross-sectional study. Environ Health. 2006;.21:5-10

Keifer M, McConnell R, Pacheco AF, et al. (1996) Estimating underreported pesticide poisonings in Nicaragua. Am J Ind Med. 1996;30:195-201

Keifer M, Murray D, Amador R, et al. (1996a) Solving the pesticide problem in Latin America: a model for health sector empowerment. New Solutions. 26-31

Keifer M, Rivas F, Moon JD, Checkoway H. (1996b) Symptoms and cholinesterase activity among rural residents living near cotton fields in Nicaragua. Occup Environ Med. 53(11):726-9.

Kesavachandran CN, Fareed M, Pathak MK, Bihari V, Mathur N, Srivastava AK. (2009) Adverse health effects of pesticides in agrarian populations of developing countries. Rev Environ Contam Toxicol. 200:33-52. Review.

Kishi M, Hirschhorn N, Djadjadisastra M, Satterlee LN, Strowman S, Dilts R. (1995) Relationship of pesticide spraying to signs and symptoms in Indonesian farmers. Scand J Work Environ Health.21:124-33

Kishi M. (2002) Farmers' perceptions of pesticides, and resultant health problems from exposures. Int J Occup Environ Health. 8(3):175-81.

Kroeger A, González M, Ordóñez-González J. (1999) Insecticide-treated materials for malaria control in Latin America: to use or not to use? Trans R Soc Trop Med Hyg. 93(6):565-70.

Lacayo-Romero M, van Bavel B, Mattiasson B. (2006) Degradation of toxaphene in aged and freshly contaminated soil. Chemosphere. 63(4):609-15.

Leveridge YR. (1998) Pesticide poisoning in Costa Rica during 1996. Vet Hum Toxicol. 40:42-4

Liebman AK, Juárez PM, Leyva C, Corona A. (2007) A pilot program using promotoras de salud to educate farmworker families about the risk from pesticide exposure. J Agromedicine. 12(2):33-43.

Litchfield MH. (2005) Estimates of acute pesticide poisoning in agricultural workers in less developed countries. Toxicol Rev 24:271-78.

London L, Bailire R. (2001) Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries. Int J Epidemiol. 30:564-70.

London L, de GS, Wesseling C, Kisting S, Rother HA, Mergler D. (2002a) Pesticide usage and health consequences for women in developing countries: out of sight, out of mind? Int J Occup Environ Health. 8(1):46-59.

London L, Kisting S. (2002) Ethical concerns in international occupational health and safety. Occup Med. 17(4):587-600.

London L. (2003) Human rights, environmental justice, and the health of farm workers in South Africa. Int J Occup Environ Health. 9(1):59-68.

López L, Blanco L, Aragón A, Partanen T.(2009) Insecticide residues on hands: assessment and modeling with video observations of determinants of exposure—a study among subsistence farmers in nicaragua. J Occup Environ Hyg. 6(3):157-64.

Lu C, Rodríguez T, Funez A, Irish RS, Fenske RA. (2006) The assessment of occupational exposure to diazinon in Nicaraguan plantation workers using saliva biomonitoring. Ann N Y Acad Sci.1076:355-65.

Macfarlane E, Chapman A, Benke G, Meaklim J, Sim M, McNeil J. (2008) Training and other predictors of personal protective equipment use in Australian grain farmers using pesticides. Occup Environ Med. 141-6. Epub 2007 Aug 17.

Ministry of Agriculture and Agroforestry. MAGFOR, Nicaragua, 2001 Informe anual de estadísticas. In http://www.magfor.gob.ni/

Maddy KT, Edmiston S, Richmond D. (1990) Illness, injuries, and deaths from pesticide exposures in California 1949-1988. Rev Environ Contam Toxicol. 114:57-123.

Mancini F, Van Bruggen AH, Jiggins JL, Ambatipudi AC, Murphy H. (2005) Acute pesticide poisoning among female and male cotton growers in India. Int J Occup Environ Health.11:221-232.

Mancini F, Jiggins JL, O'Malley M. (2009) Reducing the incidence of acute pesticide poisoning by educating farmers on integrated pest management in South India. Int J Occup Environ Health. 15(2):143-51.

