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QUANTITATIVE EVALUATION OF PREVENTION STRATEGIES IN PUBLIC HEALTH

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Abstract

Various schemes of prevention measures in public health are developed and analyzed on the basis of a general mathematical model. Features related to cost issues, including primary and secondary prevention interventions, differential survival experiences and communicable diseases are in turn used to show the potentialities of the theoretical framework. A numerical application is presented with reference to Italian cancer data.

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1. Introduction and Motivations

Health is widely acknowledged as an economic good representing a pre-requisite for individual well-being and economic productivity. Public policy actions focussed on its promotion and improvement are an essential factor to sustainable economic welfare and prevention measures are often the keys to successful health policies. Socio-economic studies provide wide evidence of the positive impact of health promotion on relevant economic variables such as labour supply, productivity, wages and earnings (for a review see Suhrke et al., 2005); however, unlike direct health services, health promotion programs entail a long-term distribution of the benefits that makes them less profitable to private firms. It is, therefore, the public sector that takes most of the charge of prevention programs and sound tools for cost reductions and resource management are becoming more and more crucial in a long-term perspective under increasing public budget constraints.

A large number of studies in the literature (based on standard statistical modelling or developing original mathematical approaches) provide specific, disease-related evaluation tools for the impact of prevention measures on various public health and socio-demographic aspects of community life (see, among many: Boily et al., 2007, Goldie S. et al., 2006, Zethraeus N., 2007). However, in the framework of overall planning, public health policy makers often need uniform and comparable tools to evaluate the global impact of prevention interventions on budget issues and community life. As clearly explained in Goldie (2003), "No clinical trial or single cohort study will be able to simultaneously consider all of these components. Cost-effectiveness analysis and disease-simulation modeling, capitalizing on data from multiple sources, can serve as a valuable tool to extend the time horizon of clinical trials, to evaluate more strategies than possible in a single clinical trial, and to assess the relative costs and benefits of alternative policies to reduce mortality". Only few studies examine the impact of prevention on public health expenditure in a comprehensive model-theoretical approach, where the effects of global resource allocation are evaluated (see, for instance, Davies R. et al., 2003, Haddix A. et al., 2003, Mackinnon D. and Dwyer J., 1993).

This paper offers a modelling approach to the general problem of design and evaluation of prevention measures under an essentially budget-management perspective. Various design aspects of prevention must be taken into account when organizing and scheduling public

health interventions, out of which the demographic structure of the reference population and the disease epidemiology are the most relevant. Specific issues to be included in a modelling approach are the distinction between primary and secondary prevention measures, direct and indirect costs of disease treatment, decision strategy indicators. However, while a primary prevention analysis only involves a simple community model with individual costs, secondary prevention schemes involve variable treatment costs, unit prevention costs and a clear epidemiological picture: the disease prevalence in the reference population and a multistate distribution of pre-clinical, asymptomatic conditions among affected individuals.

The scheme used in the following starts in section 2 with a simple primary prevention model and expands it to a multistate, secondary prevention evaluation model. Section 3 presents an application to overall Italian cancer data. In section 4 extensions of the general model are discussed to further include more complex situations, involving disease prevalence instability, sorted risk groups and differential survival experiences. Conclusions and materials for further developments and applications are presented in section 5.

2. General Prevention Models

As remarked in the previous section, primary and secondary prevention measures act at different population/disease level and interactions. In this section prevention evaluation schemes for primary and secondary interventions will be presented with regard to expenditure and savings obtained by a public health system, without selection of admission of the affected individuals to treatment (i.e.: all affected individual of the reference population have equal access to clinical treatment). A further hypothesis used in the following is that the disease prevalence in absence of prevention interventions is stable and constant over the time horizon considered; consequences of dropping this hypothesis will be briefly analysed in section 5, where possible extensions of the model will be presented.

A simple scheme of primary interventions may be thought of as an information campaign directed to the general population or a sorted proportion of it. It involves a roughly per capita expenditure and results into a reduction of the disease incidence and prevalence, at variable levels, corresponding to the effectiveness of the campaign.

Let $P = p + \bar{p}$ be the total number of individuals in a population, divided into $p = \beta P$ individuals that will eventually become affected by some disease under study (β being the known prevalence of the disease in the general population) and $\bar{p} = (1 - \beta)P$ individuals that will not develop the disease. A public health system that must treat all affected individuals has a predictable, total, disease-related cost \bar{C} given by

$$\bar{C} = A_0 + Ap \quad (1)$$

where A_0 is a general fixed system cost and A is the variable treatment cost per affected individual.

