



**PUBLIC HEALTH PREVENTION
STRATEGIES.
A MATHEMATICAL MODEL.**

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ABSTRACT

This paper presents and discusses schemes of prevention measures in public health. A mathematical model is purposely designed to outline various features related to cost issues and a numerical application to Italian cancer data is used to show the flexibility and utilization of the model.

Classification JEL: I18, C63, H89

Keywords: Public Health, Mathematical Modelling, Prevention Measures, Cost Analysis

1. INTRODUCTION AND MOTIVATION

Whatever be the health system structure, public-based, or based on a public-private partnership, embedded prevention issues are becoming more and more crucial in a long-term perspective of cost reductions and optimal resource management. Several studies in the literature (based on standard statistical modelling or developing original mathematical approaches) provide specific, disease-related analysis of the impact of prevention measures on various public health and socio-demographic aspects of community life (see, among many: Boily et al., Goldie S. et al., Zethraeus N.) however, very few of them single out the general economic impact on public health expenditure budget in a comprehensive model-theoretical approach (see, for instance, Davies R. et al., Haddix A. et al., Mackinnon D. and Dwyer J.).

This paper presents a general mathematical model of the effects of prevention strategies on health care global costs, when patients are classified at various stages of severity of a disease under study. In fact, illness severity, risk exposure and diagnostic delay are often factors that increase the costs of care: effective prevention strategies can greatly contribute to cost reductions and/or optimization of the care delivery systems.

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The model is based on an underlying, evidence-based staging of the disease of interest. This preliminary structure is designed to further accommodate issues such as competing costs between care and prevention and the related expenditure policy measures.

2. THE GENERAL PREVENTION MODEL

Let $P = p + \bar{p}$ be the total number of individuals in a population, divided into p individuals affected by some 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.

A public health system that must treat all affected individuals has a total, disease-related cost \bar{C} given by

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

where A_0 is a general fixed system cost and α_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 (1) is supposed to be induced by the disease symptomatology: i.e., affected individuals enter the cost function (1) 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



$$\varepsilon = e \frac{P}{\sum_{i=1}^n \beta_i P} = e \left(\frac{1}{\sum_{i=1}^n \beta_i} \right) \quad (2)$$

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 $\mathbf{\Pi} = [\pi_{ij}]_{i,j=1..n}$ such that:

$$\sum_{i=j+1}^n \pi_{ij} \leq 1 \quad \text{and} \quad \pi_{ij} \begin{cases} = 0 & i < j \\ 1 - \sum_{i=j+1}^n \pi_{ij} & i = j \\ \pi_{ij} & i > j \end{cases} \quad (3)$$

where the expressions in (2) are trivially generated by the hypotheses that the disease prevalence does not change within the time horizon considered and that 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 (3), the estimated total system cost, when prevention measures are put in place, is thus given by

$$\hat{C} = A_0 + \sum_{i=1}^n \alpha_i \beta_i P + \sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j P - \sum_{i=2}^n \sum_{j=1}^{i-1} \alpha_i \pi_{ij} \beta_i P + \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j P \quad (4)$$

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.

For the prevention measures to induce a saving S in the budget of the system, the following positivity condition must be met

$$S = \bar{C} - \hat{C} > 0 \quad (5)$$

which, by using (1) and (4), becomes

$$-\sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j + \sum_{i=2}^n \alpha_i \beta_i \sum_{j=1}^{i-1} \pi_{ij} - \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j > 0 \quad (6)$$

By reordering and inverting the indexes of the second term of left hand side, condition (6) becomes

$$-\sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_i \pi_{ji} \beta_j + \sum_{i=1}^{n-1} \sum_{j=i+1}^n \alpha_j \pi_{ji} \beta_j - \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j > 0$$

i.e.,

$$\sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \pi_{ji} \beta_j - \varepsilon \sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j > 0$$

and solving for ε :

$$\varepsilon < \frac{\sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \pi_{ji} \beta_j}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j} \quad (7)$$



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. Now, using (2), (7) can be expressed in terms of the unit cost e of prevention operations:

$$e \frac{1}{\sum_{i=1}^n \beta_i} < \frac{\sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \pi_{ji} \beta_j}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j} \Rightarrow e < \frac{\sum_{k=1}^n \beta_k}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \pi_{ji} \beta_j} \sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \pi_{ji} \beta_j \quad (8)$$

