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A Review on Endocrine Disruptors: A Historic Perspective Epidemiological Studies

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Abstract

Reliable appraisal of risk factor exposure is a prerequisite for efficient prevention. A street survey conducted in Jeddah, Saudi Arabia, included questions for measuring the prevalence of tobacco smoking. When entering the data, occurrence of long sex specific sequences of questionnaires suggested non-random sampling. The objective of this paper was to propose a method for diagnosing non-randomness, and measuring its impact on the prevalence of smoking and on the quality of collected data.

The distribution of the length of observed sequences of questionnaires collected among male respondents was compared with expected length under the hypothesis of random selection. For groups of sequences with significant difference between observed and expected length, two specific categories were set up according to the sign of the difference. A third category included sequences without significant length difference. The proportion of smokers and of missing information was compared between the low and the long length categories. Adjusted differences of these proportions was obtained by a logistic regression model.

Given that short sequences were underrepresented and long sequences were overrepresented, there was a sampling bias towards long sequences. Adjusted difference for the prevalence of tobacco smoking was 8.7% (95% confidence interval (CI95)-0.3%; 18.7%). For missing data, it was 3.9% (CI95) 0.3%; 8.4%).

Adequate sampling design, and sex specific training of interviewers were recommended for reducing biases associated with non-randomness due to the selection procedure. Obtained impact of non-randomness might suggest to adjust the crude prevalence of smoking obtained in this survey.

Keywords: Endocrine disruptors; Epidemiology; Tobacco smoking

Introduction

In Western countries, non-communicable diseases (NCDs) have long been the leading causes of death. Increasing risk factor prevalence and aging are determinants of the extension of NCDs in developing countries [1,2]. The WHO's Global Health Observatory data show that about 36 million deaths were attribu to NCDs. It represents 63% of 57 million deaths in 2008 [3]. Use of tobacco, obesity, hypertension, blood lipids and psychological stress were identified as major risk factors for NCDs. Interventions promoting healthy lifestyle without tobacco, balanced diet, and physical activity contributed to reduce morbidity and mortality attribu to NCDS [4]. Quality of surveillance depends on data availability and on policy adequacy for promoting healthy lifestyle behaviors. Both are tied to cultural factors and to available resources [5,6].

In the Kingdom of Saudi Arabia, the Directorate of Health Affairs, Province of Jeddah (Department of Public Health) decided to collecting data on health status, behavior, attitude and knowledge in order to designing an appropriate health education campaign.

Two main objectives underlie a survey performed before a primary prevention program: research and action. Firstly, the survey aims to provide the distribution of health status, behaviors, attitudes and knowledge in the population. This would help to identify the priorities for deciding which actions should be implemented. The distribution of risk-factor exposure in the population is necessary for setting up quantified objectives of interventions aiming to promote healthy lifestyle, and to change undesirable behaviors. As a baseline assessment, it might also contribute to the evaluation of the health education program when comparing obtained results with further surveys, provided that the study design would be appropriate.

Secondly, the survey might contribute to sensitizing the population to health concern. The usefulness of such data collection would not be restricted to professionals in charge of the analysis. It should also increase health awareness of people participating to the survey. This objective was also to be considered when designing data collection for public health purposes.

"Action-research" best describes the whole process of a prevention program, from data collection and data analysis up to health education activities and continuous program evaluation.

In Jeddah, data were collected by a street survey involving more than 2000 respondents. It was conducted by interview, before health education. This procedure was chosen for optimizing both healthy lifestyle awareness, and the feasibility of the interviews. The Tobacco Control Program of the Ministry of Health in Riyadh was in charge of data entry, and of subsequent statistical analysis. The first concern was about selection bias, a likely drawback in a street survey.

When entering the data, it appeared that long sequences with identical gender category were not uncommon. Such a finding might reflect sex clustering. This was likely for a street survey conducted in an Arabic country: in public areas, it is common to have separate male sections, women sections, and family sections. This situation might have been interacting with the randomness of the sample.

Randomness in the selection procedure of respondents would produce independent and asymptotically identical distributions among samples. In a population survey with balanced sex distribution, long sequences of identical sex category among respondents would be unlikely, provided that the hypothesis of randomness was true (H0).

A sequence of units with an identical characteristic is called a run. Investigation of randomness by run tests appeared early in the

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statistical literature [6]. More recent papers reviewed existing methods and extended them to multivariate run tests [7-11]. In this investigation, the run length was the number of subsequent men responding to an interviewer. A simple comparison between the observed and the expected distribution of run length under H0 is a simple tool for diagnosing absence of randomness due to respondent selection. This comparison might also clarify which statistical units were likely to have been included according to a correct selection procedure or not.