Thus, given a per capita prevention expenditure e and a corresponding proportion γ of individuals positively responding to the prevention measures, the total cost (1) becomes

$$\hat{C} = A_0 + A(1 - \gamma)p + eP \quad (2)$$

Note that the term P does not include already affected individuals, as they are not the object of the prevention actions and are, therefore, included in the fixed cost term A_0 .

Using (1) and (2), a system saving is thus attained if

$$S = \bar{C} - \hat{C} = A\gamma p - eP > 0 \quad \Rightarrow \quad e < A\gamma\beta \quad (3)$$

which provides an exact evaluation of the profitability of a prevention investment: in fact, this turns out to be economically profitable only when the variable treatment costs and/or the disease prevalence are high enough to compensate for the prevention costs.

A more complex modelling scheme is to be used to evaluate secondary prevention measures as these interventions aim at different results and involve various, disease-related types of individuals. In this case the reference population, target of these prevention measures, includes those already affected individuals at asymptomatic, pre-clinical stages aiming at an early detection of the disease and at its early treatment (Simeonsson, 1991).

Let now be the total population given by $P = p + \bar{p}$ with p asymptomatic individuals already affected by the disease under study at n increasing levels of severity, and \bar{p} healthy individuals, and let β_i $i=1, \dots, n$ be the known prevalences of each level of severity of the disease in the population.

Similarly to (1), the public health system in absence of prevention measures has a predictable, total, disease-related cost \bar{C} given by

$$\bar{C} = A_0 + \sum_{i=1}^n \alpha_i \beta_i P \quad (4)$$

where A_0 is a general fixed system cost and $\alpha_i, i=1, \dots, n$ are the variable treatment costs per affected individual and related to the n levels of severity of the disease. Note that the distribution of individuals in (4) is supposed to be induced by the disease symptomatology: i.e., affected individuals enter the cost function (4) at a level corresponding to detectable symptoms.

Possible prevention measures can be thought of as some form of screening over the entire population P to detect all affected individuals before their disease becomes symptomatic (i.e., at a lower level of severity). Let e be the unit cost of the prevention operations; the total cost of prevention is therefore given by

$$eP = e \left(\sum_{i=1}^n \beta_i P + \bar{p} \right)$$

and the prevention cost per affected individual actually detected is then given by

$$\varepsilon = e \frac{P}{\sum_{i=1}^n \beta_i P} = e \left(\frac{1}{\sum_{i=1}^n \beta_i} \right) \quad (5)$$

The effects of prevention on the number of affected individuals are thus given by their redistribution among the n levels of severity (with the corresponding changes in the treatment costs) according to a lower triangular transition matrix $\Pi = [\pi_{ij}]_{i,j=1..n}$ such that:

$$\sum_{i=j+1}^n \pi_{ij} \leq 1 \quad \text{and} \quad \pi_{ij} \begin{cases} = 0 & i < j \\ 1 - \sum_{i=j+1}^n \pi_{ij} & i = j \\ \pi_{ij} & i > j \end{cases} \quad (6)$$

where underlying hypotheses are:

- the disease prevalence does not change within the time horizon considered,
- prevention measures do not interact with the symptomatology of the disease (i.e.: the level of severity detected by prevention measures cannot be higher than the level corresponding to detectable symptoms).

By using (4), the total system cost, when prevention measures are put in place, is thus given by

$$\hat{C} = A_0 + \sum_{i=1}^n \alpha_i \beta_i P + \sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j P - \sum_{i=2}^n \sum_{j=1}^{i-1} \alpha_i \pi_{ij} \beta_i P + \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j P \quad (7)$$

where the variable treatment cost of the i -th level of severity is now given by the algebraic sum of

- $\alpha_i \beta_i P$: the cost of individuals detected at symptomatic level of severity;
- $\sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j P$: the cost of individuals detected at the i -th level of severity with a higher symptomatic level of severity;
- $\sum_{j=1}^{i-1} \alpha_i \pi_{ij} \beta_i P$: the cost of individuals with i -th symptomatic level of severity detected at a lower level of severity;

- $\varepsilon \sum_{j=i+1}^n \pi_{ji} \beta_j P$: the prevention costs per individual with i -th symptomatic level detected at a lower level of severity.

