

Measures of material and social circumstances to adjust for deprivation in small-area studies of environment and health: review and perspectives

Roberto Pasetto^(a), Letizia Sampaolo^(a) and Roberta Pirastu^(a,b)

^(a)Dipartimento di Ambiente e Connessa Prevenzione Primaria, Istituto Superiore di Sanità, Rome, Italy

^(b)Dipartimento di Biologia e Biotecnologie, Università di Roma "Sapienza", Rome, Italy

Summary. The present review describes and critically analyzes the main characteristics of deprivation indices (DIs), meant as measures of material and social circumstances at a population level, used to adjust for deprivation in small-area studies of environment and health. A systematic search strategy in the period 1990-2009 was run on PubMed/Medline and Embase databases, and 41 articles were selected. In most of the reviewed studies DIs appear to be pragmatically applied and information is not adequate to evaluate whether the use of DIs is efficient. Suggestions for the use of DIs are given foreseeing that more data on exposure, outcomes and other predictive factors will be acquired, and information will be growingly available to disentangle the complex interplay between exposure, health and deprivation.

Key words: environmental exposure, socioeconomic factors, confounding factors, review.

Riassunto (*Indicatori di condizioni materiali e sociali per aggiustare per deprivazione negli studi di piccola area su ambiente e salute: rassegna e prospettive*). La presente rassegna descrive e analizza criticamente le principali caratteristiche degli indici di deprivazione (ID), intesi come indicatori di circostanze materiali e sociali a livello di popolazione, utilizzati negli studi di piccola area su ambiente e salute per aggiustare per deprivazione. È stata eseguita una strategia di ricerca sistematica sulle basi di dati PubMed/Medline ed Embase per il periodo 1990-2009. Dalla bibliografia risultante sono stati selezionati 41 articoli. Nella maggior parte degli articoli gli ID risultano applicati in modo pragmatico e le informazioni fornite non sono sufficienti per valutare se l'aggiustamento risulti efficiente o meno. Alla luce di quanto emerso vengono forniti suggerimenti per l'uso degli ID, prevedendo che nel prossimo futuro saranno maggiormente disponibili sia i dati sull'esposizione, gli outcome e altri fattori predittivi, che le informazioni per comprendere la complessa interrelazione tra esposizione, salute e deprivazione.

Parole chiave: esposizione ambientale, fattori socioeconomici, fattori di confondimento, rassegna.

INTRODUCTION

Deprivation can be defined as “a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which an individual, family or groups belong” [1]. It is a multidimensional concept in which two main domains can be distinguished: material and social circumstances. Following Townsend, the first involves “the material apparatus, goods, services, resources, amenities and physical environment and local life”, the second “the roles, relationships, functions, customs, rights and responsibilities of membership of society and its subgroups” [1].

Area-based measures of material and social circumstances, defined as deprivation indices (DIs), are indicators of relative deprivation at a population level. They were developed in Great Britain in the '80s to describe and study inequalities in health [2, 3].

In small-area studies of environment and health, potential confounding from deprivation is present in many cases being its role predictive of several diseases [4, 5]. For example the risk is higher in more disadvantaged categories for respiratory cancers (nose, larynx and lung), and cancers of the mouth, pharynx, oesophagus, and stomach [6, 7]. This is a major problem especially since any risk from typical environmental pollution tends to be small, and may be swamped by deprivation because deprived population may concentrate in polluted areas [4]. To appropriately adjust for material and social circumstances, DIs have been extensively used since the mid '90 [4, 8].

In small-area research, territorial unit at study is identified in various ways depending on data availability which is variable in different countries; data for numerator – events at study – and for denominator – population at study – must be available at the

same area level. According to Carstairs, “the specific value of small-area analysis is that it permits the examination of data for population which tend to be more homogeneous in character and in their environmental circumstances than are larger and more widely spread populations” [9].

In the present paper the main characteristics of DIs in small-area studies of environment and health are reviewed; their application is analysed; suggestions for future studies are made.

METHODS

Coherently with the paper aim, the authors identified keywords, an initial search strategy, and determined the studies inclusion/exclusion criteria. Ecological studies were considered eligible if small-area designed, and evaluating the association between environmental exposure and mortality or morbidity. Since DIs have been extensively used from the mid '90s in ecological small-area studies, it was agreed to settle a 1995-2007 time range for publication date. No publication language limit was set. Then an informal trial search was fixed on PubMed

database The following terms were used: small-area, deprivation, socio-economic, epidemiology, morbidity, mortality, cancer, proximity, environment.

By this search relevant studies were retrieved and selected, and further articles were taken into account by examining bibliography included in the selected studies, or because already known to the authors. Aware that some relevant and well-known articles were missing, the authors considered that potential articles citing DI were also to be retrieved, even if not specifically addressing to it as main investigative topic. Therefore, a systematic search strategy simultaneously taking into account the four basic concepts was set up: a) measure of material and social circumstances (DI); b) study design (small-area); c) geographic location of exposed populations (proximity to the source of exposure); d) potential environmental exposure. Points a) and b) were included in the following main search filter, from which occupational studies were excluded:

((“small-area” OR “small area” OR *ecologic* OR *ecological* OR *environment* OR *environmental*) AND ((*socioeconomic* OR “socio economic” OR “social and

Table 1 | Full search strategy executed on PubMed/Medline database and repeated on Embase – Ovid Interface – to perform a systematic review of the literature published from January 1990 to November 2009

#1 (“small area” OR “small-area” OR “ecological study” OR “ecological studies”)
AND
#2 (socioeconomic OR “socio economic” OR deprivation OR poverty))
OR
#3 (socioeconomic factors OR “lifestyle factors” OR socioeconomic indicator” OR “socioeconomic indicators” OR “deprivation studies” OR “deprived sites” OR health status OR residence characteristics OR “socioeconomic deprivation score” OR poverty OR poverty areas OR housing OR “socioeconomic status” OR catchment area (health) OR “population data” OR “socioeconomic data” OR “socioeconomic inequity” OR “neglected areas” OR “neglected populations” OR “socioeconomic differences” OR “socioeconomic conditions” OR “socioeconomic disparity” OR “socioeconomic position” OR “socioeconomic deprivation” OR “educational inequality” OR “socioeconomic inequality” OR “unequal social distribution” OR “impoverished neighbourhoods” OR “impoverished neighbourhoods” OR “ecological comparisons” OR “socioeconomic disadvantage” OR “ecological evaluation” OR social class OR social isolation)
AND
#4 (“high risk factories” OR “environmental crisis” OR “landfill sites” OR “chemical industry” OR petroleum OR “iron industry” OR “steel industry” OR “coke industry” OR “industrial complexes” OR “oil refineries” OR “power plants” OR “mine industry” OR “mining industry” OR “ship industry” OR “ships industry” OR “naval industry” OR cokeworks OR “coke works” OR air pollution OR asbestos OR “pesticide factory” OR “pesticides factory” OR “pesticides factories” OR “mineral fibers” OR “mineral fibres” OR electromagnetic fields OR elf OR “television transmitters” OR “radio transmitters” OR radiofrequency OR radiofrequencies OR “radio frequency” OR “radio frequencies” OR waste disposal OR sewage OR landfills OR incinerated OR incinerator OR incinerators OR “natural radiation” OR “natural radioactivity” OR radon OR “coke plant” OR “coke plants” OR “solid waste” OR “military sites” OR “industrial areas” OR foundry OR foundries OR “petrochemical industry” OR “waste combustion plant” OR “waste combustion plants” OR radio OR television OR “environmental pressure” OR “high power transmitter” OR “high power transmitters” OR “sewage plant” OR “sewage plants”)
OR
#5 (coke OR extraction and processing industry OR coal mining OR sewage OR refuse disposal OR electromagnetic fields OR radio waves OR television OR asbestos OR air pollution OR aerosol OR incineration OR environmental pollution OR hazardous waste OR odors OR odours OR chemical industry OR hazardous substances OR air pollutants OR environmental exposure OR environmental pollutants OR book industry OR tanning OR textile OR tobacco industry)
AND
#6 (exposure OR proximity OR distance OR “living near” OR “residents near” OR indwelling OR environmental illness OR “resided near” OR “close to” OR “residents living within” OR “proximity of residence” OR “populations living within” OR “populations living in areas” OR municipality OR municipalities OR “population of” OR “populations of” OR “distance from” OR “living within” OR census OR areas OR “residents living close to” OR “area of residence” OR “deaths within” OR “cancers within”)
#1 AND (#2 OR #3) AND (#4 OR #5) AND #6
Limits: Publication Date from 1990/01/01