Marquart J, Brower DH, Gijsbers JH, Links HM, Warren N, Van Hemmen JJ. (2003) Determinants of Dermal Exposure Relevant for Exposure Modelling in Regulatory Risk Assessment. Ann. occup. Hyg., 47(8)599–607.

Martins CB, de Andrade SM, de Paiva PA. (2006) Accidental poisoning among children and adolescents in a county in southern Brazil. Cad Saude Publica. 22:407-14.

Mc Connell R, Pacheco Anton AF, Magnotti R. (1990) Crop duster aviation mechanics: high risk for pesticide poisoning. Am J Public Health. 80(10):1236-9.

McConnell R, Cordon M, Murray DL, Magnotti R. (1992) Hazards of closed pesticide mixing and loading systems: the paradox of protective technology in the Third World. Br J Ind Med. 49(9):615-9.

McConnell R, Hruska A. (1993) An epidemic of pesticide poisoning in Nicaragua: implications for prevention in developing countries. Am J Public Health. 83:1559-62

McConnell R, Keifer M, Rosenstock L. (1994) Elevated quantitative vibrotactile threshold among workers previously poisoned with methamidophos and other organophosphate pesticides. Am J Ind Med. 25:325-334.

McConnell R, Delgado E, Cuadra R,et al. (1999a) Organophosphate neuropathy due to methamidophos: biochemical and neurophysiological markers. Arch Toxicol. 73:296-300.

McConnell R, Pacheco F, Wahlberg K, et al. (1999b) Subclinical health effects of environmental pesticide contamination in a developing country: cholinesterase depression in children. Environ Res. 81(2):87-91

Meyrat A. (1992) Diversifying crops: the Nicaraguan experiment. People Planet. 1(3):23.

Ministry of Health of Nicaragua. (1990) Boletín Epidemiológico del Programa de Plaguicidas. MINSA Nicaragua.1:1-12

Ministry of Health of Nicaragua.(1995) Boletín Epidemiológico de Intoxicaciones por plaguicidas. MINSA- Nicaragua. 9:1-20

Ministry of Health of Nicaragua. (2001) Boletín Epidemiológico del Programa de Plaguicidas. MINSA Nicaragua: 18:1-16.

Ministry of Health of Nicaragua. (2002) Encuesta de Establecimientos de Nicaragua 2000. MINSA. Managua, Nicaragua.

Ministry of Health of Nicaragua. (2003) Análisis de Situación de Salud, MINSA. Managua, Nicaragua.

Ministry of Health of Nicaragua. (2005) Monitoring and evaluation forms. Pesticide program reports. Managua, Nicaragua.

Miranda J, Lundberg I, McConnell R et al. (2002a) Onset of grip- and pinch-strength impairment after acute poisonings with organophosphate insecticides. Int J Occup Environ Health 8:19-26.

Miranda J, McConnell R, Delgado E, et al. (2002b). Tactile vibration thresholds after acute poisonings with organophosphate insecticides. Int J Occup Environ Health. 8(3):212-9.

Miranda J (2003). Neurotoxicity after poisonings with organophosphate pesticides in Nicaragua. Doctoral Thesis. Karolinska Institute. Stockholm, Sweden

Miranda J, McConnell R, Wesseling C, et al. (2004) Muscular strength and vibration thresholds during two years after acute poisoning with organophosphate insecticides. Occup Environ Med. 61(1):1-6.

Murphy H, Hoan NP, Matteson P et al. (2002) Farmers' self-surveillance of pesticide poisoning: a 12-month pilot in northern Vietnam. Int J Occup Environ Health. 8:201-11.

Murray DL. (1984) Social problem-solving in a revolutionary setting: Nicaragua's pesticide policy reforms. Policy Stud Rev. 4(2):219-29.

Murray D. (1994) Cultivating Crisis. The Human Cost of Pesticides in Latin America, pp. 21-26. University of Texas Press, Austin, Texas.

Murray D, Wesseling C, Keifer M et al. (2002) Surveillance of pesticide-related illness in the developing world: putting the data to work. Int J Occup Environ Health. 8:243-8.

Nagami H, Nishigaki Y, Matsushima S et al. (2005) Hospital-based survey of pesticide poisoning in Japan, 1998-2002. Int J Occup Environ Health. 11:180-184.