A system saving is thus attained if

$$S = \bar{C} - \hat{C} > 0 \quad (8)$$

which, by using (4) and (7), becomes

$$-\sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j + \sum_{i=2}^n \alpha_i \beta_i \sum_{j=1}^{i-1} \pi_{ij} - \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j > 0 \quad (9)$$

By using some simple algebra and solving for ε we have

$$\varepsilon < \frac{\sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \pi_{ji} \beta_j}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j} \quad (10)$$

Thus an economically sound prevention policy can be effectively set up when the cost of one asymptomatic detected individual is smaller than the average cost reduction, weighed by the newly detected prevalences of each level of severity. In the absence of further, specific information on the morbidity of the disease under study at various levels of severity (i.e.: no direct or indirect information available on the π_{ij} terms), the assumptions that the whole population P undergoes the prevention screening and that no biased error occurs during the screening operation, provide a reasonable ground to the conservative hypothesis that the prevalence rates β_i $i=1, \dots, n$ of the general population also apply to the various levels of severity. This implies that all transitions π_{ij} can be approximated by the corresponding prevalence rates β_j $\forall j > i, i=1, \dots, n$ and, similarly to (3), (10) can be expressed in terms of the unit cost e of prevention operations and becomes

$$e < \frac{\sum_{k=1}^{n-1} \beta_k}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \beta_i \beta_j} \sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \beta_i \beta_j \quad (11)$$

Under the hypothesis of non-decreasing costs between the disease stages and the trivial remark that $\beta_i > 0$ for at least two different i 's, $i = 1 \dots n$, then $e \geq 0 \forall \alpha_i, i = 1 \dots n$ and $e = 0$ if and only if $\alpha_j - \alpha_i = 0 \forall j > i, i, j = 1 \dots n$.

3. An Application to Italian Cancer Data

The various tumor forms are a typical example falling into most of the modelling hypotheses as in section 2; even when limited to any incidence sub-populations, these may, however, be easily detected (male-female, for instance). In the following, simple numerical examples of prevention schemes are presented, based on the model in the previous section and using cancer treatment- and cost-data from heterogeneous, external studies. Prevalence and global unit cost data corresponding to various primary tumor sites are shown in table 1.

Table 1. - Unit treatment costs and prevalence by tumor primary site.

primary	prevalence%*	unit cost (×1000€)**
<i>lung</i>	0,17	36
<i>stomach</i>	0,12	19
<i>melanoma</i>	0,27	21
<i>colon/rectum</i>	0,69	24
<i>cervix</i>	0,05	10
<i>breast</i>	2,26	17
<i>prostate</i>	1,23	19
<i>leukemias</i>	0,09	77

* A.I.R.TUM. – I tumori in Italia (2012) - <http://www.tumori.net>

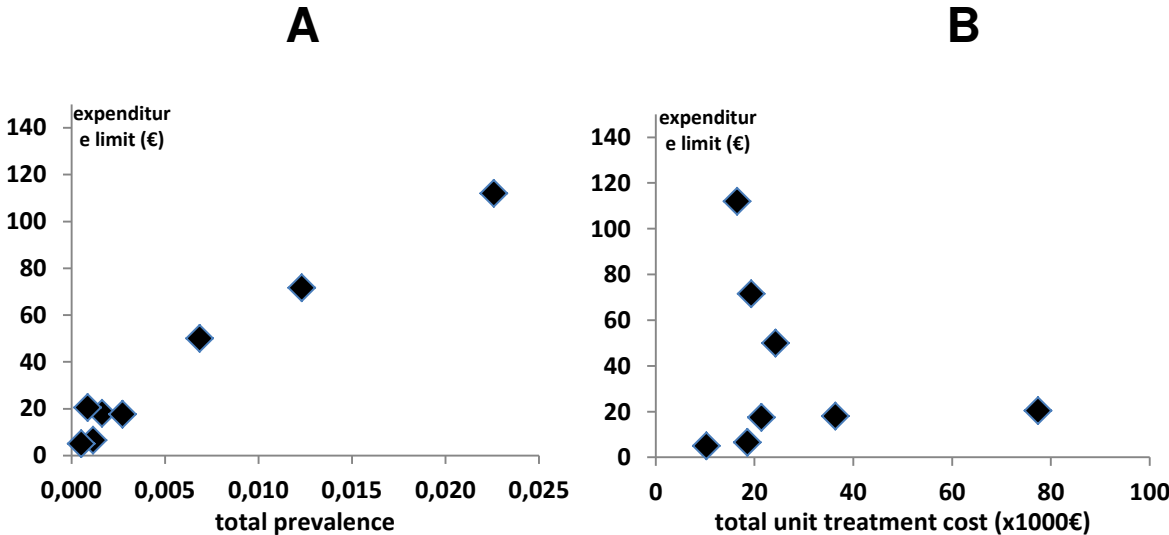
** CENSIS, from *Economist Intelligent Unit* (2010)

