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Evaluation of community-wide interventions: the ecologic case-referent study design

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Abstract. In a setting of long-standing, community-wide and generally accepted prevention activities like youth health care services in The Netherlands, evaluative research in the form of experimental studies is hardly possible. Furthermore, as most interventions will bear fruit only after several years and the effects are often described in rather vague terms, even non-experimental study designs are fraught with possible difficulties. Although a study design using aggregate data is generally considered inferior or 'incomplete', in many cases, especially in health services research, this approach can be the only one feasible to evaluate the effectiveness of preventive programmes and interventions. In this article we present the ecologic case-referent design as a potentially expedient and valid method for estimating the ecologic effect of a population-wide intervention on the outcome rate in those populations. In this case-referent design, many variables are measured at the individual level, whereas the main exposure variable is measured at an aggregate or ecologic level. Using recently published studies as an example, the advantages and drawbacks of the design are discussed using the randomised controlled trial design as the referent study design.

Key words: Ecologic case-referent study design, Effect evaluation, Evidence based medicine, Health services research

Introduction

In preventive medicine, population-wide interventions are generally recognised as an, in essence, effective means to enhance community health. Indeed, few will doubt the positive influence of water sanitation measures or will question the effectiveness of vaccination of children in reducing morbidity and mortality due to communicable diseases. In some cases proof of the effectiveness of certain measures was derived from 'natural experiments'. One of the early examples is the work of Snow, who compared cholera mortality rates in regions serviced by different water companies, thereby demonstrating the value of water sanitation [1]. A more recent example is the momentary decrease in pertussis vaccination in England, giving rise to a clear increase in morbidity due to whooping cough [2, 3].

Given the potential impact of community-wide interventions, it is remarkable to see that most are in use without sufficient evidence about their effects on health outcomes. Many of these activities have been introduced in community health years or even decades ago, and continue to be used to this day, while the effectiveness, relative to unintended effects and financial costs, is under discussion [4–7], or even proven to be non-existent [8, 9]. Still worse, community-wide interventions can have unexpected side-effects that outweigh or even reverse the intended beneficial influence [10–12]. These problems, of course, are not restricted to the field of medicine. Many are the preventive measures that have found their way into society without adequate proof of their (cost-)effectiveness [13].

Several reasons are brought forward to explain this lack of evaluative research. First, in a setting of long-standing, community-wide and generally accepted prevention activities, experimental studies are hardly possible. Furthermore, as most interventions will bear fruit only after several years and the effects are often described in rather vague terms like 'improved health', even non-experimental study designs are fraught with possible difficulties. Also, this lack of clear definitions of intended outcome makes the choice of specific outcome measurement(s) difficult and often controversial, especially if the evaluation returns a less than positive result. Moreover, many of the outcomes targeted have a low incidence or prevalence, again reducing the possible design options. Apart from these methodological arguments, because of the often high level of acceptance by professionals as well as the general public a critical appraisal of such longstanding preventive activities is often less than appreciated, even to the point of suppressing unwelcome publications [14].

For screening activities it is even harder to weigh the effectiveness, since the benefit of finding even one individual with the disease targeted has to be contrasted against the cost – financial, social, and psychological – of screening the total population at risk [13, 15–17].

In The Netherlands, a clear example of community-wide interventions in preventive medicine that sorely lack rigorous evaluation of their effectiveness is youth health care (YHC), in particular the care for the 4–19 year age group – in The Netherlands the school-going population.

In the past 50 years, these YHC services have developed from modest local initiatives to nation-wide, labour-intensive services, employing hundreds of physicians, nurses and medical assistants. By the time they leave school, every child in The Netherlands will have been exposed to a variety of preventive health and health promotion activities, administered by many different YHC workers. Most of these contacts will have been in the form of well-care visits (otherwise known as periodic health examinations) and screening activities for specific physical abnormalities.

Since the early 1960s, the way YHC services are conducted has changed profoundly, often necessitated by budgetary cutbacks. Furthermore, a shift of attention from physical to mental health problems required a fundamental change in the content of prevention activities and in the general attitude of YHC workers. Examples, however, of changes brought about on scientific grounds or due to outcomes of evaluative health services research, are rare.

