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Cost-Efficient Design of Occupational Exposure Assessment Strategies- A Review

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Abstract

When designing a strategy for collecting occupational exposure data, both economic and statistical performance criteria should be considered. However, very few studies have addressed the trade-off between the cost of obtaining data and the precision/accuracy of the exposure estimate as a research issue. To highlight the need of providing cost-efficient designs for assessing exposure variables in occupational research, the present review explains and critically evaluates the concepts and analytical tools used in available cost efficiency studies. Nine studies were identified through a systematic search using two algorithms in the databases PubMed and ScienceDirect. Two main approaches could be identified in these studies: *comparisons* of the cost efficiency associated with different measurement designs, and *optimizations* of resource allocation on the basis of functions describing cost and statistical efficiency. In either case, the reviewed studies use simplified analytical tools and insufficient economic analyses. More research is needed to understand whether these

drawbacks jeopardize the guidance on cost-efficient exposure assessment provided by the studies, as well as to support theoretical results by empirical data from occupational life.

Keywords: error, information, performance, cost, optimization.

INTRODUCTION

Acquiring sufficient information on occupational exposures is a persistent challenge in occupational epidemiologic studies. Imprecise and biased estimations of exposure averages may result in vague or even false conclusions regarding the exposure status of a group, and may thus even jeopardize groups or conditions, as in epidemiology and intervention research. Using biomechanical exposure as an example, guidance on *measurement designs* has therefore been developed during recent years to improve the information provided by occupational exposure assessments. This guidance includes considerations to the appropriateness of different measurement instruments, acknowledging possible systematic errors in using them (Burdorf and van der Beek, 1999; David, 2005; van der Beek and Frings-Dresen, 1998; Winkel and Mathiassen, 1994; Burdorf and van Riel, 1996; Stanton et al., 2005; Takala et al., 2010), and it includes discussions on sampling strategies focussing on how to deal with random sources of error (Burdorf, 1995; Mathiassen et al., 2002; Mathiassen et al., 2003; Nordander et al., 2004). The literature also includes an extensive discussion on which method is more accurate and most applicable when measuring different biomechanical exposures in working life (e.g. van der Beek and Frings-Dresen, 1998; Winkel and Mathiassen, 1994). The appropriateness and statistical efficiency of the employed measurement design, however, are not the only criteria determining whether or not a specific design will or should be employed. A measurement design should also be *cost-efficient* as pointed out and addressed decades ago by, e.g. Cochran (1977). While statistical efficiency concerns minimizing the variance of an unbiased estimator of the target exposure variable, the economic term of *cost efficiency* refers to either *technical efficiency*, i.e. generating the maximum possible “output” for the given “inputs” (measurement efforts), or *productive efficiency*, i.e. producing one unit of “output” at the lowest possible cost. In the context of exposure measurement, statistical efficiency is an appropriate measure of “output”, since it measures the amount of information generated by the measurement design. With this definition of output, cost efficiency is an appropriate comprehensive concept to use, because it emphasizes both economic and statistical performance. Notably, the concept of cost efficiency

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3 when measuring exposures differs from the term “cost-effectiveness analysis” as frequently
4 used in health economics. While cost efficiency analysis as discussed in the present paper
5 addresses an economic evaluation of measurement designs that produce information on
6 exposure variables, cost-effectiveness analysis is a methodology for economic evaluation of,
7 in particular, treatment programs. Consequently, in cost efficiency, the term “efficiency”
8 refers to a statistical concept focussing the quantity of information, while the term
9 “effectiveness” in cost-effectiveness analysis refers to the outcomes of a treatment
10 intervention on patients, for instance as measured by improved quality of life.

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12 The measurement method and the number of sampling units both affect the total cost of the
13 measurement as well as the statistical efficiency of the estimated variable. A reduction of
14 errors in exposure assessment, i.e. an improvement of statistical efficiency, can be achieved
15 by using more suitable or advanced technical instruments and/or by increasing the number of
16 sampling units. Such improvements, on the other hand, most often increase the total cost of
17 the measurement. Thus, a measurement design that generates low error (high statistical
18 efficiency) is not necessarily cost-efficient. A cost-efficient measurement design balances the
19 cost and the amount of information produced according to either technical or productive
20 efficiency criteria by, in principle, manipulating the number of sampling units at different
21 stages as well as by considering which measurement methods to employ in the statistical
22 production.

23
24 Analysis of the cost efficiency of producing information on exposure variables is an important
25 field of research, yet so far with a limited body of literature. As an example, the literature on
26 occupational biomechanical exposure assessment lacks studies devoted to the issue of how to
27 supply “sufficient” information on exposures at a “low” cost. None of the measurement
28 design studies cited above have considered cost efficiency criteria when assessing
29 occupational exposures; all have focused on appropriateness and/or statistical performance.
30 An interesting study, however, by Trask et al. (2007) was devoted to classification and
31 estimation of all important cost components associated with different methods of measuring
32 low back injury risk factors. While this study clearly demonstrated that costs differ between
33 exposure assessment technologies, it did not discuss statistical performance.