Given that tobacco smoking was associated with gender, an unbalanced sex distribution might have biased result obtained from the survey. A straightforward correction by a method of standardization would then be necessary. The same procedure might be appropriate for other characteristics like age, education or marital status.

This paper focuses on other potential biases associated with lack of randomness in the selection procedure, as opposed to peculiar distribution of respondents with respect to socio-demographic categories. It explores potential bias of obtained prevalence of smoking and also problems in the quality of collected data due to factors associated with non-randomness. Such determinants of the explored bias and of problems in the quality of the data might result from respondent and/or from interviewers.

The objective of this paper was to diagnose the distortion of randomness as obtained from the observed distribution of run length, and to quantify the impact of such a distortion on smoking prevalence and on the reliability of collected data.

The findings provide hints for improving both internal and external validity of further data collection by taking into account cultural particularities of targeted populations in Arabic countries. They refer to existing models for sampling procedures, and for the prevention of biases due to interviewing techniques.

The survey was designed by a Committee including the Supervisor General of the Tobacco Control Program, representatives of family physicians, primary health care department and primary health education department at the Ministry of Health of the Kingdom of Saudi Arabia. It was decided to interview non-probability samples of voluntary adults in one mall. Fifty interviewers - 28 female and 22 male – had been trained for gathering the data in Jeddah. During 7 consecutive days, 2083 questionnaires were collected.

The pile of questionnaires was in chronologic order when it was sent to the Tobacco Control Program in Riyadh. Data entry was checked by an Epi-info program [12]. The original order of the questionnaires was maintained up to data analysis performed by SPSS [13].

Diagnosis of non-randomness

The diagnosis of non-randomness proposed in this paper resulted from a comparison between the observed distribution of run length and the expected distribution under the hypothesis of randomness (H0). Only a detailed comparison between observed and expected distribution under the hypothesis of randomness can provide clues for further exploration, within the data set, of biases due to non-randomness. The proposed diagnostic method was consistent with the next step: measuring the impact of non-randomness on smoking prevalence and on the quality of gathered data.

The expected distribution of the probability of run length according to the number of subsequent male respondent can be expressed as a function of the number of male respondent (m), and of the total number of respondent (n). Let pm=m/n. Among the runs with length i ≥ 0, the expected proportion of runs of length i, that is E(ri), is a function of pm and of i.

E(ri)=(pm)i • (1- pm)=(pm)i - (pm)i+1 [A]

The expected distribution of the number of male respondent by run length (E(mi)) derives from equations [B] and [C]:

E(mi)=i • (pmi - pmi+1) • k [B]

where k is a constant such that

(mi)=m. [C]

In this survey, equations [B] and [C] were satisfied for pm = 953/2083, m=953, and k=1130.

For comparing the observed distribution of respondent by run length Oi with the corresponding expected distribution E(mi), a conventional chi square statistics, chi²i=(Oi-E(mi))²/E(mi), was obtained for all runs with an expected number of respondent larger than 4.5, as shown on 2. The diagnosis of non-randomness was done by a test based on these chi²s. The vector of chi²i s was then regrouped into homogeneous categories of contiguous chi²i s. The criterion for grouping contiguous run lenghts was first based on the level of significance below or above 0.05. For groups of run with a level of significance below 0.05, contiguous run length would be considered as homogeneous provided they were all either over- or underrepresented. One specific code of run length was attributed to each homogeneous group of categories, and all long runs with large lengths got the same code, as shown on 2. This code was then attributed to all respondent belonging to the same group of run length.

Outcome variables

Answers to the question “Are you a smoker?” provided two distinct outcome variables. The first variable was built from the answers corresponding to “yes”, “no” or “ex-smoker”. It was a binary variable with exposed category corresponding to answer “yes” and reference category including “no” and “ex-smoker”. The second outcome was a binary variable for identifying a missing value. This variable was used for testing the association of non-randomness with the quality of data collection. Another outcome variable about the quality of collected data was built from answers to two questions dealing with cigarette smoking. One was an open question asking for the number of cigarettes smoked a day, and the other was a closed question with pre-defined categories of the number of cigarettes smoked per day. Concordant and discordant answers among respondent to both questions were identified with a binary variable.

Independent variables: non-randomness, reliability of the data and potential confounders

Given that the largest proportion of respondent with long run were in excess when comparing with expected distribution under Ho, the reference category of non-randomness was attributed to individuals with the shortest runs. Exposed category to non-randomness was attributed to respondent included in long runs, more likely to be subject to selection. Crude association of non-randomness was first explored by the change in prevalence of tobacco smoking when comparing groups of run length. Logistic regression modeling including age in three categories (15-24; 25-49; 50+), education in two

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categories (illiterate to secondary; college or other), and marital status in two categories (married; single, divorced or widowed) was used for getting adjusted odds ratios. These adjusted odds ratios were used for computing the adjusted impact of non-randomness on tobacco smoking adjusted for potential confounders.

