

The Application of Trend Surface Models to the Analysis of Time Factors in Swiss Cancer Mortality

Cesare Cislaghi¹, Eva Negri^{1, 2}, Carlo La Vecchia^{2, 3}, Fabio Levi^{3, 4}

¹ *Istituto di Biometria e Statistica Medica, Università di Milano*

² *Istituto di Ricerche Farmacologiche «Mario Negri», Milano*

³ *Institut universitaire de médecine sociale et préventive, Lausanne*

⁴ *Registre vaudois des tumeurs, Lausanne*

There are three separate, but not independent, temporal factors influencing disease incidence and mortality: age, birth cohort and period of death. These three factors are usually analysed separately (i.e., cross-sectional presentations of age and period effect), although the estimates obtained are often distorted by the confounding effect of the third factor (i.e., cohort) [1, 2].

To overcome these difficulties, over the last years formal log-linear models have been proposed for disentangling the effect of cohort of birth, period of death and age on cancer mortality [3]. These models have been applied to the analysis of cancer incidence and mortality data from various countries (including Switzerland) [4], as well as to sociological and demographical research [5, 6].

The major conceptual problem of any such model is its inherent non-identifiability property, since there is an exact linear relationship between the three factors. Although various solutions to bypass this difficulty have been proposed, in terms for instance of analysis of identifiable linear slopes or use of various constraints on the parameters, and although some of these models can offer a simplified framework for reading and interpreting mortality data, they implicate, nonetheless, a loss of information in comparison with careful analysis of single age-specific rates (for reviews, see refs [7 and 8]).

The latter on the other hand, although by definition fully informative, are complex and difficult to read and interpret. In this paper, therefore, we present and discuss a method of representation of temporal effects in mortality based on a series of graphical rather than numerical representations of the whole matrix of age-specific rates.

Further, smoothing and modelling techniques are applied to the age/period and cohort surfaces, in order to obtain simplified pictures of the major underlying general patterns.

Material and Methods

Death Certification Data

Numbers of cancer death certifications by cause, stratified for sex and age in five-year groups for the period 1950–1984 were abstracted from files kindly provided by the Swiss Federal Office of Statistics.

From 1951 to 1968, the Swiss Classification of Causes of Deaths, 1951 Edition, was utilized for coding causes of death in details [9]. Thereafter, causes of death were coded according to the standard International Classification of Diseases (ICD), Eighth Revision [10].

To obtain internal comparability of the data, all cancers or groups of cancers were recoded according to the Eighth Revision of the ICD and grouped in 30 categories, besides total cancer mortality and a broadly heterogeneous group of “others or unspecified”. Reliable distinction between some sites or histotypes is not possible on the basis of death certification alone. In particular, we had to group all intestinal sites (colon and rectum), melanoma and non-melanomatous skin neoplasms, all uterine cancers (cervix and endometrium), all non-Hodgkin's lymphomas, all leukaemias, and all neoplasms of the brain or nerves, benign and malignant.

Estimates of the resident population for the corresponding calendar period were provided by the Swiss Federal Office of Statistics (unpublished). From these numerators and denominators, age-specific death certification rates were computed for each calendar year and quinquennium of age (from 30–34 to 75–79). Deaths at age 80 or over were not considered on account of the low reliability of death certification and population estimates at older ages [11], and those below age 30 because of small absolute numbers, which introduce serious problems of random variation and hence instability of rates. Consequently, the central years of cohorts for which at least some point was available were between 1873 and 1952.

Graphic Representations

The surface defined by the matrix of various age-specific rates can be graphically represented using different tones of grey according to the value of each single rate.

This graphic representation was based on the logarithm of rates, after appropriate smoothing using moving averages of rates of each age group across calendar years, to reduce changes of tone due to random variation alone.

Giving the values of the area to which each rate is related to its geometrical central point (or “centroid”),

continuous surfaces named “contour” maps were defined by a “smoothing” function which takes into account not only contiguous points, but also a defined number of other points in inverse relation with their distance.

In the present work, “contour” maps are represented using eight tones of grey, from light (lowest values of the rates) to dark (highest values), each including one eighth of the overall range of rates.

Further, various regression surfaces were defined on the basis of two independent variables ($x = \text{age}$, $y = \text{cohort}$), and fitted by the method of least squares to the matrix of age-specific rates of each disease considered. Progressively more complex models from first to third order were fitted, corresponding to polynomials including each term and their interactions. The number of parameters is 3 for the first order model, 6 for the second order and 10 for the third order one.