economic” OR deprivation) AND (index OR indices OR indexes) NOT (occupational OR occupations OR occupation OR job OR work OR worker OR workers) Limits: Humans.

Each concept was translated from natural English language into controlled terms, when available, and into text words and synonyms, to attain also studies not yet or selectively indexed. This explicit search strategy (Table 1) was successively run on PubMed/Medline and Embase databases to perform a systematic review of the literature published from January 1990 to November 2009. The online search yielded 152 titles and abstracts; 29 of these were original articles dealing with small-area studies and evaluating the association between environmental risks and health effects, therefore were considered pertinent and their full text was requested. Based on experts' suggestions or on studies already known to the authors and on the analysis of the bibliography included in the selected studies, 12 more articles were collected.

The selected studies were examined to describe the use of DIs in small-area studies of environment and health. Territorial unit at study, data source, component variables and reference years were analysed for each DI. For each investigation the main characteristics, *i.e.* exposure, study and reference population, health outcome, observation period and risk parameter were set forth.

RESULTS

As a result of the search strategy and selection of the papers a total of 41 articles qualified for inclusion in the review; 11 of these were conducted in Italy (4 among them are in Italian), 26 in Great Britain, two in New Zealand, one in Australia and one in Spain. Table 2 describes the main characteristics of DIs applied; index variables are described to the letter as reported in the reviewed articles.

It came into light that Italian studies use *ad hoc* DIs [10-13] and DIs developed for various epidemiological settings [14, 15]. Several among them [16-21] adopt the same index [14] but the variables are not homogeneously reported. In Great Britain studies published before 1997 apply *ad hoc* indices based on the same variables [22-24] while later only Townsend [25] and Carstairs [26] indices are used. Non-*ad hoc* DIs [27-29] are employed in New Zealand [30, 31], Australian [32] and Spanish [33] investigations.

It is known that DIs variables pertain to both material and social domains [1]: employment/unemployment is common, education is frequent among DIs, the ownership of material goods is recurrent and expressed in different ways, *e.g.* living or not in an own house, surface of dwellings or car ownership. Some DIs include also social domains like social class or single parenthood with children.

As far as the *population size*, in Great Britain in 23 of the collected studies the territorial unit is the

Enumeration District [22-24, 34-53] with an average of 400 inhabitants, in two is the Electoral Ward [54, 55], having an average of approximately 5136 inhabitants, and in the remaining one the postcode sector, where residents are on average 6600 people, is seemingly used [56]. In Italy instead, in seven studies [13, 16-21] municipality is the investigated area and the census tract is considered in four [10-12, 57]: about 70% of Italian municipalities include less than 5000 residents, while the mean of census tract population is approximately 200 residents [15]. The two New Zealand investigations acquired look at census area unit where residents range between 3000 and 8000 inhabitants [30, 31]. Lastly, in Australia the area analyzed is the postcode sector – number of residents not specified in the reviewed article [32] – and in Spain is the census tract, where the mean population under study is about 1000 subjects [33].

As far as DIs construction, it must be noted that in all studies DIs were built using variables from the National Census. Three are the main methods used to treat variables in DIs calculation (for a review of the topic see references 3 and 58). The first is to calculate standardized z-scores of *a priori* selected variables. The second is to define the major components in large datasets of variables by factor analysis. The third is to assign weights to the selected variables using the evaluation of their relative importance from a representative sample of population (*e.g.* through questionnaires submitted to health experts). The first and third can be combined.

In the reviewed articles, most DIs are derived from the sum of standardized z-scores of few selected variables. The initial value of each variable is generally defined on the basis of the proportion of population with the characteristic of interest in each territorial unit (*e.g.* education can be defined as the proportion of population with elementary degree or less). Then indices can be classified in population quantiles – the sum of populations of territorial units belonging to one class is the same for each class – or in territorial units quantiles – each class has the same number of territorial units.

For the reviewed investigations, the main characteristics in terms of exposure, study population, and reference entity are described in Table 3. Environmental exposure/s under investigation can be variously distinguished: multiple sources of pollution from industries [10, 12, 13, 16, 18, 20, 21, 35-39, 46, 51, 56], air pollution from specific pollutants [30, 31, 33, 48-50, 55], or traffic sources [44, 54], landfills [21, 40, 41, 43, 45, 47, 52, 53], incinerators [11, 23, 42, 57], asbestos/asbestiform fibres [17, 19], TV and radio transmitters [24, 32, 34] and nitrates in drinking water [35]. Study population is defined as exposed either because of the presence of environmental exposure/s in the area/s [11-13, 16, 18-21, 30-33, 35, 44, 48-50, 53, 55] or because of residence within a given distance from the putative pollution source [10, 17, 22-24, 34, 36-43, 45-

Table 2 | *Small-area environmental studies: main characteristics and components of deprivation index*

Country	Reference	Index, quantiles	Variables (literally reported as described in the studies)	Territorial unit	Source, year
Italy	Michelozzi <i>et al.</i> , 1998 [10]	<i>Ad hoc</i> Quartiles	- Occupation - Education - Unemployment - Number of family members - Overcrowding - Ownership of dwellings	Census tract	Census, 1991
	Martuzzi <i>et al.</i> , 2002 [16]	Cadum Quintiles	- Unemployed residents as a proportion of all economically active residents - Population more than 6 years with elementary degree or illiterate - Proportion of population living in rented house - Mean households surface - Residents in "single parent" household as a proportion of all households	Municipality	Census, 1991
	Chellini <i>et al.</i> , 2002 [11]	<i>Ad hoc</i> Tertiles	- Percentage unemployed - Percentage with less than seven years of formal education - Percentage with unskilled employment - Percentage living in rental housing	Census tract	Census, 1991
	Biggeri <i>et al.</i> , 2004 [17]	Cadum Quintiles	- Proportion of the unemployed active population - Proportion of subject with low educational level - Proportion of houses without an inside bath - Proportion of families who do not own their residence - Proportion of one parent families	Municipality	Census, 1991
	Parodi <i>et al.</i> , 2005 [12]	<i>Ad hoc</i> 30 quantiles	- Ratio between unemployed and employed people - Proportion of low educated people - Proportion of residents immigrated from southern Italy	Census tract	Census, 1991
	Biggeri <i>et al.</i> , 2006 [13]	<i>Ad hoc</i> Quintiles	- Proportion of population more than 6 years with elementary degree or illiterate - Proportion of unemployed active population - Mean number of occupants per room	Municipality	Census, 2001
	Minichilli <i>et al.</i> , 2006 [18]	Cadum Not specified	- Proportion of unemployed population - Proportion of population with elementary degree - Proportion of rented house - Mean households surface - Proportion of single parents with children	Municipality	Census, 1991
	Marinaccio <i>et al.</i> , 2008 [19]	Cadum Quintiles	Not reported	Municipality	Census, 1991
	Federico <i>et al.</i> , 2009 [57]	Caranci Quintiles	- Occupation - Educational level - Household condition - Density of people in 100 m ² - Families with only one parent in charge of minors	Census tract	Census, 2001
	Ianni <i>et al.</i> , 2009 [20]	Cadum Quintiles	Not reported	Municipality	Census, 1991
	Martuzzi <i>et al.</i> , 2009 [21]	Cadum Quintiles	- Unemployment - Education - Housing ownership - Surface of dwelling - Family structure	Municipality	Census, 1991
	Great Britain	Sans <i>et al.</i> , 1995 [22]	<i>Ad hoc</i> Quintiles	- Unemployment - Overcrowding - Social class of the head of the household	Enumeration district
Elliott <i>et al.</i> , 1996 [23]		<i>Ad hoc</i> Not specified	- Unemployment - Overcrowding - Social class of the head of the household	Enumeration district	Census, 1981
Dolk <i>et al.</i> , 1997 a. [24]		<i>Ad hoc</i> Quintiles	- Unemployment - Overcrowding - Social class of the head of the household not specified	Enumeration district	Census, 1981