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35 While our personal interests concern mainly biomechanical exposures in working life, the
36 present review addresses all available studies devoted to the trade-off between “cost” and
37 “efficiency” in assessment of any exposure variable. The purpose of the review is to analyse
38 statistical and economical models suggested and/or applied in the literature for analysing cost
39 efficiency in exposure assessment, so as to set a stage for future research. In order to aid the
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3 discussions, the review even considers some studies devoted to cost-efficient assessments of
4 response variables, and also points to usable methodologies from the literature on health
5 economics. The review considers cost efficiency analysis in the two applications occurring in
6 the literature: *evaluation/comparison* of alternative measurement designs and *optimization* of
7 resource allocation in statistical production.
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12 13 14 METHODS

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18 A systematic search in the medical database PubMed and the cross-disciplinary scientific
19 database ScienceDirect was conducted in February 2009, using two search algorithms:

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21 1. $[\text{cost} \cap (\text{precision} \cup \text{accuracy} \cup \text{power}) \cap \text{assessment} \cap \text{exposure}]$,

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23 2. $(\text{cost-efficient} \cap \text{validation study})$. These search algorithms identified 99 papers (78+21) in
24 PubMed and 112 (22+90) papers in ScienceDirect, primarily in the areas of epidemiology,
25 health economics and medical statistics. The relevance of the studies to the present review
26 was judged using three criteria: 1) the analysis of cost efficiency should address assessment of
27 exposure variables, 2) both “cost” and “efficiency” (or terms with equivalent meanings) must
28 be considered, 3) the analysis of cost efficiency should be based on at least one mathematical
29 model. First, the titles of all 211 papers were inspected. If the title suggested the paper to be
30 relevant according to the inclusion criteria, the abstract was examined. Thus, the abstracts of
31 183 publications were examined. On the basis of this examination, nine papers were identified
32 as relevant that fulfilled the inclusion criteria. Several other publications were considered
33 relevant to the general topic of cost efficiency analysis in data collection. These papers are
34 addressed when appropriate in the discussion below, but they were not included in the core
35 review. Reviewing the reference lists of the nine included papers did not lead to the
36 identification of additional relevant papers. Also, a citation report was retrieved for all nine
37 papers using Google Scholar, but this did not reveal any additional studies either. Thus, a total
38 of nine papers were accepted for a thorough review.
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52 In examining these nine articles, we focused on three issues: 1) the indicator of statistical
53 efficiency and the operational model applied to assess it, 2) methods used to assess “cost”,
54 and 3) the general conclusion of the cost efficiency analysis. Some studies reported empirical
55 data to illustrate their approach, but we considered these quantitative data not to be
56 generalizable, and thus have not commented them in this review.
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RESULT AND DISCUSSION

Early in the review process, we found that the identified papers employ concepts and tools that are specifically adapted either to evaluation/comparison of measurement designs or to their optimization. Since these two approaches are fundamentally different, conceptually as well as with respect to the applied methods, we chose to structure the review accordingly, and sort the nine identified papers into either category. Tables 1.a and 1.b summarize the nine studies by reporting their indicators of “efficiency”, the purpose in their cost efficiency analysis, and the underlying assumptions in the applied statistical and economical models.

For Review Only

Table 1.a Basic characteristics of the identified studies on cost-efficient exposure assessment in comparison approach

Reference	Indicator of statistical efficiency	Purpose	Statistical assumption	Economical assumption
Lemasters et al. (1996)	Precision	Comparison of 32 alternative sampling strategies	Additive random error, three-stage sampling	Total cost directly proportional to the number of measurements
Shukla et al. (2005)	Precision	Comparison of alternative sampling strategies	Additive random error, three-stage sampling	Total cost directly proportional to the number of measurements
Armstrong (1995, 1996)	Accuracy	Comparison of two measurement methods	Existence of perfect measurement, single-stage sampling	One linear cost component differing between measurement methods, same fixed cost for both measurement methods

Table 1.b Basic characteristics of the identified studies on cost-efficient exposure assessment in optimization approach

Reference	Indicator of statistical efficiency	Purpose	Statistical assumption	Economical assumption
Duan and Mage (1997)	Accuracy	Optimization of resource allocation between two measurement methods	Correlation between indirect and direct measurements, single-stage sampling	One linear cost component differing between direct and indirect measurement methods
Spiegelman and Gray (1991) Spiegelman (1994)	Discriminatory statistical power	Optimization of resource allocation between main and validation studies	Non-linear error model, single-stage sampling	One linear cost component differing between main and validation studies
Stram et al. (1995)	Precision	Optimization of resource allocation between two sampling stages	Additive random error, two-stage sampling	Two linear cost components
Whitmore et al. (2005)	Precision	Optimization of resource allocation between three sampling stages	Additive random error, three-stage sampling	Three linear cost components, fixed cost addressed