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 hypotheses 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 $\beta_j \quad \forall j > i, i=1, \dots, n$ and the second of (8) becomes

$$e < \frac{\sum_{k=1}^{n-1} \beta_k}{\sum_{i=1}^{n-1} \sum_{j=i+1}^n \beta_i \beta_j} \sum_{i=1}^{n-1} \sum_{j=i+1}^n (\alpha_j - \alpha_i) \beta_i \beta_j \quad (9)$$

3. CANCER AND PREVENTION COSTS IN ITALY. A NUMERICAL EXAMPLE

The various cancer forms are a typical example falling into most of the modelling hypotheses as in section 2; even when they may be limited to any incidence sub-populations, these may, however, be easily detected (male-female, for instance). In the following, an example of the model-at-work is presented, using cancer treatment- and cost-data derived from external studies.



As of (9), relevant data consist of prevalences and cost distributions at various stages of severity of the disease; these input data are compared to the expenditure limit computed through (9) and mapped onto graphical representations.

For the sake of homogeneity of the various primary tumors and to outline the use of the model the staging classifications have been reduced to 3 for each type of tumor. Moreover, the cost scaling between stages was supposed to amount to: $\alpha_3 = 2\alpha_2 = 4\alpha_1$ throughout, as the costs of single stagings are not immediately available.

Table 1. - *Expenditure limits by tumor primary site and related costs and epidemiology.*

primary	prevalence%*	unit cost (×1000)**	limit
<i>lung</i>	0,17	36	53
<i>stomach</i>	0,12	19	18
<i>melanoma</i>	0,27	21	40
<i>colon/rectum</i>	0,69	24	162
<i>cervix</i>	0,05	10	5
<i>breast</i>	2,26	17	596
<i>prostate</i>	1,23	19	192
<i>leukemias</i>	0,09	77	56

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

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

Figures 1 and 2 show the mapping of the model expenditure limit (as in 9) to, respectively, the disease prevalence and the average treatment cost, while figure 3 relates the unit treatment cost to prevalence. A visual inspection of the three figures shows, as expected, a clear dependence of the model expenditure limit from the pathology prevalence. On the other hand, no evident dependency is exhibited between unit treatment cost and prevalence (Fig. 3) and unit treatment cost and pathology prevalence (Fig. 2).

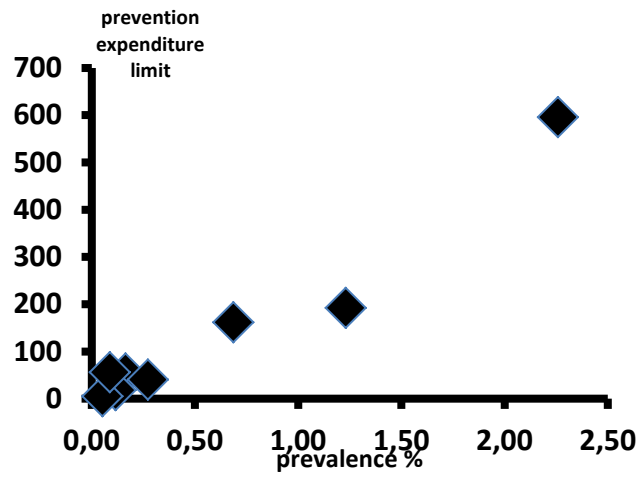


FIGURE 1. – Tumor primary sites by prevalence and prevention expenditure limit (Table 1)

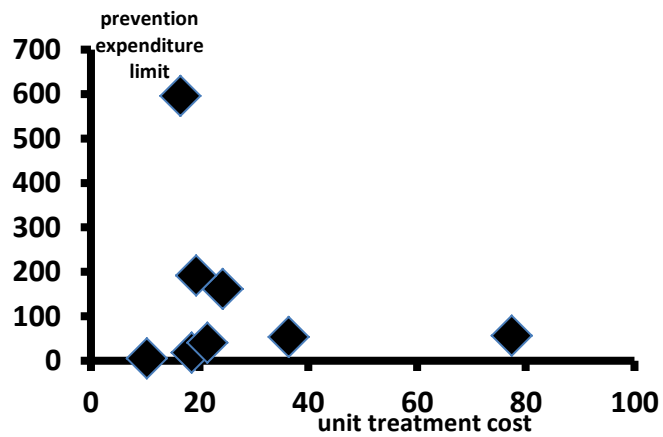


FIGURE 2. – Tumor primary sites by unit treatment cost and prevention expenditure limit (Table 1)