As in any regression analysis [12], the total variability, that explained by the model and the residual one were computed. The ratio between variance explained and total variance is the coefficient of determination, whose values range from zero for a model which does not explain anything of the variability of the rates to one when all the data lie on the regression surface.

Trend surface maps were plotted using the same eight tones of grey of the “contour” maps, plus two extreme classes for expected values beyond the range of variation of observed values.

The map of residuals was produced by the simple algebraic difference between the original “contour” map and that obtained from the model chosen. Dark areas indicate positive residuals and signs “minus” negative ones. The presence of diffuse areas of positive or negative residuals may indicate an unsatisfactory fitting, which leaves auto-correlated residuals, while scattered residuals indicate a good fitting.

The methods are more thoroughly presented and discussed in a separate paper [13], and the whole graphic procedure was implemented by means of the SYMAP system [14], and appropriate *ad hoc* developed routines. The whole set of data utilised for the present analyses (number of certified deaths, population estimates, age-specific rates) have been published in a technical volume [15].

Results and Comments

Table 1 gives the coefficients of determination for major cancer sites in the two sexes. In general, first or second order surfaces offered excellent fitting to the data, although there were a few neoplasms whose fitting was appreciably improved by the third order model.

In particular, a determination coefficient near to unity for the first order model indicates that there is no interaction between age and cohort (or that there are symmetrical interactions between period and age and period and cohort which compensate each other [13]). For selected cancer sites and sexes, three graphs are

Tab. 1. Determination coefficients for first to third degree models applied to Swiss mortality data from various cancers or groups of cancers, 1950–84.

Cancer site	Sex	Determination coefficient for polynomials of:		
		1st degree	2nd degree	3rd degree
Mouth or pharynx	M	0.94	0.98	0.98
	F	0.92	0.92	0.93
Oesophagus	M	0.96	0.98	0.99
	F	0.91	0.96	0.98
Stomach	M	0.99	0.99	1.00
	F	0.98	0.99	0.99
Intestines	M	0.99	0.99	1.00
	F	0.99	0.99	0.99
Liver	M	0.98	0.98	0.98
	F	0.93	0.95	0.96
Gallbladder and bile ducts	M	0.96	0.97	0.98
	F	0.97	0.97	0.99
Pancreas	M	0.96	0.98	0.99
	F	0.97	0.97	0.99
Larynx	M	0.94	0.96	0.98
	F	0.64	0.67	0.68
Lung	M	0.89	0.99	0.99
	F	0.95	0.97	0.98
Pleura	M	0.76	0.83	0.86
	F	0.61	0.62	0.64
Bone	M	0.83	0.90	0.92
	F	0.73	0.88	0.88
Connective and soft tissue sarcoma	M	0.72	0.75	0.76
	F	0.68	0.76	0.78
Skin, including melanoma	M	0.91	0.92	0.93
	F	0.82	0.85	0.91
Breast	F	0.89	0.98	0.99
Uterus, cervix and corpus	F	0.95	0.99	0.99
	F	0.88	0.98	0.98
Prostate	M	0.95	0.98	0.99
	M	0.04	0.46	0.49
Bladder	M	0.95	0.97	0.98
	F	0.94	0.95	0.96
Kidney	M	0.97	0.98	0.99
	F	0.95	0.97	0.97
Brain or nerves, benign or malignant	M	0.53	0.86	0.89
	F	0.59	0.84	0.88
Thyroid	M	0.93	0.94	0.96
	F	0.94	0.95	0.97
Hodgkin's disease	M	0.46	0.64	0.73
	F	0.33	0.58	0.65
All other lymphomas	M	0.91	0.93	0.96
	F	0.91	0.93	0.94
Multiple myeloma	M	0.92	0.95	0.97
	F	0.91	0.93	0.96
Leukaemias	M	0.93	0.96	0.97
	F	0.92	0.95	0.96
Total, all sites, all histologies, benign and malignant	M	0.98	1.00	1.00
	F	0.98	1.00	1.00

presented, including respectively “contour” maps, an arbitrarily selected trend surface, and the corresponding residual map. To assist reading and interpretation of these graphs, the legend in the upper left indicates that the age effect should be read across the abscissa, the cohort effect across the ordinate, and the period effect across the diagonal. Further, a brief description and comment is given of major findings for selected cancer sites.