Studies comparing measurement methods/strategies

Comparison of alternative sampling strategies

Based on variance components estimated by a random effect model, Lemasters et al. (1996) compared 32 possible alternative sampling strategies with various combinations of periods, weeks, and days that might be adopted in assessments of coal-dust exposure for an individual miner. Each of these alternatives is compared to a “pilot” strategy in terms of cost and precision. Gains or losses in “relative accuracy” are assessed using the expression $\frac{\hat{\sigma}_{\bar{x}}(choice)}{\hat{\sigma}_{\bar{x}}(pilot)} \times 100$, where $\hat{\sigma}_{\bar{x}}$ denotes the standard error of the mean. The assessed “relative accuracy” is evaluated together with the “cost saving”, which is set equal to the percentage reduction in the total number of measurements per person. The paper then identifies “the 10 best choices” among the 32 alternatives, for which the trade-off between cost savings and changed precision is most favourable. Thus, among “the 10 best choices”, the reader can identify the design that provides the highest precision for a particular budget, or the design that offers an acceptable precision at the lowest cost.

In a similar yet more advanced study, Shukla et al. (2005) also compared alternative sampling strategies in terms of cost and precision of the estimated mean, using the same structure as Lemasters et al. in assessing environmental exposure for periods, weeks, and days. In the paper by Shukla et al., the cost efficiency analysis is based on three concepts: “cost”, “precision” and “design efficiency”. Like Lemasters, the authors define “cost” as being directly proportional to the total number of measurements, while “precision” is quantified as the inverse of the standard error of the mean exposure estimate resulting from the sampling strategy. The “design efficiency” of a specific strategy is defined as its precision relative to the pilot strategy, divided by its relative cost. The alternative sampling strategies are then ranked according to their design efficiencies.

Unlike Shukla’s study, the Lemasters paper confuses the terms “precision” (reproducibility) and “accuracy” (unbiasedness) when it describes “relative accuracy” by standard errors in alternative designs. The two studies both use statistical models for estimating the precision of the mean that are based on the assumption of an additive random effect, while not discussing possible violations of this assumption. Neither of the studies considers fixed costs associated with the compared designs. Further, they equalize the cost and the number of measurements when estimating the cost of each design. This very simple approach of assessing costs has the advantage that it is easily employed for economic evaluation of different strategies. However,

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3 it does not account for the fact that the cost of measurements is only part of the total cost of a
4 strategy, and that it may vary over time. Thus, it seems improbable that the reduction of the
5 total number of measurements per worker is equivalent to the “cost saving”. The Lemasters
6 study identifies “the 10 best choices” among several investigated strategies, but the cost
7 efficiency analysis does not introduce a general method for ranking alternative designs. Thus,
8 Lemasters’ approach and results are not generally applicable in comparing measurement
9 designs. The study by Shukla et al. solves this by introducing the concept of “design
10 efficiency”.

11 12 13 14 15 16 17 18 19 20 *Comparison of two alternative measurement methods*

21 In two similar studies, Armstrong (1995, 1996) formulated principles for comparing the cost
22 efficiency of two exposure assessment methods. His approach is based on the concepts
23 *asymptotic relative efficiency* (ARE), *validity coefficient* (ρ_{xz}) and *reliability* (ρ_{xz}^2). In the
24 context of Armstrong’s studies, asymptotic relative efficiency is given an extended definition
25 as the ratio of the total costs of two measurement designs that achieve equal statistical power,
26 i.e. that yield the same precision of an estimated mean exposure. The validity coefficient of an
27 approximate exposure measure Z is its correlation with the “true” exposure X , and the
28 reliability of Z as a measure of X is the square of the validity coefficient. In comparing an
29 “approximate” and a “perfect” exposure measurement, Armstrong suggests the following
30 model:
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$$39 \quad ARE_{Z/X} = \rho_{xz}^2 [(C_I + C_X) / (C_I + C_Z)] \quad [1]$$

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42 In this equation, c_I denotes the basic cost of including a subject, while c_X and c_Z refer to the
43 cost of getting a perfect and an approximate measurement, respectively, from that subject.
44 Armstrong states that Z and X are equally efficient when $ARE = 1$, and that X is preferable
45 if $ARE < 1$, which occurs when $\rho_{xz}^2 < [(C_I + C_Z) / (C_I + C_X)]$. For comparing an approximate
46 exposure measure Z_1 with a more accurate one Z_2 , he suggests another model:
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$$51 \quad ARE_{1/2} = (\rho_{xz_2}^2 / \rho_{xz_1}^2) [(C_I + C_{Z_2}) / (C_I + C_{Z_1})] \quad [2]$$