Computation of impact of non-randomness

The impact of non-randomness on the prevalence of smoking, on missing values, and on discordance about the number of cigarettes smoked per day was the adjusted difference obtained between groups of participants included in the exposed and in the reference category of non-randomness.

Controlling for potential confounders of crude difference and confidence interval for outcome variables was based on adjusted odds obtained by multivariate analysis. Consider a binary outcome variable like tobacco smoking. Let us call df the crude difference of the proportion of smokers with respect to a binary factor f, like non-randomness, partitioning statistical units into exposed category (1) and reference category (0).

df = p1-po [D]

Adjustment of this difference makes use of the natural logarithm (Loge) of odds ratio βf, as obtained from a logistic regression model including a vector of →γ s, that is Loge of the odds ratios for potential confounders:

Loge ζ = α + βf + Σγi [E]

In equation [E], ζ is the estimate of the odd of smoking among exposed, and α holds for the natural logarithm of the odd of smoking among non-exposed. Estimate of adjusted difference of proportions Adj (df) was computed from parameters α and βf resulting from the logistic regression model provided in equation [E]:

Adj (df) = [eα +βf/(1+eα +βf)]–[eα/(1+eα)] [F]

The confidence interval results from the same formula where βf is replaced by its lower and by its upper limit provided in the output when performing the logistic regression procedure with appropriate software [14].

The same procedure was used for exploring outcome variables reflecting the quality of data collection: missing versus valid answer to the question on smoking, and discordant versus concordant answers to two separate questions on the number of cigarettes smoked per day.

Among the total of 2083 participants to the survey, 953 were male respondent, that is a proportion of 45.8%. Prevalence of smoking among men and statistical association with age, education and marital status are provided in 1.

Two characteristics were significantly associated with a lower prevalence of smoking at the level of 5%: age 50 or more, and another level of education than college, that is illiterate to secondary, or not specified.

The proportion of missing values among answers to the same question about tobacco smoking was significantly associated with one variable at the level of 5%: it was about twice higher for not married men.

Diagnosis of non-randomness based on run length among male respondent

The observed proportion of male respondent, that is 953/2083, was used for computing the probability of run length under the hypothesis of randomness (H0). Expected number of respondent given in 2 were obtained for all probabilities of run length larger than 10-4.

The chi² obtained by summing up all categories with expected value larger than 4.5 amounts to 187.6***. Given the result obtained in 2, the coding of homogeneous groups was attributed to three distinct categories of run length. The runs shorter than 3 were significantly underrepresented, whereas runs longer than 6 were significantly overrepresented.

The selection procedure increased long runs and limited the number of respondents belonging to short runs.

Respondent included in short runs were considered to be less likely subject to the selection procedure responsible for the excess in long runs. In further analyses, respondent belonging to short runs were considered as the reference category.

Impact of non-randomness on the prevalence of smoking

As shown on 3, the prevalence of smoking was higher among respondent belonging to long runs. When testing the absolute increase of 8.7% against 0, the p-value was 0.06.

The joint distribution of both the binary variable “smoker” versus “not smoker” or “ex-smoker”, and the binary variable short run versus long run provided a crude odds ratio of 1.4. The crude increase in the prevalence of smoking among respondent associated with long run was 8.7%. The 95% confidence interval (CI95) was - 0.3%; 18.3%.

Adjustment of this crude estimate based on a logistic model including socio-demographic variables provided a similar result (see first section of 4). The adjusted increase in the proportion of smokers associated with long run was 9.0%, CI95: -0.4%; 18.7%.

Selection procedure and quality of the data

The section 2 of 4 provides the result of the analysis of the statistical association between missing value for the question “Are you a smoker?”, and the run length. There was a significant association between low randomness in the selection of interviewees and missing data at the level of 0.05. The crude difference was 7.6% (95% C.I. 0.5%; 14.3%). The adjusted difference in proportions of missing values due to long run was 3.9% (95%C.I. 0.3%; 8.4%).

The section 3 of 4 shows that there was no significant statistical association between discordant answers to the questions about cigarette smoking and run length (odds ratio=1.0; p=0.903). The difference adjusted for socio-demographic variables amounts to 0.5%.

Among explored socio-demographic variables, the marital status was significantly associated with low quality of the data as measured by missing values and by discordance.

Discussion

There are many determinants of biased result in public health surveys. A classical reference [15] mentioned coverage, nonresponse, sampling, interviewer, respondent, instrument and mode. After reviewing the method used in this paper for diagnosing non-randomness, the discussion focuses on sources of bias suspected from the obtained statistical association of run length with prevalence of smoking and with quality of the data. Considered potential

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determinants of such biases include factors due to respondent and to interviewers.