Nevertheless, in the face of an increasing demand for evidence based medicine [18, 19], an effort has to be made to substantiate the effectiveness claimed by YHC workers. It is fortunate therefore, that circumstances largely unrelated to the development of health and health-related behaviour in school-going children created considerable regional variation in type and frequency of YHC activities. Thus a natural experiment was created, which facilitated the development of a suitable study design.

In this paper we propose the ecologic case-referent design to address the problem of ex-post evaluation of effectiveness of preventive health interventions. The design is applicable in situations of substantial interregional variability in the prevention strategies used. However, it can also be used in situations where this variability exists at a lower level (i.e. between departments within an organisation) or at a higher level (for instance in an international comparative study). Moreover, it may be appropriate for situations in clinical medicine (hospitals, general practice). In this paper, however, we will restrict ourselves to preventive health interventions at the community or regional level.

In all cases, the most important question to be answered is whether at the aggregate level the variability in interventions is reflected in a variability in relevant health outcomes. The core hypothesis, therefore, is that, in order to be worthwhile, advocated interventions should lead to detectable and relevant effects on population morbidity and/or mortality relative to propagated alternative interventions for the same health, or health-related problem.

The situation

As indicated before, in this type of research a randomised controlled trial (RCT), or any other form of experimentation, is not feasible. Apart from that, several publications have pointed out the drawbacks of this design for studying the effectiveness of interventions [20–28]. However, the RCT in itself is still rated as paradigmatic in studying the occurrence of an event in relation to a dichotomous intervention that is randomly assigned to study subjects to ensure comparability of study groups. Therefore, the general principles underlying a well-conducted RCT should also apply to alternate study designs [29]. The resulting rate ratio will then provide a meaningful estimate of the effectiveness of the intervention (relative to its alternative) under the conditions reflecting the basic principles of evaluative research: (1) relevance, (2) validity, and (3) power and efficiency:

a. Relevance: the study has to be relevant regarding intervention, projected outcome, and population targeted. Actual and specific YHC interventions, therefore, should be studied with a view to the intended effects on the (quality of the) health of children.
b. Validity: the study should provide an unbiased estimate of the effectiveness of specific YHC interventions. This means that populations with different types of intervention have to be similar in baseline risk and distribution of potential confounders. In other words, the counterfactual rate in the population exposed should be the same as that in the referent population. Furthermore, information on determinant status should have no bearing on outcome measurement and *vice versa*.
c. Power and efficiency: the number of children should be large enough to detect relevant differences across the determinant categories. The efficiency of the design can be enhanced by sampling from populations that are more or less at the ends of the continuum of the health outcome under study (for instance 'severe depression' vs. 'no symptoms of depression at all'). Also, where possible, use of available data from (national) registries should be considered.

Generally speaking, aspects of study design, data collection and data analysis should be chosen in a manner such that the burden to investigator, study population and/or society, is minimised, conditional on the requirements stated above.

The proposed approach

As the focus of the study is on evidence regarding effectiveness at the aggregate level – is the regional variation in occurrence of disease related to the variation in preventive health activities – the ecologic approach seems apparent. The necessary information on intervention characteristics, outcome events and co-variables (confounders) can be obtained at an individual and group level, and/or by judiciously collecting data from the preventive services, (national) registries and (annual) reports. Provided all necessary data can be acquired, efficiency considerations, especially in the case of low prevalence or incidence of the outcome targeted, lead to the potentials of the case-referent approach for studying effectiveness at the individual level, notwithstanding the original purpose of the investigation to provide information at the aggregate level.

Both lines of thought lead to an ecologic case-referent design in which individual and aggregate level measurements are combined in an efficient way to provide an accurate and unbiased estimate of the effect of a preventive health intervention on the regional occurrence of the health outcome targeted.