National Institute of Statistics and Census. (2002) Encuesta de Medición de Nivel de Vida, EMNV 2001. INEC Publication. Managua, Nicaragua.

Osorio AM. (2002) Surveillance systems for pesticide intoxications. Int J Occup Environ Health. 8: 1-13.

Panamerican Health Organization. (1994) Epidemiología Ambiental: Un proyecto para América Latina y El Caribe, ECO-OPS-OMS, México.

Panamerican Health Organization (2000). Plaguicidas y Salud en Honduras. OPS/OMS, Plagsalud. Honduras.

Panamerican Health Organization Organización Panamericana de la Salud. (2000) Informe Final de la XVI Reunión del Sector Salud de Centroamérica y República Dominicana (RESSCAD). Honduras.

Panamerican Health Organization. (2002) Boletín Epidemiológico. 2002;3. www.paho.org/spanish/sha/be_v23n3-plaguicidas.htm (accessed 3 April 2008)

Panamerican Health Organization Orga. (2003 a) Efectos de los plaguicidas en la salud y el ambiente en Costa Rica. OPS/ Ministerio de Salud. San José, Costa Rica.

Panamerican Health Organization. (2003 b) Exclusión en Salud en Países de América Latina y El Caribe. Serie Extensión de la Protección Social en Salud # 1. OPS-ASDI. Washington DC.

Plan Nacional de Desarrollo (2001). Gobierno de Nicaragua, Managua, Nicaragua.

Perry MJ, Layde PM. (2003) Farm pesticides: outcomes of a randomized controlled intervention to reduce risks. Am J Prev Med. 24(4):310-5.

Pérez CJ, Alvarado P, Narváez C, et al. (2000) Assessment of insecticide resistance in five insect pests attacking field and vegetable crops in Nicaragua. J Econ Entomol. 93(6):1779-87.

Pimentel David, McLaughlin L, Zepp A et al. (1991). Environmental and Economic Effects of Reducing Pesticide Use. BioSci 41;402-409

Rajasuriar R, Awang R, Hashim SB et al. (2007) Profile of poisoning admissions in Malaysia. Hum Exp Toxicol. 26:73-81.

Rao P, Gentry AL, Quandt SA, Davis SW, Snively BM, Arcury TA. (2006) Pesticide safety behaviors in Latino farmworker family households.Am J Ind Med. 49 (4):271-80.

Rautiainen R, Lehtola M, Day L, et al. (2008) Interventions for preventing injuries in the agricultural industry. Cochrane Database Syst Rev. 23;(1):CD006398

Reed DB, Browning SR, Westneat SC, Kidd PS. (2006) Personal protective equipment use and safety behaviors among farm adolescents: gender differences and predictors of work practices.J Rural Health. 22(4):314-20

Reeves M, Schafer KS. (2003) Greater risks, fewer rights: U.S. farmworkers and pesticides. Int J Occup Environ Health. 9(1):30-9.

Roberts DM, Karunarathna A, Buckley NA, Manuweera G, Sheriff MH, Eddleston M. (2003) Influence of pesticide regulation on acute poisoning deaths in Sri Lanka. Bull World Health Organ. 81(11):789-98. Epub 2004 Jan 20.

Rodríguez T, Younglove L, Lu C, et al. (2006) Biological monitoring of pesticide exposures among applicators and their children in Nicaragua. Int J Occup Environ Health. 12(4):312-20.

Rodríguez MM, Bisset JA, Fernández D. (2007) Levels of insecticide resistance and resistance mechanisms in Aedes aegypti from some Latin American countries. J Am Mosq Control Assoc. 23(4):420-9-15.

Romero ML, Dorea JG, Granja AC. (2000) Concentrations of organochlorine pesticides in milk of Nicaraguan mothers. Arch Environ Health. 55(4):274-8.

Rosenstock L, Keifer M, Daniell WE, McConnell R, Claypoole K. (1991) Chronic central nervous system effects of acute organophosphate pesticide intoxication. The Pesticide Health Effects Study Group. Lancet. 27;338(8761):223-7.

Rugama R, Calero S, Fomsgaard I, Lacayo ML, Martinez V, Pitty J. (1993) Levels of organochlorine residues in blood plasma from three populations in Nicaragua. Bull Environ Contam Toxicol. 51(1):153-9.