Mouth or pharynx (Figure 1a). Among older males, the “contour” map shows some tendency toward decreasing mortality for more recent cohorts, whereas the pattern is, if anything, opposite at younger ages, although random variability makes the interpretation of trends at younger ages extremely difficult. Thus, in the second order surface, besides a major impact of age, there is a diverging cohort/period effect. Second order residuals are scattered, thus indirectly confirming the excellent fitting of the model. The pattern is similar for females, although less consistent in consequence of smaller absolute numbers of deaths (data not shown).

Oesophagus (Figure 1b). In the “proximal” map for males there are clear cohort and period effects mostly in older ages, which are apparently diverging from the effects observed at younger ages. These effects are evident on the second and, mostly, on the third order surfaces, which show a major cohort component in older males and a substantial interaction with age. The overall trends are similar for females (data not shown), although based on substantially lower numbers of certified deaths, and constitute a confirmation of the different impact of the major risk factors for oesophageal cancer (tobacco and alcohol) in subsequent Swiss generations [16]. In particular, the decreasing cohort pattern among older generations may well reflect the downward trends in alcohol consumption in Switzerland in the first half of the century [17].

Stomach. In both sexes (Figure 2a given for females only) there were substantial decreases over period and, chiefly, over cohort (mostly in older generations), which are clearly evident in the second degree surface whose residuals are extremely limited and scattered. Similar decreases for gastric cancer mortality have been observed in most developed countries, but the levels reached by Swiss females are among the lowest in Western Europe [18]. No defined factor has been linked to such major decreases, although it is likely that diet has played an important role [11].

Intestines, chiefly colon and rectum. Besides the obvious age effect, there was a suggestion of downward trend chiefly on a period basis, which was somewhat greater in females (Figure 2b). The first order coefficient was already extremely close to unity (Table 1), indicating the absence of major age/cohort interaction, at least in terms of graphical representation.

Liver (Figures 3a and 3b). The pattern of trends in the “contour” as well as in subsequent degree surfaces was largely heterogeneous in the two sexes, since there was a major period and, chiefly, cohort increase in older males, but a substantial decrease in older females. The data for the two sexes are more similar at younger ages, where an earlier increase was followed by a subsequent stabilization. There is no obvious explanation for the diverging pattern in the two sexes, although it is conceivable that these trends are, at least in part, influenced by misclassification of secondaries, since

the liver is a frequent site of secondaries, particularly from cancer of the lung [11].

Gallbladder and bile ducts. In males, no clear pattern was evident, besides the obvious age effect (data not shown). In females (Figure 4a), whose rates are about twice that of males, there was a rather complex and unstable “contour” map, which could be summarized in the third order surface map in terms of a modest downward trend over period. The reasons for this decline are not defined, nor it is known how much the trends observed are influenced by the recent increases in cholecystectomy rates.

Pancreas. In both sexes (Figure 4b given for males only) the “contour” as well as the second and third order surfaces show an effect of age only at younger ages, but a substantial increase (chiefly on a cohort basis) at older ones. Since the upward trends are restricted to the older age groups, it is difficult to state how much of the increase is real and how much influenced by improved certification, considering that cancer of the pancreas is particularly difficult to diagnose [11]. There are nonetheless important similarities between the pattern observed in pancreatic cancer mortality and that of lung cancer, which may reflect the influence of the aetiological factor in common, i.e., tobacco [19].

Larynx. For males (Figure 5a), there was a substantial decrease on a period/cohort basis at older ages, and a general stability at younger ones. The overall pattern is thus similar to that previously described for cancers of the mouth or pharynx and oesophagus, and further underlines the similarity in risk factors for all neoplasms of upper digestive and respiratory tract (chiefly, alcohol and tobacco, although their relative importance may well be quantitatively different for various sites). Mortality rates were extremely low in females (data not shown) and, consequently, the pattern was largely inconsistent.

Pleura. The pattern in mortality from cancer of the pleura, even in males (Figure 5b), is difficult to interpret on account of the limited numbers of certified deaths and, chiefly, of changes in the International Classification of the Diseases, which may well have introduced spurious trends in certified mortality. Thus, the interpretation of the “contour” map is extremely difficult on account of problems of random variability, but the pattern emerging from the third order surface indicates important period and cohort effects, which however should be considered with due caution on account of the previously mentioned certification problems.