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54 The more accurate measure Z_2 is preferable if $(\rho_{xz_2}^2 / \rho_{xz_1}^2) > [(C_I + C_{Z_2}) / (C_I + C_{Z_1})]$.
55 Armstrong (1996) concludes, therefore, that “*investment in increased precision is worthwhile*
56 *up to the point at which the proportional increase in the total cost per subject exceeds the*
57 *proportional gain in ρ_{xz}^2 , the square of the validity coefficient (reliability)”*. Further, he
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3 stresses that the expression ρ_{xz_1}/ρ_{xz_2} in [2] cannot generally be replaced by $(\rho_{z_1z_2})$, which
4 means that it is always necessary to have access to a perfect measurement when comparing
5 two alternative methods, if both are approximate.
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9 The terms “power” (the probability of rejecting a null hypothesis that is, in fact, false),
10 “accuracy” and “precision” as indicators of statistical efficiency are interchangeably
11 employed by Armstrong, which is confusing, given the sources of error actually addressed by
12 the study. Armstrong’s suggested models for comparing the cost efficiency of alternative
13 measurement methods are based on the concept “asymptotic relative efficiency”, which is
14 theoretically advantageous. However, it presents difficulties in practice, since it involves the
15 terms “validity coefficient” and “reliability”, which are principally unknown whenever the
16 “true exposure” is inaccessible. Thus, in principle, Armstrong’s comparison approach cannot
17 clearly identify the most cost-efficient measurement method when “the true exposure” is not
18 available. Despite the development of advanced instruments during recent years, perfect
19 measurements are not possible in most situations. Realizing this, Armstrong (1996) relaxes
20 the requirement for a “perfect measurement” to the “most accurate” when exemplifying his
21 approach in an assessment of exposure to nitrogen dioxide. Armstrong’s model for calculating
22 total cost for each measurement method includes a fixed cost, which is important when
23 comparing alternative designs. However, as Lemasters et al. and Shukla et al., Armstrong
24 assumes that the cost associated with using either method is linearly related to the number of
25 measurements.
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41 Studies optimizing resource allocation

42 *Optimal allocation of resources between two measurement methods*

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44 Duan and Mage (1997) have addressed the approach of combining direct and indirect methods
45 for assessment of pollution exposure. The direct measurement method is superior in precision
46 but expensive, while the indirect exposure estimation is cheaper but associated with a larger
47 error. The combined approach is a way to balance the drawbacks of either method. The
48 sample of subject is principally separated into two sub-samples: a dual sample and an
49 indirect-only sample. Both measurement methods are used simultaneously in the dual sample,
50 while only the indirect method is used in the indirect-only sub-sample. The dual sample is
51 used to estimate the relationship between the direct measurements and the indirect estimates.
52 The estimated relationship is then applied to the indirect-only sample to calibrate the indirect
53 estimates, thus predicting the direct measurements that were never carried out. Finally, the
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3 direct measurements in the dual sample and the predicted direct measurements in the indirect-
4 only sample are combined into an estimate of mean exposure in the entire target population.
5 Duan and Mage provide an algorithm that can be used to determine the optimal allocation of
6 subjects between the dual and the indirect-only samples, in the sense that it minimizes the
7 measurement error subject to a linear budget constraint. The optimal fraction of direct
8 measurements, $f_{(D)}^*$, depends on the costs of collecting the indirect data and the direct data for
9 each individual in the dual sample, $c(I)$ and $c(D)$, and the correlation between the direct
10 measurements and indirect estimates, ρ_T^2 , as follows:
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$$18 \quad f_{(D)}^* = \sqrt{c(I)(1 - \rho_T^2) / c(D)\rho_T^2} \quad [3]$$

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20 The formula states, as could be expected, that if an indirect measurement is a good predictor
21 of the direct measurement, i.e. if ρ_T^2 is large, and if the cost of the indirect measurement is low
22 compared to that of the direct measurement, then the optimal sample allocation will call for a
23 small number of expensive direct measurements.
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28 Duan and Mage's study constitutes a step forward as compared to the results by Armstrong in
29 introducing analytical tools to optimize the fraction of direct measurements. The confusion
30 between "precision" and "accuracy" found in the Lemasters and Armstrong studies is also
31 seen here, since the authors measure the "precision" of the mean exposure estimate by its
32 mean square error, which also includes the bias of an estimator. Duan and Mage's statistical
33 modeling of "approximate mean square error" is thus potentially advantageous, provided that
34 the sub-sample selected for direct measurements is representative to the entire population.
35 Surprisingly, the optimal sample allocation fraction is allowed to exceed one without
36 imposing the additional constraint $f_{(D)}^* \leq 1$.
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47 *Optimal allocation of resources between main and validation studies*