(Continued)

Table 2 | (Continued)

Dolk <i>et al.</i> , 1997 b. [34]	<i>Ad hoc</i> Quintiles	- Unemployment - Overcrowding - Social class of the head of the household	Enumeration district	Census, 1981
Parslow <i>et al.</i> , 1997 [35]	Townsend 2 categories	- Unemployment - Car ownership - Owner occupation - Overcrowding	Enumeration district	Census, 1991
Wilkinson <i>et al.</i> , 1997 [36]	Carstairs Quintiles	Not reported	Enumeration district	Census, 1981 Census, 1991
Dolk <i>et al.</i> , 1999 [37]	Carstairs Quintiles	Not reported	Enumeration district	not specified
Harrison <i>et al.</i> , 1999 [54]	Townsend Not specified	Not reported	Ward	not specified
Wilkinson <i>et al.</i> , 1999 [56]	Carstairs Quintiles	Not reported	Not specified	Census, 1981 Census, 1991
Dolk <i>et al.</i> , 2000 [38]	Carstairs Quintiles	- Proportion of unemployed males - Proportion of persons without access to a car - Proportion of persons in overcrowded households - Proportion of persons in households with the head of households in social class IV or V	Enumeration district	Census, 1981 Census, 1991
Aylin <i>et al.</i> , 2001 [39]	Carstairs Quintiles	Not reported	Enumeration district	Census, 1991
Elliott <i>et al.</i> , 2001 [40]	Carstairs Tertiles	Not reported	Enumeration district	Census, 1991
Jarup <i>et al.</i> , 2002 [41]	Carstairs Tertile	Not reported	Enumeration district	Census, 1991
Cresswell <i>et al.</i> , 2003 [42]	Carstairs Quintiles	Not reported	Enumeration district	Census, 1991
Morris <i>et al.</i> , 2003 [43]	Carstairs Tertiles	Not reported	Enumeration district	Census, 1991
Maheswaran <i>et al.</i> , 2003 [44]	Carstairs Quintiles	- Percent of men unemployed - Percent of persons with no car - Percent of persons in overcrowded houses - Percent of persons with household head in social class IV or V	Enumeration district	Census, 1991
Morgan <i>et al.</i> , 2004 [45]	Carstairs Quintiles	Not reported	Enumeration district	not specified
Hodgson <i>et al.</i> , 2004 [46]	Carstairs	Not reported	Enumeration district	not specified
Palmer <i>et al.</i> , 2005 [47]	Townsend Quintiles	Not reported	Enumeration district	not specified
Maheswaran <i>et al.</i> , 2005 a [48]	Townsend Quintiles	- Proportion of economically active residents who were unemployed - Proportion of households without a car - Proportion of households not owner-occupied - Proportion of overcrowded households	Enumeration district	Census, 1991
Maheswaran <i>et al.</i> , 2005 b [49]	Townsend Quintiles	- Proportion of economically active residents who were unemployed - Proportion of households without a car - Proportion of households not owner-occupied - Proportion of overcrowded households	Enumeration district	Census, 1991
Maheswaran <i>et al.</i> , 2006 [50]	Townsend Quintiles	Not reported	Enumeration district	Census, 1991
Hodgson <i>et al.</i> , 2007 [51]	Carstairs Quintiles	- Percentage of men unemployed - Percentage of persons with no car - Percentage of persons in overcrowded houses - Percentage of persons with household head in social class IV or V	Enumeration district	Census, 1991

(Continued)

Table 2 | (Continued)

	Elliott <i>et al.</i> , 2007 [55]	Carstairs Deciles	- Unemployment - Car ownership - Overcrowding - Social class	Ward	Census 2001
	Jarup <i>et al.</i> , 2007 [52]	Carstairs Quintiles	Not reported	Enumeration district	Census, 1991
	Elliott <i>et al.</i> , 2009 [53]	Carstairs Not specified	- Unemployed head of household - Car ownership - Overcrowding - Low social class	Enumeration district	not specified
New Zealand	Scoggins <i>et al.</i> , 2004 [30]	NZDep1996 Quartiles	Proportion of people: - Aged 18-59 years unemployed - Aged 18-59 years without any qualifications - No access to a telephone - Aged 18-59 years receiving a means-tested benefit - Living in households with equivalised income below an income threshold - With no access to a car - Not living in own home - Living in households above equivalised bedroom occupancy threshold - Aged less than 60 years living in a single-parent family	Census tract	Census, 1996
	Sabel <i>et al.</i> , 2007 [31]	NZDep2001 Quartiles	- Employment status - Education - Income - Access to transport and communication services - Home characteristics	Census Area Unit (CAU)	Census, 2001
Australia	McKenzie <i>et al.</i> , 1998 [32]	C86SES /Ross index Not specified	44 variables in 5 domains for SLA and CD - Income - Education - Occupation - Wealth - Power/Prestige	Postcode level	Census, 1986
Spain	Barceló <i>et al.</i> , 2009 [33]	<i>Ad hoc</i> Domínguez-Berión quartiles	- Percentage of people aged ≥ 16 years without a job or actively - Percentage of the total employed population aged ≥ 16 years who are earning wages in temporary jobs searching for a job with respect to the total economically active population - Percentage of total population aged ≥ 16 years who are manual workers - Percentage of people aged ≥ 16 years with < 5 years of schooling or > 5 years but with no completion of compulsory education with respect to the total population aged ≥ 16 years	Census tract	Census, 2001

SLA: statistical local area; CD: collection district

47, 51, 52, 54, 56] *e.g.* residents within 7.5 km from cokeworks [38, 39], within 2 km from landfills [40, 41] or within 3 km from a combustion plant [42].

The exposed population is identified at a single point in time – usually census year [10-12, 16, 22-24, 30, 34, 35, 39, 44, 55], at two points in time – mainly decennial census year [20, 36, 37, 41, 51, 56], or over several years [21, 32, 33, 38, 40, 42, 43, 45, 47-50, 52, 53, 57].

In the articles included in the review the comparison entity is represented either by the national or local population or by population resident farther than a given distance: *e.g.* residents more than 2 km from landfills [40, 41] or more than 3 km from a combustion plant [42].