Lung. For males (Figure 6a), both the “contour” and the second order surface show an age effect only at younger ages, with a cohort component progressively stronger with advancing age. The picture is different in females (Figure 6b), since for the first calendar period there is an effect of age only, whereas in more recent years the dominant pattern is the upward cohort one. Thus, lung cancer patterns well reflect the different

trends in smoking for the two sexes, since smoking rates increased in males during the first half of the century and then stabilized, whereas the increase of smoking among females was a more recent phenomenon [20].

Bone. In both sexes (Figure 7a given for males only) there were substantial decreases on a period and, chiefly, cohort basis. It is not known, nonetheless, how much of the decrease is real (and attributable, for instance, to improved survival), and how much is due to improved diagnoses and hence progressive elimination of misclassification and certification of secondaries [11].

Connective and soft tissue sarcomas. Although, on account of small numbers of certified deaths, the "contour" maps are largely inconsistent in both sexes (data shown in Figure 7b for males only), the general pattern emerging from the third degree surface suggests a major cohort/period increase at older ages, but not in younger middle age. In this case, too, it is difficult to state how much of the increase is due to improved diagnosis and certification, and how much is real. Although the causes of these neoplasms are largely undefined, in fact, some recent evidence suggested that soft tissue sarcomas are associated to exposure to phenoxyacids and other herbicides [21], whose utilization has largely increased over the last decades.

Skin, including melanoma. In both sexes (data shown for females only, Figure 8a) the "contour" maps show a major increase at younger ages, chiefly on a cohort basis. At older ages, the pattern is scattered and largely inconsistent. The third order surface shows very clearly the major cohort increases at younger ages, whereas at older ages the pattern is different across periods, with some (period) decrease in earlier years considered, and some increase over more recent years. This composite pattern is likely due to the heterogeneous trends in the different histotypes, since the substantial increases at younger ages are chiefly attributable to the rise in melanoma common to most developed countries and believed to be related to intermittent exposure to sunbathing and, perhaps, changes in clothing [22]. In contrast, the earlier decline at older ages may be attributable to decreasing mortality from squamous cell cancer, on account of improved treatment and, perhaps, more accurate certification, with progressive elimination of secondaries [11].

Breast, females (Figure 8b). In the "contour" map, little systematic effect is evident at younger ages, but there is some tendency toward increasing mortality over period from older middle age onwards. This pattern is clearly evident in the third degree surface map, with some moderate upward trend in the period effect. Corresponding residuals were scattered, thus confirming the excellent fitting of the model.

Uterus, cervix and corpus (Figure 9a). The "contour", as well as the subsequent degree trend surface models, show a clear downward trend over period, and some decrease in the cohort effect (or some age/period

interaction) at older ages, too. Although it is difficult, on the basis of death certificate alone, to reliably distinguish between cancers of the cervix and corpus uteri, most of the decreases observed (chiefly at younger ages) are attributable to declines in mortality from cervical cancer [4, 16]. The pattern observed at older ages, if not due to a real cohort effect, could be explained in terms of period interaction on the age curve, possibly on account of the later start of the decline in cervical cancer mortality for older women, or to the increased hysterectomy rate over the most recent calendar years [23].

Ovary (Figure 9b). The "contour" map shows some systematic decrease over more recent periods in the younger age groups, and an inconsistent pattern at older ages. This age/period interaction is reflected in the large improvement in model fitting from the first to the second degree. In the second order surface, besides a period/cohort decline at younger ages, some increase was evident at older ages, chiefly on a cohort basis. Second order residuals were scattered, further confirming the excellent fitting of the model. It is difficult to define how much the rise at older ages is attributable to improved diagnosis and certification [11], and how much of the decline at younger ages reflects the favourable impact of oral contraceptive use [24], or some therapeutic improvement.

Prostate (Figure 10a). In the "contour" map, the age effect is overwhelming, in the absence of major systematic patterns in period and cohort effects. In the second order surface, some moderate period increase is evident at older ages, probably explainable in terms of better diagnosis and certification [11, 25].

Testis (Figure 10b). The "contour" map, although largely scattered on account of small absolute numbers, shows clear excess mortality at younger and older ages, and a minimum in middle age. Not surprisingly, therefore, the fitting of the first order surface is extremely poor, and, although somewhat improved, it is largely unsatisfactory even for higher order models. The third order surface shows a period increase in earlier calendar years (probably attributable to increased incidence), followed by a substantial decline (probably due to improved therapy [26]). There were systematic declines over period in the older age groups, too, and no clear pattern in middle age, where most of the residuals were concentrated.