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49 In two similar studies of cost-efficient designs for assessing exposure and response variables
50 in epidemiologic research, Spiegelman and Gray (1991), and Spiegelman (1994) suggested a
51 complicated error model for determining optimal sample sizes for a main study, n_1 , and a
52 validation study, n_2 . The optimization problem involves minimizing
53 $(r_D + r_X)n_1 + (r_x + r_X)n_2$ for a specified discriminatory statistical power, π , determining
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59 constraints $1 - \Phi\left(\frac{z_{1-\alpha/2}\sqrt{V_L(n_1, n_2)} - \beta_U + \beta_L}{\sqrt{V_U(n_1, n_2)}}\right) \geq \pi$ and $\Phi\left(\frac{-z_{1-\alpha/2}\sqrt{V_U(n_1, n_2)} - \beta_L + \beta_U}{\sqrt{V_L(n_1, n_2)}}\right) \geq \pi$,
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3 where r_D , r_X , and r_x are the unit costs for assessing the (binary) response variable, the
4 imperfect exposure measurement, and the superior exposure measurement, respectively.
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6 $z_{1-\alpha/2}$ is the $1-\alpha/2$ (confidence level) percentile of the standard normal distribution, and
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8 $V_L(n_1, n_2)$ and $V_U(n_1, n_2)$ are the variances of the estimated regression coefficient β between
9 exposure and response under the two alternative values β_L and β_U , respectively. In a simple
10 explanation, the power constraints reflect an epidemiologic study designed to discriminate
11 between two values of relative risk obtained by two different measurement methods.
12 Spiegelman's optimization approach thus attempts to provide a cost-minimized, yet powerful
13 epidemiologic study, where both superior and imperfect measurement methods are used to
14 assess a continuous exposure variable, similar to the dual sampling idea also addressed by
15 Duan and Mage (1997). As expected, the optimal resource allocation between the main study
16 and the external validation study depends on many parameters, such as the desired confidence
17 level, unit cost components, distance between two alternative values of relative risk,
18 magnitude of hypothesized values of parameters, and the specified non-linear model of
19 measurement error.
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22 The choice of "discriminatory power" as an indicator of efficiency is highly relevant when
23 assessing relationships between response and exposure variables using approximate and more
24 accurate methods for measuring exposures. However, the constraint inequalities in the
25 Spiegelman papers results in the optimization problem having no closed-form mathematical
26 solution for n_1 and n_2 . This is unfortunate, since closed-form solutions provide elementary
27 demand functions for the number of sampling units, which are discrete and offer the potential
28 for sensitivity analysis. An alternative approach in epidemiologic studies is to assume a fixed
29 or maximized precision of regression coefficients instead of inequalities, which can lead to
30 closed-form solutions (Reilly, 1996). Like in the studies by Armstrong and by Duan and
31 Mage, Spiegelman's cost model is based on the assumption of the measurement costs for each
32 method being linearly related to the number of measurements; that is, the cost does not vary
33 with replicate measurements or between subjects.
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54 *Optimizing a two-stage sampling strategy*

55 For the purpose of sampling diet records in a nutrition study, Stram et al. (1995) suggest an
56 analytical tool for determining a cost-efficient strategy in terms of the number of subjects, n ,
57 and the number of recording days per subject, m . In optimizing this two-stage sampling
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strategy, the authors minimize the variance $\frac{1}{n} \left(\frac{\sigma^2}{m} + \sigma_\varepsilon^2 \right)$ of the mean exposure subject to a fixed total cost, $C = n(S + R(m-1))$, and an implicit constraint, $m \geq 1$, where σ^2 and σ_ε^2 are the variabilities in nutrient consumption within and between subjects, respectively, S is the cost of recruiting a new subject and obtaining the first 1-day record, and R is the cost of making an additional measurement on a subject who has already been measured once. The optimal number of recording days when $S > R$ depends on the ratios of variances and costs as follows:

$$m = \sqrt{\frac{\sigma^2}{\sigma_\varepsilon^2} \left(\frac{S}{R} - 1 \right)} \quad [4]$$

The unusual specification of the cost model in Stram's study leads to an optimal allocation that has a *global* solution only in the case of $S > R$. If $S < R$ or $S = R$, for instance if the cost of recruiting a subject is negligible, the variance has a *local* minimum when m takes its smallest possible value, i.e. $m = 1$. Stram et al. do not state whether any economical assumptions or theories can explain that they separate the cost of the first-day recording from the cost of additional recordings, and instead add it to the cost of recruiting a subject. When optimizing a two-stage sampling strategy, the costs of primary and secondary sampling units usually appears as separate parts of the total sampling cost (Cochran, 1977). In that case, the cost model could take the form $C = n[S + Rm]$, where S denotes the average cost of recruiting a subject and R stands for the average cost of one measurement from a subject. The demand function for m would then be $m = \sqrt{\frac{\sigma^2}{\sigma_\varepsilon^2} \cdot \frac{S}{R}}$, which has a global solution also in the case of $S < R$ and $S = R$.

Other studies besides the one by Stram et al. have addressed optimization of a resource allocation between two sampling stages, either when assessing a continuous response variable (Shoukri et al., 2003) or when addressing two different treatment conditions (Allison et al., 1997). As in Stram's study, these papers optimize a two-stage sampling strategy by manipulating the number of subjects and the number of replicates per subject. However, rather than addressing the precision of a mean value, they express statistical performance through the size of the intraclass correlation coefficient (Shoukri et al.) or through the correlation between replicate measurements (Allison et al.) The estimated total cost in the studies consists of costs associated with recruitment and observations (Shoukri et al.) or treatments (Allison et al.). The optimization model in Shoukri's study is appropriate for