While no staging data are required in this simplified application of the primary prevention scheme as from (3), the secondary prevention scheme requires cost and prevalence distribution data for the application of (11). In the next, for the sake of homogeneity of the various primary tumor sites and in order to outline the use of the model, the staging classifications have been reduced to 3 for each type of tumor on the basis of epidemiological and clinical data drawn from the existing medical literature. However, as the detailed cost distribution at each stage is not immediately available, various distributional hypotheses were applied to the data in table 1 and the resulting expenditure limits were computed according to (11).

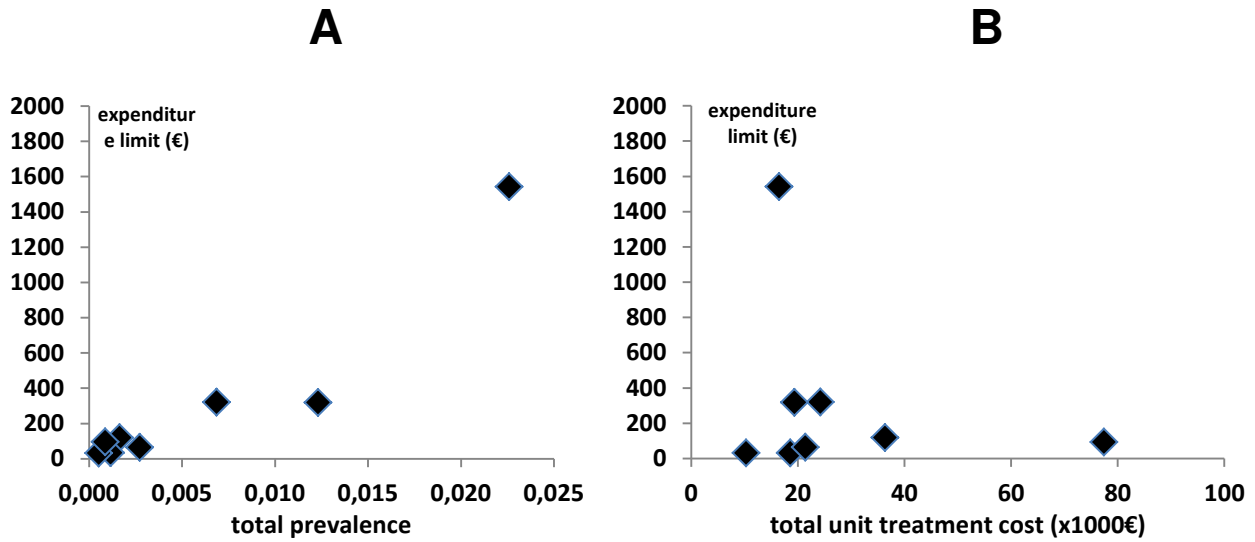
Figures 1, A and B, show two examples of primary prevention schemes where: A) the expenditure limits are mapped against the corresponding total prevalences, and B) the expenditure limits are mapped against the total unit treatment costs.

Figures 2 and 3, A and B, show two examples of secondary prevention schemes with different distributional hypotheses among the stages, where, as above: A) the expenditure limits are mapped against the corresponding total prevalences, and B) the expenditure limits are mapped against the total unit treatment costs.