Method for diagnosing non-randomness

There was no sorting of the questionnaires by sex from the time they were gathered up to data entry. Given that obtained summary chi² value was huge, the hypothesis of randomness (H0) was to be rejected.

When comparing expected with observed distribution of run length, it appeared that the selection procedure of most respondent included in long runs did not fit criteria leading to randomness. However, the classification of all respondent in the long run category as exposed to non-randomness was likely to be imperfect: Among the 202 respondent included in the long run category, 37.2 (18%) were expected under the null hypothesis.

When comparing expected with observed distribution according to run length, a lower frequency in the short run group might be due to exclusion of short runs or to preferential inclusion of longer runs. In this street survey, it was considered that this latter process was corresponding to the way some interviewers had been choosing interviewees. The sampling procedure was considered as biased towards long runs. This implied to use the shorter runs group as the reference category when measuring the impact of non-randomness by the following difference: the proportion of smokers among respondent belonging to the long run group minus the proportion of smokers in the short run group.

The result obtained by the method of adjustment were checked with a stratified analysis of the two by two s exploring the links between run length and outcome variables: smoking and missing values. Marital status was a suspected confounder because it was likely to be associated with both long run and smoking. The stratification according to marital status did not change much the summary Mantel-Haenszel odds ratio in comparison with the crude odds ratio for both outcome variables. This result confirmed what was obtained by the method of adjustment based on logistic regression.

Factors of bias due to respondent only

Among available socio-demographic variables, age and education were associated with prevalence of smoking, and marital status was associated with missing values among answers to the question: 'Are you a smoker?'. Such factors might have been confounders when exploring the link between non-randomness with tobacco smoking and with missing values. As a matter of fact, after adjustment by modeling with logistic regression, the statistical associations of non-randomness with smoking and with missing values were very close to crude estimates. This means that characteristics of the respondent did not explain the obtained impact of non-randomness on the prevalence of smoking and on the missing values.

When exploring the link between non-randomness and discordance among answers to the two questions dealing with the number of cigarettes smoked, only respondent having answered "yes" to the question "Are you a smoker?" could be considered. It appeared that the statistical association was unlikely (p=.90). This result does not support the hypothesis of a link between non-randomness and reliability of the data provided by the respondent.

All obtained results do not support the hypothesis that confounding factors only related to respondent characteristics might explain the measured impact of non-randomness. It is likely that the determinants of the measured impact of non-randomness on smoking prevalence and on the proportion of missing values was due to some interviewers and/or to interaction between some interviewer and some respondent.

Factors of bias due to interviewers

Review of interviewer's effect showed the large spectrum of concern in the literature [16]. In Jeddah's survey, the large number of interviewers might explain some dispersion in the procedures applied for selecting the people and/or in the quality of data collection. Identical training of a large group of interviewers might have produced a variety of individual results. This might have led to specific selection procedures associated with different level of quality of the data collected by the different interviewers. The relative difference in the prevalence of tobacco smoking amounted to 23%. It may be due to chance (p=.06), or reflect a bias introduced by interviewers. The same consideration might also apply to the difference in the proportion of missing values for the question "Are you a smoker" (p=.02).

Conclusion

It appeared that sampling, nonresponse and interviewer were likely sources of errors when appraising the prevalence of smoking in the street survey conducted in Jeddah.

For sampling, the range of alternative methods is huge. In a study restricted to people attending a mall, a recommended procedure would be to randomly identify eligible people for the survey at each entrance of the mall. A previous observation of the frequency of people entering the mall during a couple of days might help for defining the precise procedure. It might take into account the proportion of people to be included in the sample. Then a fix ratio could be applied for choosing eligible respondent. An alternative method based on the expected run length of subsequent interviewees might also be used. Such a method might be based on the random selection in the cumulative probability function of the runs weighted by the number of individuals.

External validity of measured prevalence of tobacco smoking was a major concern for studies aiming to stimulate the development of adequate prevention policy at a national level. [17-24] Recommended procedures applied in such surveys might contribute to the preparatory steps for deciding on a sound sampling procedure, and also for adequate training and selection criteria of interviewers. Understanding of the grounds for standards to be applied is crucial for adapting the procedures to the cultural context of a survey. Interviewer gender effects were considered as a major concern in Islamic areas. [24,25] Gender specific training might be considered for improving the quality of data collected in some Islamic countries. Such a procedure might also facilitate gender specific intervention by appropriate health educators.

Adjustment for non-randomness of obtained crude results might be considered for getting a better appraisal of the prevalence of smoking in Jeddah's survey.

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