Bladder. In the "contour" map (Figure 11a given for males only), no consistent trend was observed in younger and middle age, but substantial rises were evident at older ages, chiefly on a cohort basis. This pattern is comparable in the two sexes, well reflected in the third order surface, and is similar to those observed for cancer of the lung and other tobacco-related neoplasms, such as pancreas and kidney [19].

Kidney. In both sexes, there was no consistent trend at younger ages but substantial rises, chiefly in terms of cohort effect, at older ones, which are clearly apparent on the third order surface (Figure 11b given for males

only). Thus, this pattern is again consistent with that of most other tobacco-related neoplasms [19].

Brain or nerves, benign and malignant. In both sexes (data presented for females only, Figure 12a) no distinct pattern was evident at younger ages, but substantial rises, on a period and, chiefly, cohort basis were observed at older ages. The absence of trends at younger ages but the major increases at older ones is consistent with an important influence of improved diagnosis and certification on these trends, following the introduction of computerized transaxial tomography and other diagnostic techniques [11]. Third order residuals were rather concentrated in older middle age, indicating the non optimal fitting of the model.

Thyroid. The important feature in thyroid cancer mortality in both sexes (data presented in Figure 12b for females only, since rates for this neoplasms are higher in women) was the substantial decline, rather scattered in the "contour" map, but with a major period component in the trend surface models. The third surface order shows an age/period interaction at older ages since rates were not declining in earlier periods, and provides an excellent fitting, as confirmed by the largely scattered residuals. These steady declines should be related to the fact that Swiss thyroid cancer rates were exceedingly high early this century, and have been decreasing since then [16], probably following the reduced prevalence of iodine deficiency [27, 28], although generalized improvements in diet and advances in treatment of the disease may have had some impact, too.

Hodgkin's disease. The "contour" maps are similar in the two sexes (data shown for males only, Figure 13a), with a rather scattered pattern, although it is possible to identify a tendency toward declining rates over time at younger ages, and increasing rates at older ones. Consequently, the fitting of trend surface models was relatively unsatisfactory. In terms of reading and interpretation, the clearest picture is offered by the second order model, which shows earlier increases followed by clear declines over period/cohort at younger ages, and increases at older ones. This could be explained in terms of improvements in diagnosis and, subsequently, treatment at younger ages, and more accurate diagnosis and certification in the old. Further, biased trends may have been introduced by some systematic misclassification in the distinction between Hodgkin's and non Hodgkin's lymphoma [29].

All other lymphomas. As for Hodgkin's disease, it is evident from the "contour" maps some recent tendency toward decreasing rates over time in the younger age groups, but steady increasing mortality in older ages. In the second order surfaces (shown for males only, Figure 13b) this different pattern at various ages is clearly apparent, although there is a defined area of elevated residuals in middle and older middle age for earlier calendar periods. The interpretation of these trends is similar to that given for Hodgkin's disease, i.e., improved treatment at younger ages and

better diagnosis and certification at older ones, although due caution is required on account of problems of misclassification in general and within various lymphomas [29].

Multiple myeloma. The "contour" maps are largely inconsistent in younger and middle ages, but show substantial increases at older ages over most recent calendar periods. This is well reflected in the third order surface (Figure 14a given for males only), which shows major increases over period and, mostly, cohort at older ages. It is possible that the cohort effect seen at older ages is largely due to an age/period interaction, and essentially reflects progressive improvements in certification at older ages over most recent periods, following the introduction of serum electrophoresis and other enzymatic techniques, in whose absence several deaths from multiple myeloma were incorrectly attributed to infections or renal insufficiency [11].

Leukaemias. The pattern observed for leukaemias is similar to that previously described for other lymphoreticular neoplasms, i.e., recent substantial decreases at younger ages but consistent increases at older ones, chiefly in earlier calendar periods. This is reflected in the third order surface for males (Figure 14b), whose excellent fitting is confirmed by the corresponding scattered residuals. As in the case of multiple myeloma, it is conceivable that the apparent cohort effect at older ages is the product on an age/period interaction and, in fact, only an age effect is evident in more recent periods. The interpretation of these trends should again be considered in terms of improved treatments in the young and diagnosis/certification in the old.