Table 3 also shows the studies outcomes and risk parameters. The outcomes under investigation are the following: cause-specific mortality [10, 16-20, 30, 33, 37, 44, 46, 50, 51, 55], cancer incidence/hospital admissions for specific diseases [12, 23, 24, 31, 32, 34, 35, 39, 41, 48, 49, 54, 56, 57], cancer mortality and incidence [11, 13, 22, 36], adverse reproductive effects and/or congenital anomalies [21, 38, 40, 42, 43, 45, 47, 52, 53].

The study results are expressed as standardized mortality ratio (SMR), standardized incidence ratio (SIR), relative risk (RR) or odds ratio (OR). In 22 articles the results are presented with and without adjustment for DI [10-13, 17, 20, 30, 31, 33, 37, 40-42, 44-46, 48-50, 52, 53].

Table 3 | *Small-area environmental studies and deprivation: study characteristics*

Country	Reference	Environmental exposure	Study population (reference period for population estimate)	Reference population	Health outcome (period)	Risk parameter (DI adjusted)	
Italy	Michelozzi <i>et al.</i> , 1998 [10]	Multiple sources of air pollution (landfill, petrochemical refinery, waste incinerator)	Residents within 10 km from the plants (1991 census)	Municipality (2.7 million inhabitants)	Mortality (1987-93)	SMR (crude and adjusted)	
	Martuzzi <i>et al.</i> , 2002 [16]	Multiple sources of air, soil, and water pollution – risk areas	Residents in the municipalities in risk areas (1991 census)	Regional or local population	Mortality (1990-94)	SMR (crude and adjusted)	
	Chellini <i>et al.</i> , 2002 [11]	Sewage plant	Residents in census units (1997 demographic office)	Municipality	Cancer Mortality (1987-96) Cancer incidence (1987-94)	SMR (crude and adjusted)	
	Biggeri <i>et al.</i> , 2004 [17]	Asbestiform fibres	Residents in the municipalities around a volcanic area	Local population	Mortality (1980-97)	SMR (crude and adjusted)	
	Parodi <i>et al.</i> , 2005 [12]	Cokework	Residents in municipalities (1991 census)	Local population	Lung cancer incidence (1986-97)	SIR (crude and adjusted)	
	Biggeri <i>et al.</i> , 2006 [13]	Multiple sources of air, soil, and water pollution – risk areas	Residents in the municipalities in risk areas (2001 census)	Local population	Mortality (1997-2001) Morbidity (2001-03)	SMR (crude and adjusted)	
	Minichilli <i>et al.</i> , 2006 [18]	Multiple sources of air, soil and water pollution – risk area	Residents in municipalities in the risk area (not specified)	Local population	Mortality (1990-2000)	SMR (adjusted)	
	Marinaccio <i>et al.</i> , 2008 [19]	Asbestos	Residents in Italian municipalities (not specified)	National population	Mortality (1980-2001)	AR (crude and adjusted)	
	Federico <i>et al.</i> , 2009 [57]	Incinerator (solid urban, non special)	Residents in a municipality (1991-2005 individual data)	National population	Cancer incidence (1991-2005)	SIR (adjusted)	
	Ianni <i>et al.</i> , 2009 [20]	Multiple sources of air, soil and water pollution – risk area	Residents in municipalities in the risk area (1991 and 2001 census)	Local population	Mortality (1997-2001)	SMR (crude and adjusted)	
	Martuzzi <i>et al.</i> , 2009 [21]	Authorized landfills and illegal dumping sites	Residents in the municipalities (mortality not specified; births 1996-2002 - Caserta and Naples provinces)	Local population	Mortality (1994-2001) Congenital anomalies (1996-2002)	RR (adjusted)	
	Great Britain	Sans <i>et al.</i> , 1995 [22]	Multiple sources of pollution (petrochemical, refinery, steel plant)	Residents within 7.5 km (1981 census)	National population	Mortality (1981-91) Cancer incidence (1974-84)	SMR and SIR (adjusted)
		Elliott <i>et al.</i> , 1996 [23]	Incinerators (household, commercial, industrial)	Residents within 7.5 km (1981 census)	National population	Cancer incidence (England 1974-86; Wales 1974-84; Scotland 1975-87)	SIR (adjusted)
Dolk <i>et al.</i> , 1997 a. [24]		Radio FM and television transmitters	Residents within 10 km (1981 census)	National population	Cancer incidence (England 1974-86; Wales 1974-84; Scotland 1975-87)	Smoothed SIR (adjusted)	
Dolk <i>et al.</i> , 1997 b. [34]		Radio FM and television transmitter	Residents within 10 km (1981 census)	National population	Cancer incidence (1974-86)	SIR (adjusted)	
Parslow <i>et al.</i> , 1997 [35]		Nitrate in drinking water	Residents in water supply zones (1991 census)	Local population	Childhood diabetes mellitus incidence (1978-94)	SIR (adjusted)	
Wilkinson <i>et al.</i> , 1997 [36]		Chemical plant (pesticides and fertilizers)	Residents within 7.5 km (1981 and 1991)	National population	Cancer mortality (1981-92) Cancer incidence (1977-89)	SMR and SIR (adjusted)	
Dolk <i>et al.</i> , 1999 [37]		Cokeworks	Residents within 7.5 km (1981 and 1991 censuses)	Regional population	Mortality (1981-92)	SMR (crude and adjusted)	
Harrison <i>et al.</i> , 1999 [54]		Main roads and petrol stations	Residents within 100 m (0-15 years old; 1990-94 West Midlands)	- Residents more than 100 m from main roads and/or petrol stations - Local population	Childhood cancer (1990-94)	OR and SIR (adjusted)	
Wilkinson <i>et al.</i> , 1999 [56]		Oil refineries	Residents within 7.5 km (1981 and 1991 censuses)	National population	Lymphomatopoietic cancer incidence (England and Wales 1974-89; Scotland 1975-91)	SIR (adjusted)	
Dolk <i>et al.</i> , 2000 [38]		Cokeworks	Residents within 7.5 km (live, stillbirths, deaths 1981-92)	Local population	Perinatal, infant mortality, and low birth weight (1981-92)	O/E ratios (adjusted)	
Aylin <i>et al.</i> , 2001 [39]		Cokeworks	Residents within 7.5 km (1991 census)	Local population	Hospital admission for respiratory and cardiovascular disease (1992-95)	RR (adjusted)	

(Continued)

Table 3 | (Continued)