Schenker MB, Orenstein MR, Samuels SJ. (2002) Use of protective equipment among California farmers. Am J Ind Med. 42(5):455-64.

Solomon G, Ogunseitan OA, Kirsch J. (2000) Pesticides and human health: a resource for health care professionals. Physicians for Social Responsibility and Californians for Pesticide Reform. California, USA.

Strong LL, Thompson B, Koepsell TD, Meischke H. (2008) Factors associated with pesticide safety practices in farmworkers. Am J Ind Med. 51(1):69-81.

Sweezy S. Nicaragua´s Revolution in pesticide policy. (1986) Environment 28;7-36

Tagwireyi D, Ball DE, Nhachi CF. (2006) Toxicoepidemiology in Zimbabwe: pesticide poisoning admissions to major hospitals. Clin Toxicol (Phila). 44:59-66.

Thundiyil J, Stober J, Besbelli N et al. (2008) Acute pesticide poisoning: a proposal classification tool. Bull of the World Health Organization. 86:205-209.

van der Hoek W, Konradsen F. (2005) Risk factors for acute pesticide poisoning in Sri Lanka.Trop Med Int Health. 10(6):589-96.

van Wendel de Joode B, De Graaf IAM, Wesseling C, Kromhout H. (1996) Paraquat exposure of knapsack spray operators on banana plantations in Costa Rica. Int J Occup Environ Health. 2(4):294-304.

Vaughan M. (1993) Plaguicidas, Ambiente y Desarrollo. Ministerio del Ambiente y los Recursos Naturales ECOT/PAF/PAA/NIC: Nicaragua.

Villarino MA, Garcia O, Fussell W, Preston K, Wagner GG. (2003) An initial survey of the cattle grub Dermatobia hominis (L. Jr.) in Nicaragua. Prev Vet Med. 12;61(4):333-8.

Weinberg JL, Bunin LJ, Das R. (2009) Application of the industrial hygiene hierarchy of controls to prioritize and promote safer methods of pest control: a case study. Public Health Rep. 124 Suppl 1:53-62.

Weinger M, Lyons M. (1992) Problem solving in the fields: an action oriented approach to farmworker education about pesticides. Am J Ind Med. 22:677-90.

Wesseling C, Castillo L, Elinder CG. (1993) Pesticide poisonings in Costa Rica. Scand J Work Environ Health. 19:227-35

Wesseling C. (1997) Health effects from pesticide use in Costa Rica – an epidemiologic approach. Stockholm, Sweden.

Wesseling C, Mc Connell R, Partanen et al. (1997) Agricultural pesticide use in developing countries: health effects and research needs. Int J Health Services. 27: 273-308.

Wesseling C, van Wendel de Joode B, Monge P. (2001a) Pesticide-related illness and injuries among banana workers in Costa Rica: a comparison between 1993 and 1996. Int J Occup Environ Health. 7:90-97

Wesseling C, Aragón A, Castillo L et al. (2001b) Hazardous pesticides in Central America Int J Occup Environ Health. 7:287-94. Review

Wesseling C, Corriols M, Bravo V. (2005) Acute pesticide poisoning and pesticide registration in Central America.Toxicol Appl Pharmacol. 207:697-705. Review.

World Health Organization. (1990) Public Health Impact of Pesticides Used in Agriculture. WHO-UNEP. Geneva. 85-89.

World Health Organization. (1992) The Public Health Impact of Pesticides Use in Agriculture, pp. 46. World Health Organization, Geneva.

World Health Organization. (2004) Epidemiology of pesticide poisoning: harmonized data collection of data on human pesticide exposure in selected countries. Geneva: International Programme on Chemical Safety/WHO.

World Health Organization. (2005) The WHO recommended classification of pesticides by hazards and guidelines to classification. Geneva, WHO.

Yassin MM, Abu Mourad TA, Safi JM. (2002) Knowledge, attitude, practice, and toxicity symptoms associated with pesticide use among farm workers in the Gaza Strip. Occup Environ Med. 59 (6):387-93.

Zapata AL, Santamaria M, Alvarez M, Salazar S, Muller U. (1996) Organochlorine pesticide residues in cow's milk, Nicaragua Bol Oficina Sanit Panam. 120(6):483-90