Total, all sites, all histologies (benign and malignant). For total cancer mortality in males (Figure 15a) there is clearly a major impact of age, and the minor effects of cohort or period are restricted to some decrease in the young, mostly over more recent periods, and some increase at older ages, with a substantial stability in middle age. This is well illustrated by the second order surface, which covers practically the whole of the variability. For females (Figure 15b), the declines are observed in all subsequent age groups, principally on a period basis. The different pattern of trends for the two sexes are largely due to the greater and earlier impact of increasing mortality for lung and other tobacco-related neoplasms in males, which counterbalanced the favourable trends of stomach, intestines and other minor sites (e.g., thyroid, lymphomas and leukaemias). Further, the downward trends in mortality from cancer of the (cervix) uteri have contributed to the overall encouraging trends for females, too [30].

Discussion and Conclusions

The methods of graphic representation described and applied in this work to the analysis of Swiss cancer mortality provide a synthetic and original tool for analysing and interpreting the role of different temporal components in mortality rates. There is, in fact, a

conceptual non-identifiability property within any age/period/cohort model, due to the fact that the three factors are not independent, and hence definition of any two implies knowledge of the third [7, 8].

On the other side, although it is clear that the whole of information is contained in the matrix of age-specific rates, their accurate reading and interpretation is often complex and time-consuming.

Thus, the simplified representation of the matrices in graphic form represents a useful instrument for descriptive purposes. Further, it allows fitting of trend surface models, which assist in the identification of general patterns and major underlying components [13]. In fact, even the lower order models utilized (including three to ten parameters) provided, for most cancer sites, an excellent fitting to the data. Further, they allowed immediate identification of residuals (i.e., high or low mortality points), which are often obscured within the overall variability of the original data, as well as estimates of first-order interactions between the three factors (although the parameter of the main effects remained still undetermined).

In conclusion, we would like to stress that these methods should be essentially interpreted and utilized as a summary guide to illustrate and understand general patterns of age, period and cohort components in (cancer) mortality, and they offer the possibility of immediate examination of single age-specific rates, although of course they cannot conceptually solve the inherent problem of identifiability of the three components.

Summary

To study different temporal components on cancer mortality (age, period and cohort) methods of graphic representation were applied to Swiss mortality data from 1950 to 1984. Maps using continuous slopes ("contour maps") and based on eight tones of grey according to the absolute distribution of rates were used to represent the surfaces defined by the matrix of various age-specific rates. Further, progressively more complex regression surface equations were defined, on the basis of two independent variables (age/cohort) and a dependent one (each age-specific mortality rate). General patterns of trends in cancer mortality were thus identified, permitting definition of important cohort (e.g., upwards for lung and other tobacco-related neoplasms, or downwards for stomach) or period (e.g., downwards for intestines or thyroid cancers) effects, besides the major underlying age component. For most cancer sites, even the lower order (1st to 3rd) models utilised provided excellent fitting, allowing immediate identification of the residuals (e.g., high or low mortality points) as well as estimates of first-order interactions between the three factors, although the parameters of the main effects remained still undetermined. Thus, the method should be essentially used as summary guide to illustrate and understand the general patterns of age, period and cohort effects in (cancer) mortality, although they cannot conceptually solve the inherent problem of identifiability of the three components.

Résumé

Les modèles de régression spatiale pour l'analyse des tendances de la mortalité suisse par cancer

Les différentes composantes chronologiques (âge, période et génération) de la mortalité cancéreuse suisse 1950–1984 ont été étudiées à l'aide de méthodes de représentation graphique. On présente, d'abord, une série de cartes dites «contour», définies par des pentes continues et basées sur huit tonalités de gris en fonction de la distribution absolue des taux; ces cartes fournissent une représentation des surfaces déterminées par la matrice des différents taux spécifiques pour l'âge. Ensuite, des équations de régression spatiale de degrés de complexité progressivement croissants ont été définies, incluant deux variables indépendantes (âge et génération) et une dépendante (chaque taux de mortalité spécifique pour l'âge). Des structures générales de la mortalité par cancer ont été ainsi identifiées; elle permettent de mettre en évidence, à côté du rôle prépondérant de l'âge, d'importants effets de génération (par exemple: croissants dans le cas du poumon et des autres néoplasies associées au tabac, ou en diminution pour l'estomac) ou de période (par exemple: en diminution pour les cancers intestinaux et thyroïdiens). Pour la plupart des localisations cancéreuses, même les modèles d'ordre inférieur utilisés (du 1^{er} au 3^e) ont fourni une adaptation très satisfaisante aux données, permettant ainsi l'identification immédiate des résidus (par exemple: des points de haute ou faible mortalité) et l'estimation des interactions de premier ordre entre les trois facteurs (bien que les paramètres des effets principaux restent indéterminés). Cette méthode devrait principalement permettre d'illustrer et d'interpréter de manière synthétique des effets d'âge, de période et de génération sur la mortalité (cancéreuse), bien qu'elle ne puisse résoudre conceptuellement les problèmes d'identification des trois composantes, inhérents à la méthode.