	Elliott <i>et al.</i> , 2001 [40]	Landfills (hazardous waste, non special, unknown)	Residents within 2 km (terminations 1988-98; births and stillbirths 1983-98)	Residents more than 2 km from landfills	Congenital anomalies (1983-98) Hypospadias and epispadias, (1993-95) Hospital admission (1993-97) Stillbirths (1983-98) Low birth weight (1983-98)	RR (crude and adjusted)
	Jarup <i>et al.</i> , 2002 [41]	Landfills	Residents within 2 km (1981 and 1991 censuses)	Residents more than 2 km from landfills	Selected cancer incidence (England and Scotland 1983-97; Wales 1983-94)	RR (crude and adjusted)
	Cresswell <i>et al.</i> , 2003 [42]	Waste Combustion plant	Residents within 3 km (live births 1985-99)	Residents 3-7 km from the plant	Congenital anomalies (1985-99)	RR (crude and adjusted)
	Morris <i>et al.</i> , 2003 [43]	Landfills (special waste)	Residents within 2 km (CA and terminations 1988-94; hospital admissions 1993-95; births and stillbirths 1983-98)	Residents more than 2 km from landfills	Congenital anomalies (1988-94) Stillbirths and low birth weight (1983-98)	RR (crude and adjusted)
	Maheswaran <i>et al.</i> , 2003 [44]	Main roads	Residents in enumeration district by distance to main roads - < 200 m; 200-500 m; 500-1000 m (> = 45 years old; 1991 census)	Residents more than 1 km to main roads	Stroke mortality (1990-92)	RR (crude and adjusted)
	Morgan <i>et al.</i> , 2004 [45]	Landfills (hazardous waste)	Residents within 3 km (singleton live birth registration 1986-99)	Residents 3-7 km from landfills	Low birth weight (1986-99)	OR (crude and adjusted)
	Hodgson <i>et al.</i> , 2004 [46]	Industrial plants (various chemicals)	Residents within 2 km (not specified)	Local population	Kidney disease mortality (1981-99)	SMR (crude and adjusted)
	Palmer <i>et al.</i> , 2005 [47]	Landfills (household, commercial, industrial; Wales)	Residents within 2 km (births 1983-97)	Residents more than 4 km from landfills	CA (1983-97)	SRR (adjusted)
	Maheswaran <i>et al.</i> , 2005 a [48]	Air pollution (PM ₁₀ , NOx, CO)	Residents in enumeration district (1994-98 Sheffield health authority estimates)	Quintile of PM10, NOx, CO modeled exposure	Stroke hospital admissions (1994-99)	RR (crude and adjusted)
	Maheswaran <i>et al.</i> , 2005 [49]	Air pollution (PM ₁₀ , NOx, CO)	Residents in enumeration district (1994-98 Sheffield health authority estimates)	Quintile of PM10, NOx, CO modeled exposure	Coronary heart disease hospital admissions (1994-99)	RR (crude and adjusted)
	Maheswaran <i>et al.</i> , 2006 [50]	Air pollution (NOx)	Residents in enumeration district (1994-98, Sheffield health authority estimates)	Quintile of NOx modeled exposure	Stroke mortality (1994-98)	RR (crude and adjusted)
	Hodgson <i>et al.</i> , 2007 [51]	Mercury emitting industries	Residents within the modelled ambient mercury contours (1981 and 1991 censuses)	Local population	Kidney disease mortality (1981-2001)	SMR (adjusted)
	Elliott <i>et al.</i> , 2007 [55]	Air pollution (black smoke SO ₂)	Residents in wards (1991 census)	National population	Mortality (1982-98)	RR (crude and adjusted)
	Jarup <i>et al.</i> , 2007 [52]	Landfill sites (special, nonspecial or unknown waste)	Residents within 2 km (live births, late fetal deaths and terminations 1989-98)	Residents more than 2 km from landfills	Down syndrome registrations (1989-98)	RR (crude and adjusted)
	Elliott <i>et al.</i> , 2009 [53]	Landfill sites (special, nonspecial or unknown waste)	Residents within 2 km (terminations 1988-98; births and stillbirths 1983-98)	Residents more than 2 km from landfills	Hypospadias and epispadias, cardiovascular defects, neural tube defects and abdominal wall defects (1983-98)	OR (crude and adjusted)
New Zealand	Scoggins <i>et al.</i> , 2004 [30]	Air pollution (NO ₂)	Residents in CAUs- Census Area Unit (1996, Auckland)	Residents in low pollution CAUs	Mortality (1996-1999)	O/E (adjusted) OR (crude and adjusted)
	Sabel <i>et al.</i> , 2007 [31]	Air pollution (PM10)	Residents in CAUs- Census Area Unit (1996 and 2001 Christchurch)	NA Cluster analysis	Respiratory system and appendicitis admissions (1999-2004)	O/E in cluster (crude and adjusted)
Australia	McKenzie <i>et al.</i> , 1998 [32]	Exposure to RFR-radio frequency radiation	Residents in LGA (Local Government Area, 1972-1990, Sidney)	Residents in low radio frequency radiation LGAs	Leukemia incidence (1972-1990)	RR (adjusted)
Spain	Barceló <i>et al.</i> , 2009 [33]	Air pollution (TSP, PM10, NO ₂ , SO ₂ , CO)	Residents in census tracts (1994-2003, Barcelona Metropolitan Area)	National population	Mortality: all causes, COPD, ischemic heart disease, lung cancer, bladder cancer, thyroid cancer, lymphoma (1994-2003)	Smoothed SMR (BYM model crude and adjusted)

SMR: standardized mortality risk; SIR: standardized incidence; RR: relative risk; OR: odds ratio; O/E: observed/expected.; SLA: statistical local area; CD: collection district

Lastly, as far as the reference year for DI calculation, in six papers it is not specified [37, 45-47, 53, 54], and in 16 more studies DI variables are from the Census in the same year of identification of the exposed population [10, 12, 13, 16, 22-24, 30, 31, 34-36, 38, 39, 44, 56], in the remaining papers the DI year precedes the identification of population (*e.g.* in [11] DI year is 1991 and population is identified in 1997) or is included in the period of population enumeration (*e.g.* in [32] DI year is 1986 and population was represented by residents in 1972-1990).

DISCUSSION

The use of DIs: critical aspects

DIs can be constructed in various ways and calculated at various area levels. Different area-based DIs show unlike associations with health effects from different causes [59, 60].

It is expected that the use of DIs to adjust for deprivation in small-area environment and health studies should result in better risk estimates. This holds true if the following conditions are present: a) exposure is causally associated with outcome; b) DI is a proxy for factors causally associated with outcome; c) exposure and DI are associated - exposed and unexposed areas are different in respect to DI. The risk estimates of most of the 22 reviewed studies reporting adjusted and unadjusted results for deprivation do not significantly differ. An example of an exception is found in two studies assessing the association between air pollution and lung cancer [33, 55]. In these studies conditions a) and b) are defined [61, 62]. In one of them also condition c) is ascertained as it shows correlation between some air pollutants and deprivation [33].

The interplay between environmental exposure, deprivation and health is complex. One element of the complexity is the possible reverse causality between deprivation and health. It can occur when studying health effects of long-term environmental exposures, since the worsening in health status caused by environmental exposures can result in downgrading in socioeconomic status. On the other hand, a Great Britain study shows that areas with similar long standing economic disadvantage do not have similar high mortality rates, being some of them *resilient* to external disadvantage factors. According to Tunstall, "these areas might be doing 'better than expected' or 'overachieving'". This status implies that there may be protective factors or practices in particular areas, which weaken the usually strong relationships between economic adversity and poor health" [63]. Then again, a Dutch investigation documents that some deprived areas are healthier, and wealthy areas are instead unhealthier than expected on the basis of their socio-economic level [64]. The relationship between deprivation and health may also potentially be confounded by phenomenon of selective migration into deprived

neighbourhoods of people already in poor health status [65]. Conversely, other studies highlight the apparent clustering of hazardous and polluting sites in areas inhabited by ethnic minorities. The consequence is that socially disadvantaged people become subject to the additional burden of a more polluted or hazardous environment, thus providing evidence of environmental inequities [66-68]. A recent study exemplifies interplay complexity and environmental inequalities. It shows that populations living closer to waste facilities are also the more deprived and both adjusted and unadjusted mortality excesses are higher among them. The authors suggest the possible occurrence of effect modification by deprivation [69].

In studies of environment and health where deprivation is thought at play another point to be considered is that mortality and morbidity could be influenced by past and by present deprivation as well [4]. This influence is disease-specific, since under or over control for deprivation could occur if DIs time patterns should not fit the relevant time window of the study. An additional issue to be taken into account is that the relationship between deprivation and health could be different in various areas within a country [63].

In the light of the above issues when adjusting for deprivation in environment and health studies it is advisable to report both adjusted and unadjusted results, to explicit relevant time windows of the investigation conducted, and to document overtime socioeconomic characteristics of the area at study.