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3 assessing continuous variables in two-stage sampling procedures, but does not apply to
4 sampling at three stages, for instance subjects, days and units within days. The study by
5 Allison et al. identifies solutions to a number of additional basic optimization problems with
6 applications in health economics, besides the two-stage allocation issue. Another similar study
7 is available, addressing how to optimize a general two-stage sampling strategy for conducting
8 a reliability study (Eliasziw and Donner, 1987). However, the results of this study are not
9 directly applicable to sampling strategies for mean exposure assessment.
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17 *Optimizing a three-stage sampling strategy*

18 Using a three-stage sampling procedure (county, n_1 , census block, n_2 , household, n_3) for
19 assessment of human environmental exposure to metals and volatile organic compounds,
20 Whitmore et al. (2005) aimed at determining the optimal numbers of sampling units to
21 achieve a given level of precision at a minimum cost. The analytical tools applied in sampling
22 optimization consisted of a linear cost model $C = C_0 + n_1 C_1 + n_1 \bar{n}_2 C_2 + n_1 \bar{n}_2 \bar{n}_3 C_3$ and a variance
23 model assuming random effects $Var(\bar{y}) = \frac{\sigma_1^2}{n_1} + \frac{\sigma_2^2}{n_1 \bar{n}_2} + \frac{\sigma_3^2}{n_1 \bar{n}_2 \bar{n}_3}$; where $\sigma_1^2, \sigma_2^2, \sigma_3^2$ are the
24 variance components at the three stages; C_1, C_2, C_3 are the variable costs of adding one more
25 county, census, and household, and C_0 is a fixed cost, which, while not specified in
26 Whitmore's work, could include equipment costs or the salaries of the key executives that run
27 the research. The authors transform the variance formula above to an error model based on
28 intraclass correlations for the first and second sampling stages, ρ_1 and ρ_2 . The authors then
29 provide the optimal sample sizes for the second and third stages, \bar{n}_2 and \bar{n}_3 , as functions of
30 variance components (or intraclass correlations) and unit costs:
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$$45 \bar{n}_{2,opt} = \sqrt{\frac{C_1(1-\rho_1)\rho_2}{C_2\rho_1}} = \sqrt{\frac{C_1\sigma_2^2}{C_2\sigma_1^2}} \quad 46 \bar{n}_{3,opt} = \sqrt{\frac{C_2(1-\rho_2)}{C_3\rho_2}} = \sqrt{\frac{C_2\sigma_3^2}{C_3\sigma_2^2}} \quad [5]$$

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49 The authors conclude that greater variability and/or lower costs at a certain sampling stage
50 calls for a larger sample size at that stage.
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52 Like Stram's solution, the solution in Whitmore's sampling optimization problem does not
53 provide the optimum sample size for first-stage sampling units, i.e. counties in the case of
54 Whitmore. However, the optimal number of samples at this stage can be obtained from the
55 variance model in the optimization problem. Whitmore et al. chose to describe the precision
56 of the mean exposure estimate also by using intraclass correlations because "*intraclass*
57 *correlations tend to be more stable for similar outcomes than the variance components*
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3 *themselves*". Obviously, optimization based on intraclass correlations will give the same result
4 as optimization using raw variance components, and the authors do not present empirical
5 evidence to support that optimization will be easier or more correct if using intraclass
6 correlations, to compensate for the increased difficulties in translating results into practical
7 sampling advice.
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11 Addressing continuous response variables, Foster and Asztalos (2001) also developed a
12 methodology for optimizing a three-stage sampling strategy based on the same cost and
13 variance models as in Whitmore et al. The authors optimized sampling strategies both in
14 terms of minimizing cost at a constant precision, and in terms of maximizing precision under
15 a budget constraint. The cost and precision of the optimal strategies are compared with some
16 non-optimal sampling strategies. The principles for optimization are useful also for exposure
17 studies.
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25 26 GENERAL DISCUSSION 27 28 29 30