Zusammenfassung

Räumliche Regressionsmodelle zur Analyse der Entwicklung der schweizerischen Krebssterblichkeit

Mit Hilfe graphischer Darstellungsmethoden wurden die verschiedenen zeitlichen Komponenten (Alter, Geburtskohorte und Periode) der schweizerischen Krebssterblichkeit von 1950 bis 1984 untersucht. Zuerst werden sogenannte Isolinien-Karten («contour maps») vorgestellt mit stufenlosem Übergang von acht Grautönen entsprechend der absoluten Verteilung der Raten. Diese Karten stellen graphisch die Matrix der verschiedenen altersspezifischen Raten dar. Anschliessend wurden räumliche Regressionsgleichungen mit zunehmender Komplexität definiert mit den zwei unabhängigen Variablen Alter und Geburtskohorte, und als abhängiges Merkmal, jede einzelne Sterberate pro Alter. Das auf diese Weise dargestellte, generalisierte Muster der Entwicklung der Krebssterblichkeit zeigt neben dem hohen Einfluss des Alters auch einen deutlichen Kohorteneffekt (z. B. zunehmend bei Lungenkrebs und bei anderen tabakbedingten Neubildungen oder abnehmend bei Magenkrebs). Auch der Einfluss der zeitlichen Periode wird deutlich (z. B. bei Darm- und Schilddrüsenkrebs). Bei den meisten Tumorlokalisationen wurde das Datenmaterial bereits mit Modellen niedriger (d. h. erster bis dritter) Ordnung befriedigend abgedeckt. Dies erlaubt eine rasche Identifizierung der Residuen (z. B. der Punkte mit hoher oder niedriger Mortalität) sowie eine Schätzung der Interaktion erster Ordnung zwischen den drei erwähnten Faktoren. (Die Parameter der Haupteinflussfaktoren bleiben jedoch undefiniert). Das hier vorgestellte Verfahren ermöglicht es, in einer visualisierten Synthese die Effekte von Alter, Periode und Geburtskohorte auf die Krebssterblichkeit zu verdeutlichen. Es kann jedoch – methodenbedingt – das Problem der Identifizierung dieser drei Einflussfaktoren nicht lösen.

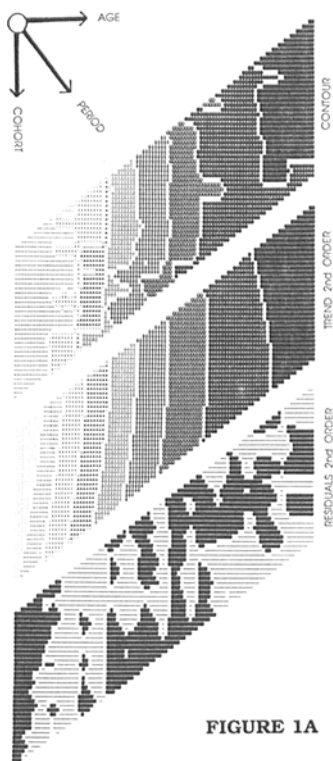


FIGURE 1A

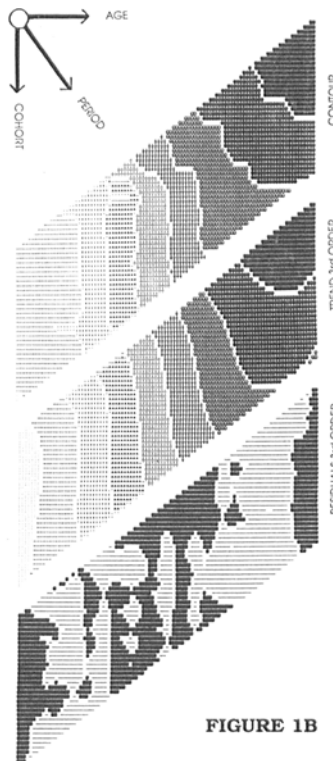


FIGURE 1B

Fig. 1. Age, period and cohort surfaces for a) oropharyngeal and b) oesophageal cancer in males aged 30–79. Switzerland, 1950–84.