Another critical aspect in the use of DI is related to the *population size* of the territorial unit as reducing it does not automatically lead to a better estimate of deprivation. In fact, smaller units are more homogeneous but DI becomes unstable due to greater sensitivity to local variation [4]. Population size should also be considered in relation to the *contextual effect* of deprivation. In fact, since this effect is meant as an overall socioeconomic neighbourhood influence [7], *population size* should be carefully selected to better understand the contextual effect. Deprivation at area level could be not only a *proxy* for individual socioeconomic status but also a measurement of the *contextual area effect*. In fact, sometimes measures of socioeconomic conditions at area level were found to be associated to the health outcomes at study independently from individual socioeconomic status [70, 71].

As far as the characteristics of the studies included in the present review, the great majority have been conducted in Great Britain and Italy. In the former, DIs applied in studies after 1997 have been Townsend's and Carstairs' based on clearly stated variables. In the latter instead, the variables used in the construction of DI are not homogeneously reported. However, it appears that in the great majority of studies performed in a given area the construction of *ad hoc* indices considering the local socioeconomic context is not taken into account.

It should also be pointed out that the choice of a Census year seems to derive from a pragmatic evaluation of data availability, without considering the relevant time window related to the study hypothesis; it is clearly shown, for example, in a study indicating that the more appropriate socioeconomic indicator refers to ten years before breast cancer diagnosis [71].

Another observation is that in the majority of the reviewed studies DIs are classified in quintiles but rarely information is given about the basis on which quintiles are made and the reason why they are chosen. Generally, quantiles appear to be adopted to avoid the potential residual confounding, and to have stable reference rates for each deprivation category; the latter is an issue that should be weighted in case of rare diseases or small reference populations.

In the majority of the studies adjustment for deprivation is carried out by indirect standardization. The quantiles of DIs and the reference rates for the analyzed outcomes should pertain to the same territorial unit, but the studies in the review do not grant appropriate information about this issue.

Systematic bibliographic research: critical aspects

By matching the results of the two bibliographic searches carried out, it was ascertained that the systematically conducted bibliographic search was lacking of some relevant articles that were instead included in the initial search. By examining how both the obtained articles and the missing ones were indexed some consideration came into light. The main difficulty in information retrieval originated from the fact that there was no applicable controlled term to express the concept of small-area study, unless it was referred to analyzing the variation in utilization of health care in small geographic or demographic areas; for the concept of DI the problem was similar; so, the articles dealing with these two concepts could only be achieved if such terms, or their synonyms, were included in the title or abstract. It must be considered that most of the articles identified through PubMed/Medline and Embase come from countries where DIs have been in use for a long time, therefore they are applied in the studies although the term itself is not found in the title and/or abstract; this implies that such articles are not in the hit list with this search approach. It also came out that different researchers assign different meaning, and associate similar but not equal variables to the concept of DI. In addition, in the MeSH Thesaurus a term adhering to the meaning of deprivation as a multidimensional index is not provided. In the systematic search strategy DI was therefore translated with “socioeconomic factors”, and the terms included under the related tree structure, as well as a combining of synonyms and related terms for this other concept, were also added.

It is an opinion shared by the majority that for systematic reviews the combining of online searches, bibliographic examination of the articles already owned, and experts opinion is the best approach for a comprehensive information retrieval [72]. This method proves to be even more appropriate when, as it is in this case, the topic of the study foretells a challenging bibliographic research.

CONCLUDING REMARKS

The present review describes DIs used to adjust for deprivation in small-area studies of environment and health in the last fifteen years. To the authors' knowledge this is the first attempt to exhaustively examine such a relevant topic in environmental epidemiology. A main remark is that this review makes clear the difficulty in understanding whether adjusting from deprivation using DIs was efficient or not to assess confounding from socioeconomic factors. The various DIs were adopted from studies looking at health resource allocation or health inequalities, where the role of the environment on health was not the main investigative topic. Therefore the application of DIs appears to have been pragmatic without considering the specific aim of the studies. Time, a key feature in epidemiology, does not appear to have been taken into account either in the choice of DIs or in the interpretation of the results.

In adjusting for deprivation the potential for under or over control is possible and it is specific for

BOX | Suggestions to apply DIs in future studies

If applicable, when designing a small-area study of environment and health, consider

- to perform an *a priori* evaluation of the interplay between environmental exposure – deprivation – other known predictive factors – health outcome at study;
- to choose proper time of data used to construct DI to reflect the relevant time windows in the interplay between environmental exposure – deprivation – health outcome at study;
- for local studies, to develop DIs which represent measure of material and social circumstances at the macro-area of reference instead of DIs developed at a national level;
- deprivation at area level not only as a proxy for individual socioeconomic status but also as a measure of contextual deprivation;
- to select territorial unit for DI balancing the following needs: (i) represent individual level socioeconomic status, or contextual deprivation, and (ii) define a stable index;
- to evaluate the feasibility for developing a DI for measurement of the contextual deprivation other than DI as a proxy for measurement of individual socioeconomic status.

When preparing a small-area manuscript of environment and health

- report details of *a priori* evaluation;
- describe the main characteristics of DI: variables used to construct DI as reported in methodological papers, time of reference for the selected DI, territorial unit;
- report both unadjusted and DI adjusted results.

a given environmental exposure-disease association. Over/under control is less of a problem in discussing results, if the more specific and the stronger is the exposure disease association, and the rarer and higher is the exposure [4].

The use of DIs is increasing and expanding to many countries. In the years to come, at different area level, improved exposure information and time-series data on exposure, outcomes and other predictive factors will be growingly available. This enhanced data availability, together with better knowledge on the relationship between deprivation and health, will make possible studies aimed at disentangling the complex interplay between environmental exposure, health and deprivation. In this context one of the main areas to be developed will be the application of mixed design studies combining ecological and individual data [5, 73]. To deal with this challenge, future studies should foresee an *a priori* assessment of every element at play. Even though the *a priori* knowledge is often incomplete and analytical solutions to tackle with complex interplay are not always

available, this approach has the strength to point out the information we ideally have to collect, giving a framework to discuss the final results. A novel tool proposed to perform a formal *a priori* evaluation is the direct acyclic graphs (DAG) analysis [74-76]. In the BOX suggestions are given for the use of DIs in small-area environment and health studies at the light of their use in the past, the above discussion and the possible scenarios in the next future.

Acknowledgments

The authors acknowledge the helpful and constructive comments to the article made by Francesco Mitis and Dolores Catelan.

Conflict of interest statement

There are no potential conflict of interest of any financial or personal relationship with other people or organizations that could inappropriately bias conduct and findings of this study.

Received on 31 March 2010.

Accepted on 10 May 2010.