31 Strikingly, most of the cost efficiency studies identified in this review were published more
32 than ten years ago. This shows that while the interest in identifying exposure measurement
33 designs worth their price is obvious in both research and practice, little effort has been
34 devoted to developing this issue. However, the few identified and reviewed studies are very
35 valuable as a basis for further research in that they offer the initial necessary theories and
36 methods. They clearly demonstrate the need of developing cost-efficient designs of exposure
37 assessment strategies by analysing their economic and statistical performance in a systematic
38 fashion. This requires data on cost components and sources of error, and also well-behaved
39 economical and statistical models. The review also demonstrated that additional theories and
40 experiences within microeconomics and sampling statistics, including empirical data, will be
41 necessary to further develop cost efficiency analysis.
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50 As noted previously, cost efficiency analyses, regardless of their specific approach and
51 application, strive to achieve a balance between the cost and statistical performance of a
52 measurement design. However, the specific concepts and methods chosen for the cost
53 efficiency analysis depends on whether the aim is to evaluate and compare alternative
54 designs, as pursued by some of the reviewed studies, or to determine an optimal allocation of
55 resources between different measurement efforts as attempted by others. Since the reviewed
56 papers are so few and disparate, it is not justified to derive any more specific guidelines for
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3 what might be the optimal exposure measurement design in a particular occupational setting.
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5 The concept of “efficiency” in the reviewed studies was expressed by indicators such as
6
7 “precision”, “accuracy” or “statistical power”. Some studies suffered from *confusion* in the
8
9 definition and operationalization of these indicators of “efficiency”. Such confusion can be
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11 observed in the work of Lemasters et al. (1996), Armstrong (1995, 1996), and Duan and Mage
12
13 (1997), as explained in the specific reviews of these studies. Which indicator of “efficiency”
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15 to select in a particular study depends on the specific purpose and limitations of the study. For
16
17 optimization of a resource allocation, the most useful indicator of efficiency is “precision”, as
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19 employed by Whitmore et al. (2005) and Stram et al. (1995), since a possible bias of a
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21 particular exposure assessment method does not influence how to optimally allocate samples.
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23 The concept of “statistical power” can only be employed in an optimization approach with
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25 some difficulty, as in the studies by Spiegelman and Gray (1991) and Spiegelman (1994). For
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27 evaluating and comparing different measurement methods, on the other hand, it is appropriate
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29 to use indicators that include both systematic and random sources of error or, as a minimum,
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31 to assume that exposure assessment is non-biased only after assuring that the possible bias is
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33 negligible compared to the uncertainty associated with data. Likewise, including fixed costs
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35 associated with exposure measurement is important when evaluating or comparing
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37 measurement designs. In their comparisons, Armstrong (1995, 1996) did consider fixed costs,
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39 while Lemasters et al. (1996) and Shukla et al. (2005) did not. In studies addressing optimal
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41 resource allocation, on the other hand, fixed costs do not need to be included in the proposed
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43 cost model, as all fixed costs will disappear in the differentiation contained in the optimization
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45 procedure and thus do not influence optimal allocation.
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47 Modern mixed-model statistics has, in the past decade, gained increasing intention as a tool
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49 for identifying exposure determinants with a satisfying predictive ability, mainly for the
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51 purpose of exposure control and intervention (Burdorf, 2005). However, determinants that are
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53 “cheap” to obtain and, at the same time, correlate well with “true” exposures also represent a
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55 potentially cost efficient avenue for exposure assessment. Besides the studies addressing cost
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57 efficient allocation of subjects to indirect/imperfect and direct/superior exposure
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59 measurements (Duan and Mage, 1997; Spiegelman, 1994; Spiegelman and Gray, 1991), none
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of the studies in the present review discuss this possibility of modeling “expensive” exposure
variables by “cheap” determinants. Various ideas for exposure modeling have been analyzed
with regards to statistical performance (e.g. Chen et al., 2004; Mathiassen et al., 2005; Preller
et al., 1995), while the possible and probable economic benefits of exposure modeling
remains an issue for future research.

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5 All together, the reviewed studies showed two typical and common characteristics:
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8 **Simplification**

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10 All of the reviewed studies assume that the total cost of data collection is linearly related to
11 the number of subjects and measurements per subject. In the studies by Lemasters et al.
12 (1996) and Shukla et al. (2005), this linearity is particularly simplified in assuming a straight-
13 forward equivalence between the number and the cost of measurements. However, the
14 recruitment costs may well differ between subjects, for instance because they live at different
15 distances from researcher's laboratory and thus cause different travelling cost, or because
16 different efforts need to be invested in convincing them to participate. The cost of
17 measurements for a particular subject can also vary, for instance as a result of subjects getting
18 more familiar with measurement procedures, and thus saving working time. Costs can also
19 vary over time not only due to the effect of economical factors as inflation rate but also due to
20 changes of exposure patterns. An appropriate economic model should therefore allow for cost
21 variations. A linear development of input costs exhibits a constant return to scale for exposure
22 measurements irrespective of the applied measurement technique, because the *marginal cost*,
23 i.e. the cost of one additional unit of measurement, is equal to the average cost at each level of
24 output. This assumption is a simplified view of statistical production. When adopting a linear
25 cost function, the optimized sampling strategy will be the same irrespective of whether
26 marginal costs of sampling units or their average costs are addressed in the cost model
27 (Whitmore et al., 2005). However, calculation of the total cost of a study would be incorrect if
28 the statistical production does not exhibit constant return to scale.
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31 Generally, the reviewed studies do not discuss whether the underlying assumptions of the
32 statistical models used for assessing precision of the mean exposure estimates were met; and
33 all studies employ a standard additive random effect model. It should be investigated more
34 thoroughly whether errors at different stages of sampling are, indeed, additive, and which
35 consequences a violation might have for the cost efficiency analysis. Further, variabilities at
36 the different stages of sampling are assumed to be homogeneous in the exposure studies as
37 well in the response and intervention studies, which may also in many cases be a critical
38 assumption.
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41 In studies aiming at sampling optimization, the selection of simple cost and error models may
42 be the result of a strive to obtain easy mathematical solutions to the optimization problem.
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44 With complex cost and error models, the mathematical form for optimizing sample sizes is
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3 also more complicated, so that operations may not lead to closed-form optimal solutions
4 without the use of additional assumptions. In many cases, numerical analysis, such as “non-
5 linear multiparameter constrained optimization subroutine” in the studies by Spiegelman et al.
6 (1991, 1994), may then be the most viable alternative.
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10 11 **Incompleteness**