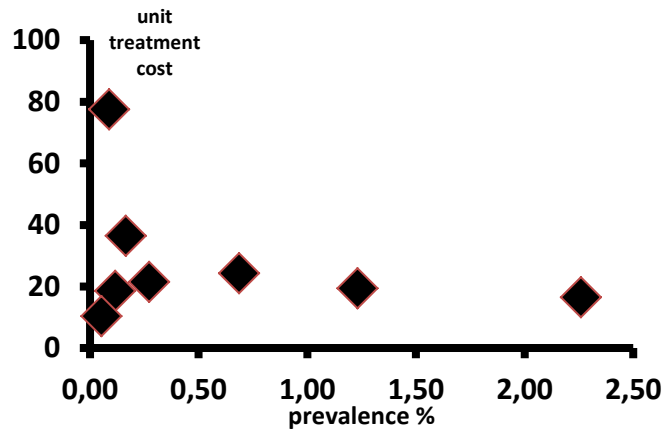


FIGURE 3. – *Tumor primary sites by prevalence and unit treatment cost (Table 1)*

Preliminary results from this simple numerical application highlight the roles of unit treatment cost and of the disease prevalence in the definition of the prevention expenditure limit. In fact, while the unit cost enters (9) only as a cost redistribution among classes of severity 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 thus a larger probability of not wasting prevention resources in the search of an unlikely event.

4. THE GEOMETRY OF PREVENTION

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, (9) can be re-written as

$$e < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha} \mathbf{B}_1 \boldsymbol{\beta} \quad \text{or} \quad e < -2 \frac{\mathbf{1}'_n \boldsymbol{\beta}}{\text{tr}(\mathbf{B}_1^2)} \boldsymbol{\alpha} \mathbf{B}_2 \mathbf{1}_n \quad (10)$$

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 (10) 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 (10) map, respectively, a prevalence profile and an unscreened individual onto the cost space, the degenerate condition accounting for the condition in (5).

This vector setting of the prevention expenditure limit (9) may be effectively used, by direct modifications of $\boldsymbol{\beta}$ and $\mathbf{1}_n$, to accommodate complex prevention schemes, such as selections of risk group sub-populations and communicable (infectious or hereditary) diseases. In these cases we can introduce such modifications to the vectors as, for instance,

- risk groups: $\mathbf{1}_n \Rightarrow \mathbf{r} = (r_1, r_2, \dots, r_n)$ may be the hazard ratios of n exposed sub-populations
- group survival: $\mathbf{1}_n \Rightarrow \mathbf{L} = (L_1, L_2, \dots, L_n)$ is the cost-adjusted, expected total life span of patients at various levels of severity
- infectious diseases: $\mathbf{1}_n \Rightarrow \mathbf{s}(R_0) = (s_1(R_0), s_2(R_0), \dots, s_n(R_0))$ is the scalar field of secondary cases as a function of the basic reproduction number, via an epidemic model or external epidemiological studies



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 the previous section. It is, however, interesting to notice that the matrix form expressions (10) allow for a geometrical interpretation of the prevention structure: in fact, the bilinear forms in (10) 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. 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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REFERENCES

- Boily M.-C. et al. (2007) Evaluating large-scale HIV prevention interventions: study design for an integrated mathematical modelling approach *Sex Transm Infect*, 83, 582-589
- Davies R., Roderick P., Raftery J. (2003) The evaluation of disease prevention and treatment using simulation models *European Journal of Operational Research*, 150(1), 53-66
- Goldie S., Goldhaber-Fiebert J., Garnett G. (2006) Public health policy for cervical cancer prevention: The role of decision science, economic evaluation, and mathematical modeling *Vaccine*, 24(S3), 155-163
- Haddix A., Teutsch S., Corso P. (Eds.) (2003) *Prevention Effectiveness* Oxford Univ. Press, New York
- Mackinnon D., Dwyer J. (1993) Estimating Mediated Effects in Prevention Studies *Evaluation Review*, 17(2), 144-158



Zethraeus N., Borgström F., Ström O., Kanis J. A., Jönsson B. (2007) Cost-effectiveness of the treatment and prevention of osteoporosis — a review of the literature and a reference model *Osteoporosis International*, 18(1), 9-23