For each determinant comprehensive information is collected with respect to the characteristics of the intervention offered in the relevant period. This information is then used to classify each region according to meaningful determinant categories. The regions are defined according to the geographical area in which the service providing the preventive health activities is active in the relevant time span. Cases are sampled from a (national) disease register and stratified according to the relevant confounding factors, about which information is obtained from the same register or other sources. Based on postal code, cases are then allocated to the various regions and thus to the determinant categories. A distinct advantage of this approach is that individuals do not have to be asked for permission to use the (anonymous) information needed, precluding the need for a ruling by the medical ethical board or obtaining informed consent, and thus greatly reducing cost and research time.

Subsequently, from the sample of cases the odds can be estimated for the intervention categories and compared to the referent odds in (a sample of) the population from which the cases originated, and stratified according to the same confounding factors. This referent population can be a sample of cases with another disease from the same disease register (unrelated to the intervention and with a similar probability of entering the register) or can even comprise the total relevant population by using the national census, e.g. the intervention distribution in the total collection of all regions in The Netherlands.

A crude odds ratio (OR) can then be calculated and subsequently adjusted for confounders by means of appropriate techniques (Mantel Haenzel, modelling) to provide an unbiased estimate of the aggregate level intervention effect on the outcome under study. Thus, the design will enable the evaluation of the hypothesis that the pertinent intervention strategies can lead to marked effects at the aggregate level, under the assumption that the regional decision to choose the specific preventive health strategy is unrelated to the baseline risk for the specific health outcome. Table 1 gives an overview of the main advantages and disadvantages of the ecologic case-referent study design.

Table 1. Main advantages and (possible) disadvantages of the ecologic case-referent study design

Advantages	Disadvantages (possible)
Large numbers	Difficulty in completeness of case ascertainment
Cost and time effective	
External validity	Non-differential misclassification
No selection bias	'Natural experiment' assumption with possible selection by indication and information bias
Accuracy of case ascertainment	
Partly individual-level of measurement	
Controlling for many confounders with data from registries and databases	

The ecologic case-referent model

If we denote the probability of the outcome event by R, the regression model necessary to estimate the OR of interest is:

$$\mathrm{logit}(R) = b_0 + b_x X + b_{1-i} C_{1-i} + e$$

where X is the intervention and C_i the confounding variable (i). The relative risk of interest, the effect of the intervention, is given by $\mathrm{OR} = e^{b_x}$. This estimate is unbiased provided all confounders are taken into the model, and sufficiently precise when the residual error (e) is small. Comparability at base line is ensured only if the decision to apply intervention X is unrelated to the perceived occurrence of the relevant health outcome, i.e. if the situation can be regarded as some sort of natural experiment. Normally, in evaluative research this assumption is not likely to be true: interventions are often introduced in response to a perceived or predicted outcome parameter (confounding by indication). However, in situations where there is a high degree of uncertainty about the effect of intervention and/or a large variability in *a priori* belief in these effects, as is the case in YHC, the assumption is more or less justified. In the case of a natural experiment, the expected number of confounders will approach zero. Strong risk factors, however, may lead to residual confounding merely by chance. Additional adjustment may be necessary, requiring an adequate description, at least at the aggregate level. Because the unit of analysis is the community, the number of random units will be limited and subsequent risk for residual confounding can be substantial.

The error term (e) represents the measurement error or non-differential misclassification. This error term can only be small if:

- the outcome is adequately defined, diagnosed and filed;
- the intervention contrast is sufficiently large (conceptually and operationally);
- mobility between regions is small;
- a suitable time frame is chosen.

In addition the sampling error can be reduced by using a large number of cases, referents and regions and a suitable distribution of the types of intervention.

Example studies

In four studies we used the ecologic case-referent design to evaluate the effectiveness at an aggregate level of a number of preventive activities of YHC: well-care visits, open consultation hours and screening for scoliosis [4, 5, 12, 30, 31]. Table 2 gives an overview of the various individual and ecological variables used in the four studies. In each study the research hypothesis was that the preventive activities of YHC had a positive effect on the health outcome targeted: reduced surgery for scolioses, fewer cases of (para)suicide, improved mental health and general wellbeing, improved lifestyle and a reduction of the prevalence of obesity. The table clearly illustrates the manner in which individual and aggregate level measurements can efficiently be combined to evaluate the effectiveness of long-standing, community-wide and generally accepted prevention activities like YHC for school children.