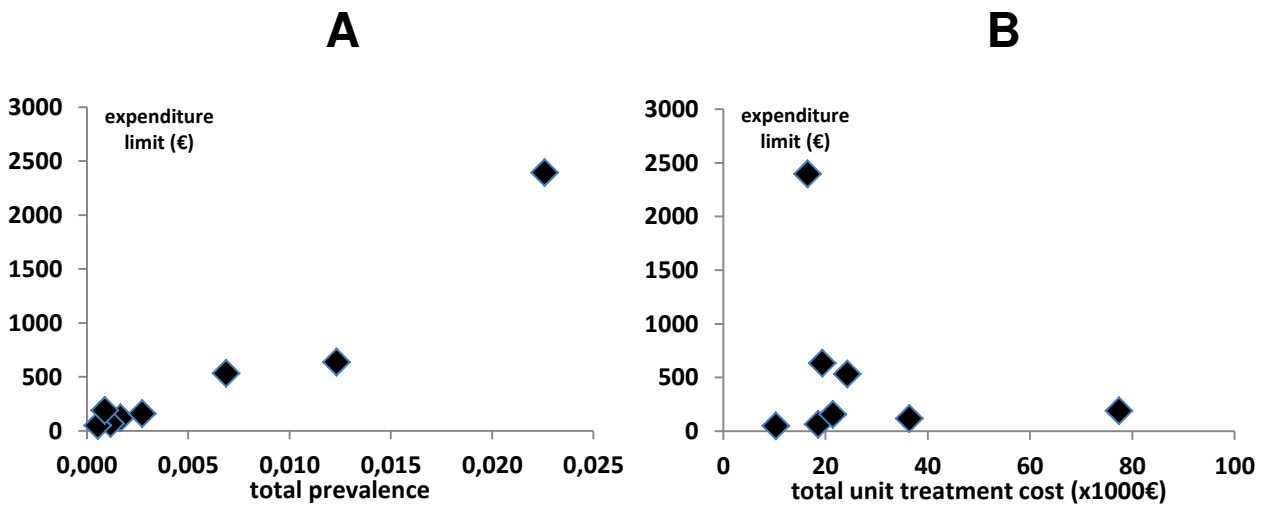
FIGURES 1 – Tumor types by primary prevention expenditure limit and A) prevalence B) unit treatment cost.



FIGURES 2 – Tumor types by secondary prevention expenditure limit and **A**) prevalence **B**) unit treatment cost, with a stage cost distribution: $\alpha_2 = 2\alpha_1; \alpha_3 = 10\alpha_2$



FIGURES 3 – Tumor types by secondary prevention expenditure limit and **A**) prevalence **B**) unit treatment cost, with a stage cost distribution: $\alpha_2 = 5\alpha_1; \alpha_3 = 1.5\alpha_2$



A visual inspection of figures 1, 2 and 3 shows that, both in the primary and the secondary prevention schemes, the expenditure limit is approximately linearly correlated to the

pathology prevalence while no direct dependency can be detected between prevention expenditure limit and the unit treatment.

The results of these simple numerical applications highlight the role of the disease prevalence in the definition of the prevention expenditure limit. In fact, while the unit cost enters (11) only as a cost redistribution among the stages and, therefore, as a relative (not absolute) budget savings, the disease prevalence is what actually provides a larger probability to detect an affected individual and of not wasting prevention resources in the search of an unlikely event.

4. Extending the Model

By defining the vectors $\boldsymbol{\beta} = [\beta_i]_{i=1,\dots,n}$ and $\boldsymbol{\alpha} = [\alpha_i]_{i=1,\dots,n}$ and the Hollow matrices

$$\mathbf{B}_1 = \begin{bmatrix} 0 & -\beta_1 & -\beta_1 & -\beta_1 & \dots & -\beta_1 \\ \beta_2 & 0 & -\beta_2 & -\beta_2 & \dots & -\beta_2 \\ \beta_3 & \beta_3 & 0 & -\beta_3 & \dots & -\beta_3 \\ \beta_4 & \beta_4 & \beta_4 & 0 & \dots & -\beta_4 \\ & & \dots & \dots & & \\ \beta_n & \beta_n & \beta_n & \dots & \beta_n & 0 \end{bmatrix}$$

$$\mathbf{B}_2 = \mathbf{B}_1 \mathbf{I}_n \boldsymbol{\beta} = \begin{bmatrix} 0 & -\beta_1\beta_2 & -\beta_1\beta_3 & -\beta_1\beta_4 & \dots & -\beta_1\beta_n \\ \beta_1\beta_2 & 0 & -\beta_2\beta_3 & -\beta_2\beta_4 & \dots & -\beta_2\beta_n \\ \beta_1\beta_3 & \beta_2\beta_3 & 0 & -\beta_3\beta_4 & \dots & -\beta_3\beta_n \\ \beta_1\beta_4 & \beta_2\beta_4 & \beta_3\beta_4 & 0 & \dots & -\beta_4\beta_n \\ & & \dots & \dots & & \\ \beta_1\beta_n & \beta_2\beta_n & \beta_3\beta_n & \dots & \beta_{n-1}\beta_n & 0 \end{bmatrix}$$