References

1. Townsend P. Deprivation. *J Soc Policy* 1987;16:125-46.
2. Whitehead M. *The health divide*. Pelican Books: London; 1988.
3. Carstairs V. Socio-economic factors at area level and their relationship with health. In: Elliott P, Wakefield JC, Best NG, Briggs DJ (Ed.). *Spatial epidemiology. Methods and applications*. New York: Oxford University Press; 2000. p. 51-67.
4. Dolk H, Mertens B, Kleinschmidt I, Walls P, Shaddick G, Elliott P. A standardisation approach to the control of socio-economic confounding in small area studies of environment and health. *J Epidemiol Community Health* 1995;49(Suppl 2):S9-S14.
5. Elliott P, Savitz DA. Design issues in small-area studies of environment and health. *Environ Health Perspect* 2008;116:1098-104.
6. Faggiano F, Partanen T, Kogevinas M, Boffetta P. Socio-economic differences in cancer incidence and mortality in social inequalities and cancer. In: Kogevinas M, Pearce N, Susser M, Boffetta P. (Ed.). *IARC Scientific Publications* 1997;138:65-176.
7. Blakely T, Hales S, Woodward A. *Poverty: assessing the distribution of health risks by socioeconomic position at national and local levels*. Geneva: World Health Organization; 2004. (WHO Environmental Burden of Disease Series, No. 10).
8. Elliott P, Dolk H. Foreword. *J Epidemiol Commun Health* 1995;49(Suppl 2):S2.
9. Carstairs V. Small area analysis and health service research. *Community Med* 1981;3:131-9.
10. Michelozzi P, Fusco D, Forastiere F, Ancona C, Dell'Orco V, Perucci CA. Small area study of mortality among people living near multiple sources of air pollution. *Occup Environ Med* 1998;55:611-5.
11. Chellini E, Cherubini M, Chetoni L, Costantini AS, Biggeri A, Vannucchi G. Risk of respiratory cancer around a sewage plant in Prato, Italy. *Arch Environ Health* 2002;57:548-53.
12. Parodi S, Stagnaro E, Casella C, Puppo A, Daminelli E, Fontana V, Valerio F, Vercelli M. Lung cancer in an urban area in Northern Italy near a coke oven plant. *Lung cancer* 2005;47:155-64.
13. Biggeri A, Lagazio C, Catelan D, Pirastu R, Casson F, Terracini B. Environment and health in Sardinia, Italy. *Epidemiol Prev* 2006;30(Suppl 1):1-96.
14. Cadum E, Costa G, Biggeri A, Martuzzi M. Deprivation and mortality: a deprivation index suitable for geographical analysis of inequalities. *Epidemiol Prev* 1999;23:175-87.
15. Caranci N, Biggeri A, Grisotto L, Pacelli B, Spadea T, Costa G. The Italian deprivation index at census tract level: definition, description and association with general mortality. *Epidemiol Prev* (in press).
16. Martuzzi M, Mitis F, Biggeri A, Terracini B, Bertollini R. Environment and health status of the population in areas with high risk of environmental crisis in Italy. *Epidemiol Prev* 2002;26(Suppl 6):1-53.
17. Biggeri A, Pasetto R, Belli S, Bruno C, Di Maria G, Mastrantonio M, Trinca S, Uccelli R, Comba P. Mortality from chronic obstructive pulmonary disease and pleural mesothelioma in an area contaminated by natural fiber (fluorocedenite). *Scand J Work Environ Health* 2004;30:249-52.
18. Minichilli F, Bartolacci S, Buiatti E, Pierini A, Rossi G, Bianchi F. Mortality in the area around Massa-Carrara 10 years after ANIC-Agricoltura and Farmoplant chemical plants were shut down. *Epidemiol Prev* 2006;30(2):120-8.
19. Marinaccio A, Scarselli A, Binazzi A, Mastrantonio M, Ferrante P, Iavicoli S. Magnitude of asbestos-related lung cancer mortality in Italy. *Br J Cancer* 2008;99:173-5.
20. Ianni E, Mignozzi K, Mitis F. Geographic epidemiologic descriptive study on the national priority site for remediation "Laguna di Grado e Marano". *Epidemiol Prev* 2009;33:27-36.
21. Martuzzi M, Mitis F, Bianchi F, Minichilli F, Comba P, Fazzo L. Cancer mortality and congenital anomalies in a region of Italy with intense environmental pressure due to waste. *Occup Environ Med* 2009;66:725-32.
22. Sans S, Elliott P, Kleinschmidt I, Shaddick G, Pattenden S, Walls P, Grundy C, Dolk H. Cancer incidence and mortality near the Baglan Bay petrochemical works, South Wales. *Occup Environ Med* 1995;52:217-24.