Strengths and weaknesses of the ecologic case-referent design

Relevance

Relevance with regard to intervention and outcome can be attained by a studied choice of the pertinent variables. In the study of the effect of screening for scoliosis, for instance, the population rate of surgery for scoliosis is a good indication of the effectiveness of the screening. Furthermore, by choosing a population based case-referent approach, the population under study is the population at risk. In several of the example studies the referent population is almost identical to the theoretical study base. This is one of the stronger features of the design.

Validity

The greatest threat to the validity of ecologic designs is the ecological fallacy. However, in the ecologic case-referent design the objective is to estimate the group-level effect of participation in an intervention programme on the population rate using a case-referent design, where cases are identified at an individual level. Therefore, this design is not subject to ecologic bias. If the objective would be to estimate the individual-level effect on the outcome risk in participants of the intervention, ecologic bias in the form of cross-level bias, specifically the sociologistic and psychologistic fallacies would be possible [32].

Generally, in an ecologic case-referent design, case ascertainment is independent of level of exposure or group. Absence of information bias with respect to the outcome measure is one of the distinct advantages of this design.

To avoid selection bias, case ascertainment has to be as complete as possible. The outcome measure must be chosen with care, clearly delineated, and possibly dichotomous in nature, as this will preclude incomplete case ascertainment. To enhance the contrast and thereby the possibility of demonstrating possible effectiveness of the intervention under study, if possible, the extreme ranges of an outcome measurement should be compared, for instance the lowest and highest quartile of a scale [30]. Care must be taken, however, to ensure that the advantages of increased contrast do not outweigh the concurrent loss of information on the outcome variable. When case ascertainment is complete and the whole of the relevant population serves as referents selection bias is unlikely.

Potential selection by indication is of more concern in non-experimental research. Therefore, it must be assured that there is no relation between the introduction of the intervention and the occurrence of the outcome, i.e. the counterfactual rates are comparable ('natural experiment'). As many community-wide interventions are introduced nationally because of a perceived problem in a population as a whole, however, a relation between intervention introduction and outcome occurrence on a regional scale, be it direct or indirect, is unlikely. Because screening for scoliosis, for instance, has been introduced and is continued irrespective of population rates for scoliosis surgery, which are the same throughout The Netherlands, selection by indication is highly unlikely [5]. Nevertheless, if the assumption of a natural experiment-type situation is questionable, that not only heightens the chance of selection by indication, but can also give rise to information bias, because, for instance, an increased awareness of the local population of a certain problem can cause a more complete case ascertainment.

Table 2. Individual and ecological variables used in various studies of the effectiveness of YHC activities in The Netherlands

Individual variables	Ecological variables
Health outcome: surgery for scoliosis [5]	
Hospital discharge records	Per YHC region
ICD-codes for surgery	Screening for scoliosis
Gender	At a national level
Postal code place of residence	General demographics (census)
Year of surgery	Information regarding (centres for) spinal surgery
Health outcome: attempted suicide (parasuicide) [12]	
Survey	Per YHC region
Self-reported suicide attempts	Open consultation hours
Various possibly confounding variables (age, gender, etc.)	Preventive activities of Regional Institutes for Ambulant Mental Welfare
Postal code schools	
	National registries
Hospital discharge records	Distribution of possibly confounding variables throughout The Netherlands
ICD-codes for parasuicide + relevant psychiatric diagnosis	General demographics (census)
ICD-codes for parasuicide + concomitant surgery	Information about admittance policy of hospitals
Gender	
Year of admittance	
Postal code place of residence	
Health outcome: suicide [12]	
National registry	Per YHC region
Age group	Open consultation hours
Area of residence (YHC region)	Mortality rates
	National registries
	Distribution of possibly confounding variables throughout The Netherlands
	General demographics (census)
Health outcome: mental health and general wellbeing [30]	
Survey	Per YHC region
Mental health and general wellbeing	Number and frequency of well-care visits
Various possibly confounding variables (age, gender, etc.)	Time elapsed since last visit
Postal code school	Open consultation hours
Health outcome: lifestyle variables [31]	
Survey	Per YHC region
Use of alcohol, tobacco and cannabis	Number and frequency of well-care visits
Eating habits	Time elapsed since last visit
Various possibly confounding variables (age, gender, etc.)	Open consultation hours
Postal code school	
Health outcome: prevalence of obesity [31]	
(Male) conscript data Ministry of Defence	Per YHC region
Age	Number and frequency of well-care visits
Height and weight	Time elapsed since last visit
Postal code place of residence	Open consultation hours
	National registries
	Distribution of possibly confounding variables throughout The Netherlands
	General demographics (census)