where \mathbf{I}_n is the $n \times n$ identity matrix, (11) can be re-written as

$$e < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha}' \mathbf{B}_1 \boldsymbol{\beta} \quad \text{or} \quad e < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha}' \mathbf{B}_2 \mathbf{1}_n \quad (12)$$

where $\mathbf{1}_n$ is the n -vector with elements all equal to 1's. Note also that \mathbf{B}_2 is skew-symmetric and both \mathbf{B}_1 and \mathbf{B}_2 are known as generalized Conference matrices.

From (12) direct, a geometric interpretation of the upper limit to prevention unit expenditures can be drawn in terms of prevalences and treatment costs. In fact, vectors $\boldsymbol{\alpha}$, $\boldsymbol{\beta}$ and $\mathbf{1}_n$ represent, respectively, the treatment cost profile of the disease under study, the prevalence profile and the profile of an unscreened individual; therefore the degenerate, bilinear forms in (12) map, respectively, a prevalence profile and an unscreened individual onto the cost space, the degenerate condition accounting for (6).

This vector setting of the prevention expenditure limit (12) may be effectively used, by direct modifications of $\boldsymbol{\alpha}$, $\boldsymbol{\beta}$ and $\mathbf{1}_n$, to accomodate complex prevention schemes, such as selections of risk group sub-populations and communicable (infectious or hereditary) diseases.

4.1 Variable Stage Survival

Let us suppose that an affected individual has a life expectancy at disease onset time t given

by $E(t) = \int_t^{\infty} \frac{S(w)}{S(t)} dw$. Since, in general, the exact time of onset of the disease is unknown, the

disease staging may be effectively used to approximate the survival experience as a discrete function of the severity rather than the time elapsed: S_i , $i=1..n$. Thus the corresponding

life expectancies $E_i = \sum_{h=i+1}^n \frac{S_h}{S_i}$ generate a new set of costs, where original average stage costs

α_i , $i=1..n$ are associated to life expectancy at each detection stage: $\alpha_i E_j$, $i \neq j$; $i, j=1..n$

and (12) turns into

$$e_s < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha}' \mathbf{B}_2 \mathbf{E}$$

where $\mathbf{E} = [E_i]_{i=1, \dots, n}$.

4.2 Communicable diseases

The extension of the model to communicable diseases prevention must account for all secondary cases that an unscreened individual may potentially generate during his whole infectious life. Not very different is the case of hereditary syndroms and affections of all sorts. Similarly to the previous section, the vector $\mathbf{1}_n$ turns into $\mathbf{1}_n + \mathbf{s} = [1 + s_i]_{i=1, \dots, n}$, where the s_i , $i = 1 \dots n$ are the average numbers of secondary cases generated by an infective individual in stage i , $i = 1 \dots n$. Therefore (12) becomes

$$e_s < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha}' \mathbf{B}_2 (\mathbf{1}_n + \mathbf{s})$$

and, still similarly to the previous case, new stage costs are generated as $\alpha_i(1 + s_j)$, $i \neq j; i, j = 1 \dots n$.

5. Final Remarks and Further Developments

The model here presented is based on health care hypotheses that apply to most public health schemes. Moreover, current ethical and social issues have no part in the approach here presented. The model is flexible enough to be further extended as to include more complex issues as shown in section 4. It is, however, interesting to notice that the matrix form expressions (12) allow for a geometrical interpretation of the prevention structure: in fact, the bilinear forms in (12) are degenerate (the matrices \mathbf{B}_1 and \mathbf{B}_2 are singular), thus mapping the

unit n -vector (representing a non-informative individual) onto the $(n-1)$ -space of treatment unit costs, where the reduction of dimensions is due to the fact that only non-zero cost differences are considered. This amounts to representing an unsorted (non-informative), affected individual in terms of cost reduction if positively sorted by some forms of prevention/screening for the disease under study. As shown in section 4, any further improvement to this model can, therefore, be attained by new geometrical definitions of the space of individuals, of the space of treatment costs or a combination of both, so as to possibly include targeted prevention measures and/or selective treatment costs.

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