23. Elliott P, Shaddick G, Kleinschmidt I, Jolley D, Walls P, Beresford J, Grundy C. Cancer incidence near municipal solid waste incinerators in Great Britain. *Br J Cancer* 1996; 73:702-10.
24. Dolk H, Shaddick G, Walls P, Grundy C, Thakrar B, Kleinschmidt I, Elliott P. Cancer incidence near radio and television transmitters in Great Britain. I. Sutton Coldfield transmitter. *Am J Epidemiol* 1997;145(1):1-9.
25. Townsend P, Phillimore P, Beattie A. *Health and deprivation: inequalities and the north*. London: Croom Helm; 1988.
26. Carstairs V, Morris R. *Deprivation and health in Scotland*. Aberdeen: Aberdeen University Press; 1991.
27. Crampton P, Salmond C, Kirkpatrick R, Scarborough R, Skelly C. *Degrees of deprivation: an atlas of socioeconomic difference*. Auckland, New Zealand: David Bateman Ltd; 2000.
28. Australian Bureau of Statistics. *Construction of an indicator of socio-economic status*. Information paper No. 15. ABS; 1986.
29. Domínguez-Berjón MF, Borrell C, Cano-Serral G, Esnaola S, Nolasco A, Pasarín MI, Ramis R, Saurina C, Escolar-Pujolar A. Constructing a deprivation index based on census data in large Spanish cities (the MEDEA project). *Gac Sanit* 2008;22:179-87.
30. Scoggins A, Kjellstrom T, Fisher G, Connor J, Gimson N. Spatial analysis of annual air pollution exposure and mortality. *Sci Total Environ* 2004;321:71-85.
31. Sabel CE, Wilson JG, Kingham S, Tisch C, Epton M. Spatial implications of covariate adjustment on patterns of risk: respiratory hospital admissions in Christchurch, New Zealand. *Soc Sci Med* 2007;65:43-59.
32. McKenzie DR, Yin Y, Morrell S. Childhood incidence of acute lymphoblastic leukaemia and exposure to broadcast radiation in Sydney—a second look. *Aust NZJ Public Health* 1998;22(3 Suppl):360-7.
33. Barceló MA, Saez M, Saurina C. Spatial variability in mortality inequalities, socioeconomic deprivation, and air pollution in small areas of the Barcelona Metropolitan Region, Spain. *Sci Total Environ* 2009;407:5501-23.
34. Dolk H, Elliott P, Shaddick G, Walls P, Thakrar B. Cancer incidence near radio and television transmitters in Great Britain. II. All high power transmitters. *Am J Epidemiol* 1997;145(1):10-7.
35. Parslow RC, McKinney PA, Law GR, Staines A, Williams R, Bodansky HJ. Incidence of childhood diabetes mellitus in Yorkshire, Northern England, is associated with nitrate in drinking water: an ecological analysis. *Diabetologia* 1997; 40:550-6.
36. Wilkinson P, Thakrar B, Shaddick G, Stevenson S, Pattenden S, Landon M, Grundy C, Elliott P. Cancer incidence and mortality around the Pan Britannica Industries pesticide factory, Waltham Abbey. *Occup Environ Med* 1997;54:101-7. Erratum in: *Occup Environ Med* 1997;54:216.
37. Dolk H, Thakrar B, Walls P, Landon M, Grundy C, Sáez Lloret I, Wilkinson P, Elliott P. Mortality among residents near cokeworks in Great Britain. *Environ Med* 1999;56:34-40.
38. Dolk H, Pattenden S, Vrijheid M, Thakrar B, Armstrong B. Perinatal and infant mortality and low birth weight among residents near cokeworks in Great Britain. *Arch Environ Health* 2000;55:26-30.
39. Aylin P, Bottle A, Wakefield J, Jarup L, Elliott P. Proximity to coke works and hospital admissions for respiratory and cardiovascular disease in England and Wales. *Thorax* 2001; 56:228-33.
40. Elliott P, Briggs D, Morris S, de Hoogh C, Hurt C, Jensen TK, Maitland I, Richardson S, Wakefield J, Jarup L. Risk of adverse birth outcomes in populations living near landfill sites. *BMJ* 2001;323:363-8. Erratum in: *BMJ* 2001;323:1182.
41. Jarup L, Briggs D, de Hoogh C, Morris S, Hurt C, Lewin A, Maitland I, Richardson S, Wakefield J, Elliott P. Cancer risks in populations living near landfill sites in Great Britain. *Br J Cancer* 2002;86:1732-6.
42. Cresswell PA, Scott JE, Pattenden S, Vrijheid M. Risk of congenital anomalies near the Byker waste combustion plant. *J Public Health Med* 2003;25:237-42.
43. Morris SE, Thomson AO, Jarup L, de Hoogh C, Briggs DJ, Elliott P. No excess risk of adverse birth outcomes in populations living near special waste landfill sites in Scotland. *Scott Med J* 2003;48:105-7.
44. Maheswaran R, Elliott P. Stroke mortality associated with living near main roads in England and Wales: a geographical study. *Stroke* 2003;34:2776-80.
45. Morgan OW, Vrijheid M, Dolk H. Risk of low birth weight near EUROHAZCON hazardous waste landfill sites in England. *Arch Environ Health* 2004;59:149-51.
46. Hodgson S, Nieuwenhuijsen MJ, Hansell A, Shepperd S, Flute T, Staples B, Elliott P, Jarup L. Excess risk of kidney disease in a population living near industrial plants. *Occup Environ Med* 2004;61:717-9.
47. Palmer SR, Dunstan FD, Fielder H, Fone DL, Higgs G, Senior ML. Risk of congenital anomalies after the opening of landfill sites. *Environ Health Perspect* 2005;113:1362-5.
48. Maheswaran R, Haining RP, Brindley P, Law J, Pearson T, Fryers PR, Wise S, Campbell MJ. Outdoor air pollution and stroke in Sheffield, United Kingdom: a small-area level geographical study. *Stroke* 2005a;36:239-43.
49. Maheswaran R, Haining RP, Brindley P, Law J, Pearson T, Fryers PR, Wise S, Campbell MJ. Small-area level ecological study. Outdoor air pollution, mortality, and hospital admissions from coronary heart disease in Sheffield, UK: a small-area level ecological study. *Eur Heart J* 2005b;26(23):2543-9.
50. Maheswaran R, Haining RP, Pearson T, Law J, Brindley P, Best NG. Outdoor NOx and stroke mortality: adjusting for small area level smoking prevalence using a Bayesian approach. *Stat Methods Med Res* 2006;15:499-516.
51. Hodgson S, Nieuwenhuijsen MJ, Elliott P, Jarup L. Kidney disease mortality and environmental exposure to mercury. *Am J Epidemiol* 2007;165:72-7.
52. Jarup L, Morris S, Richardson S, Briggs D, Cobley N, de Hoogh C, Gorog K, Elliott P. Down syndrome in births near landfill sites. *Prenat Diagn* 2007;27:1191-6.
53. Elliott P, Richardson S, Abellan JJ, Thomson A, de Hoogh C, Jarup L, Briggs DJ. Geographic density of landfill sites and risk of congenital anomalies in England. *Occup Environ Med* 2009;66:81-9.
54. Harrison RM, Leung P, Somervaille L, Smith R, Gilman E. Analysis of incidence of childhood cancer in the West Midlands of the United Kingdom in relation to proximity to main roads and petrol stations. *Occup Environ Med* 1999; 56:774-80.
55. Elliott P, Shaddick G, Wakefield JC, de Hoogh C, Briggs DJ. Long-term associations of outdoor air pollution with mortality in Great Britain. *Thorax* 2007;62:1088-94.
56. Wilkinson P, Thakrar B, Walls P, Landon M, Falconer S, Grundy C, Elliott P. Lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain. *Occup Environ Med* 1999;56:577-80.
57. Federico M, Pirani M, Rashid I, Caranci N, Cirilli C. Cancer incidence in people with residential exposure to a municipal waste incinerator: An ecological study in Modena (Italy), 1991-2005. *Waste Management* 2010;30:1362-70.

58. Bell N, Schuurman N, Hayes MV. Using GIS-based methods of multicriteria analysis to construct socio-economic deprivation indices. *Int J Health Geogr* 2007;6:17.
59. Davey Smith G, Whitley E, Dorling D, Gunnell D. Area based measures of social and economic circumstances: cause specific mortality patterns depend on the choice of index. *J Epidemiol Community Health* 2001;55:149-50.
60. Testi A, Ivaldi E. Material versus social deprivation and health: a case study of an urban area. *Eur J Health Econ* 2009; 10:323-8.
61. World Health Organization. *Air Quality Guidelines Global Update 2005*. Report on a working group meeting, Bonn, Germany, 18-20 October 2005. Copenhagen: World Health Organization; 2005.
62. Spitz MR, Wu X, Wilkinson A, Wei Q. Cancer of the lung. In: Schottenfeld D and Fraumeni JF Jr (Ed.). *Cancer Epidemiology and Prevention*, Third Edition. New York: Oxford University Press; 2006. p. 638-58.
63. Tunstall H, Mitchell R, Gibbs J, Platt S, Dorling D. Is economic adversity always a killer? Disadvantaged areas with relatively low mortality rates. *J Epidemiol Community Health* 2007;61:337-43.
64. van Hooijdonk C, Droomers MI, van Loon JAM, van der Lucht F, Kunst AE. *Soc Sci Med* 2007;64:1326-42.
65. Norman P, Boyle P, Rees P. Selective migration, health and deprivation: a longitudinal analysis. *Soc Sci Med* 2005;60: 2755-71.
66. Brown P. Race, class and environmental health: a review and systematization of the literature. *Environ Res* 1995; 69:5-30.
67. Oakes JM, Anderton DL, Anderson AB. A longitudinal analysis of environmental equity in communities with hazardous waste facilities. *Social Sci Res* 1996;25:125-48.
68. Morello-Frosch R, Pastor M Jr, Porras C, Sadd J. Environmental justice and regional inequality in southern California: implications for future research. *Environ Health Perspect* 2002;110(Suppl 2):149-54.
69. Martuzzi M, Mitis F, Forastiere F. Inequalities, inequities, environmental justice and health. *Eur J Public Health* 2010; 20:21-6.
70. Stafford M, Gimeno D, Marmot MG. Neighbourhood characteristics and trajectories of health functioning: a multilevel prospective analysis. *Eur J Public Health* 2008;6:604-10.
71. Webster TF, Hoffman K, Weinberg J, Vieira V, Aschengrau A. Community- and individual-level socioeconomic status and breast cancer risk: multilevel modeling on Cape Cod, Massachusetts. *Environ Health Perspect* 2008;116:1125-9.
72. Higgins JPT, Green S (Ed.). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2 (updated September 2009). The Cochrane Collaboration, 2009. Available from www.cochrane-handbook.org.
73. Wakefield J. Ecologic studies revisited. *Ann Rev Public Health* 2008;29:75-90.
74. Chaix B, Leal C, Evans D. Neighborhood-level confounding in epidemiologic studies. Unavoidable challenges, uncertain solutions. *Epidemiology* 2010;21:124-7.
75. Pearl J. *Causality*. New York: Oxford University Press; 2000.
76. Greenland S. Quantifying biases in causal models: classical confounding vs. collider-stratification bias. *Epidemiology* 2003; 14:300-6.