Because of the way cases and referents were chosen, other types of differential misclassification, both for exposure and confounders, are unlikely.

Non-differential misclassification, for instance because of migration, is one of the possibly more substantial sources of bias in the study. The extent to which migration bias can occur, depends upon the time lag between intervention and subsequent outcome – in the example studies ranging from 1 to 6 years.

By measuring the exposure as accurately as possible, non-differential misclassification can be further reduced. This means, one has to be certain where, when and/or by whom the intervention is implemented. It is not necessary for the intervention to be implemented in a completely identical manner in every region and/or – in this case – by every YHC worker, as long as the method used, the age at which the activity takes place, or any other variable that is of importance, is the same. After all, the purpose of the study is not to determine whether an individual youth can profit from the intervention, but whether the relevant population as a whole could have benefited by the collective approach used by the service.

As it can be safely assumed, that allocation to the relevant determinant categories is better than random (i.e. sensitivity + specificity > 1.0) the direction of the trend of the OR found cannot be reversed by non-differential misclassification [26, 27, 33–35]. That means that even a non-significant OR denoting a negative influence of the intervention on the health outcome targeted, should give rise to serious misgivings concerning an unchanged continuance of that intervention.

Power and efficiency

By using case-referent methodology, the efficiency of the design is high, whereas the number of cases and referents under study and therefore the power of the design is increased substantially by using the ecological approach. Therefore, the balance between power and costs in the ecologic case-referent design is fairly optimal.

Analysis

In the ecologic case-referent design, group- and individual-level measurements are used for inference at a group level. This does not mean, however, that multilevel analysis methods are appropriate. Multilevel studies presuppose hierarchically clustered units of analysis, where in this design there is only one unit of analysis. Therefore, methods used in multilevel analysis, like varying intercepts and/or slopes, are not applicable [36].

Discussion and conclusion

Although community intervention trials would have far greater convincing power in demonstrating the efficacy of preventive measures and interventions, in *post-hoc* evaluation of preventive health services, including YHC, such designs are inappropriate, unfeasible, and even inadequate. Designs that only use group-level measurements, although in theory sufficient to verify the effectiveness of community-wide interventions, will always be considered questionable, because proof that the bias introduced will be small enough for the result of the study to be acceptable, will be difficult to render. Therefore, a hybrid design, in which individual-level measurements are combined with group-level measurements, can possibly be more persuasive, in particular because the bias from several sources can be substantially reduced. Furthermore, the design could be augmented by collecting supplemental data on individual-level exposure from individuals randomly sampled from each group [27]. In that way, using multilevel analysis, both the individual-level effect of programme participation and the ecologic effect of the population intervention could be assessed in the same study and subsequently compared for consistency. It is clear, however, that further research into the properties of the ecologic case-referent design is necessary to assess its potential worth. The shift of attention from the individual level (back) to the population level has recently been advocated by others [37, 38]. The use of the ecologic case-referent study design could facilitate this development and provide answers to the questions raised by politicians and public health services alike, concerning the effectiveness of the myriad of preventive measures that found their way into our society. The more so, as the design is also appropriate for many other areas in and outside public health, as diverse as occupational health, law enforcement measures, health promotion, environmental regulations, and the like.

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