12 The reviewed studies have given much less attention to the cost model and economic analyses
13 than to error models and statistical interpretations. It is often not clear which cost curves (unit
14 cost, average cost or marginal cost) or which input costs (capital cost, labor cost, energy cost
15 or material cost) are considered and estimated in the cost models. The social costs of biased
16 and imprecise estimates of exposures, i.e. the *opportunity costs* of not using the most
17 productive measurement design, have never been modelled, since the outcomes have been
18 limited to statistical performance of the exposure measurement design. Further, systematic
19 methods for estimating the actual costs have not been discussed in the studies, and hence not
20 either the reliability of assessing various cost components, even though mathematical
21 techniques are available for this purpose. These techniques include approaches based on
22 Bayesian statistics (Lambert et al., 2008) or regression analysis (Lin, 2003), by which costs
23 can be estimated reliably in spite of uncertainty and incomplete data. Also, non-parametric
24 estimation methods are available to address the distributional form of measurement cost data
25 (Cooper et al., 2003).
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38 No studies have given attention to the cost and productivity associated especially with the
39 labour inputs or to further analysis of associations between (minimized) total cost and
40 statistical performance. A fundamental issue to consider when making economic decisions for
41 exposure assessment, which has not been addressed by any of the reviewed studies, is the
42 various *elasticities* associated with statistical production. Elasticities measure the dynamic
43 behaviour of cost and efficiency by a ratio of the percent change in one variable to the
44 associated percent change in another variable. Elasticities include, for instance, cost *elasticity*
45 *of output*, E_y^c , and *price elasticity of demand*, E_D^p , measuring the responsiveness of an
46 optimized function to changes in the required output and input cost, respectively. E_y^c would,
47 for instance, show the percentage change in the (minimized) cost as a result of a one percent
48 change in the required precision of the mean exposure estimate, and E_D^p would measure the
49 percentage change in demand of a measurement input, e.g. the optimal number of subjects,
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3 resulting from one percent change in its cost. Both these type of elasticities could be useful as
4 a basis for decision-making when designing exposure measurement.
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8 Also, methodologies developed for economic evaluation of competing treatment interventions
9 in the field of health economics (Tompa et al., 2008; Goossens et al., 1999) could be useful
10 when providing cost-efficient exposure measurement designs. The basic purpose of an
11 economic evaluation in this case is to ensure that the opportunity cost of implemented
12 interventions is compensated by their (positive) effects on health. In contrast to cost efficiency
13 analysis of exposure assessment, economic evaluation of alternative health care interventions
14 has a long scientific history. Since the generic issue of how to optimize economic resource
15 consumption with respect to a desirable output is shared by cost efficiency analysis and health
16 economics, research in exposure assessment could benefit from consulting the health
17 economics literature; for instance on approaches for modelling cost data, comparing the cost
18 efficiency of alternative measurement designs where the “perfect measurement” does not
19 exist, and/or optimizing resource allocation if the cost of measurement inputs, but not the
20 variabilities, are taken into consideration. Adopting approaches from health economics into
21 exposure science will present challenges in terms of replacing various dimensions of health
22 outcomes by appropriate indicators of statistical performance, while it will, at the same time,
23 offer opportunities of expressing the success of measurement designs in wider terms than
24 mere statistical performance.
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40 Distinct and well defined concepts, well-specified models for costs and error, complete cost
41 analysis, and estimation of elasticities should all be emphasized when attempting to
42 econometrically model the production of information on different exposure variables. Our
43 suggestion for future research devoted to cost efficiency analysis of exposure assessment is to
44 first formulate appropriate indices for measuring the quantity of information produced on the
45 exposure variable according to the specific need of a study, and then to construct a statistical
46 *production function* and its corresponding *cost function*, i.e. its dual cost function in
47 economics terms, so as to provide the basis for a comprehensive economic analysis. The
48 measure of the quantity of information produced should account for all sources of error and
49 not assume an “unbiased estimation” or the existence of a “perfect measurement”. Methods
50 should also be developed for evaluating the output of statistical production, e.g. statistical
51 performance, in monetary terms, so as to make it directly comparable to the total cost of data
52 collection and processing. The production and cost functions should give all information
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3 about the marginal effects of inputs on statistical production in order to facilitate decisions
4 about how to invest an increased budget or implement a saving. Another area for future cost
5 efficiency related research concerns the influence of the specifications of the statistical and
6 economical models applied on the results from comparison or optimization of measurement
7 designs. The results and principles developed by the reviewed studies might have been
8 different if other models had been applied, but the sensitivity of, for instance, an “optimal”
9 allocation to the principles and algorithms used for optimization is not known so far. This
10 includes research into the practical need of using well-specified, though complex, models for
11 estimating costs and errors, and the loss of performance when designing exposure assessment
12 strategies that deviate from the optimal choice.
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