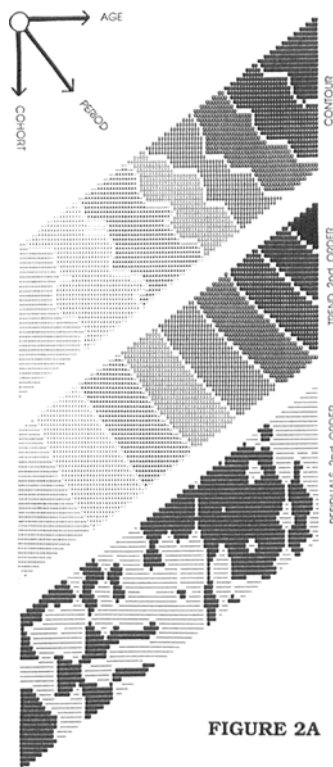


FIGURE 2A

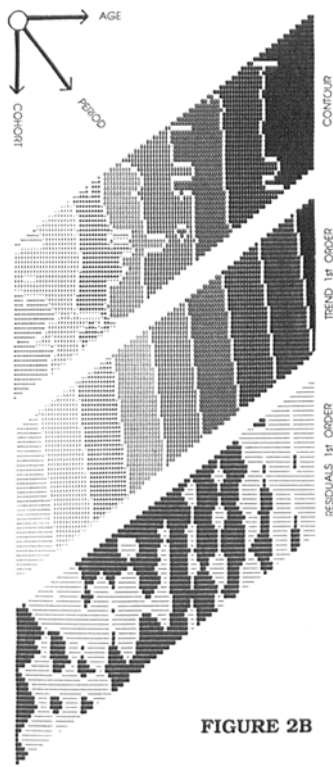


FIGURE 2B

Fig. 2. Age, period and cohort surfaces for a) gastric and b) intestinal cancer in females aged 30–79. Switzerland, 1950–84.

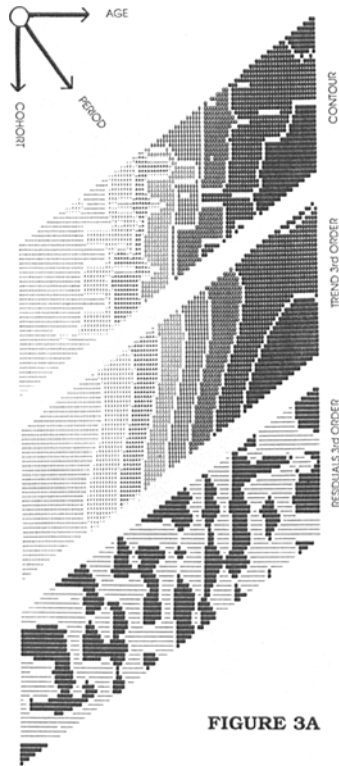


FIGURE 3A

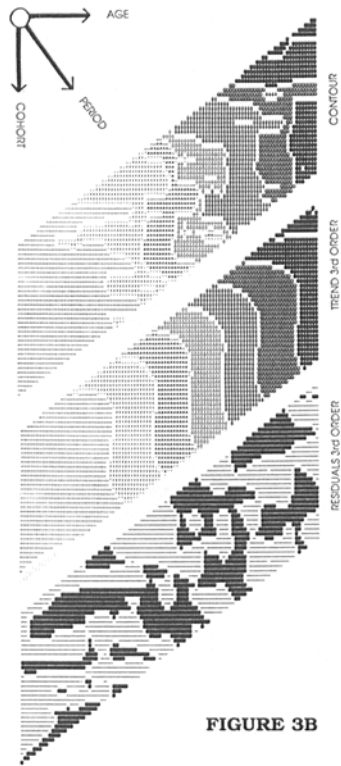


FIGURE 3B

Fig. 3. Age, period and cohort surfaces for liver cancer in a) males and b) females aged 30–79. Switzerland, 1950–84.



FIGURE 3A



FIGURE 3B

Fig. 4. Age, period and cohort surfaces for a) gallbladder in females and b) pancreatic cancer in males aged 30–79. Switzerland, 1950–84.

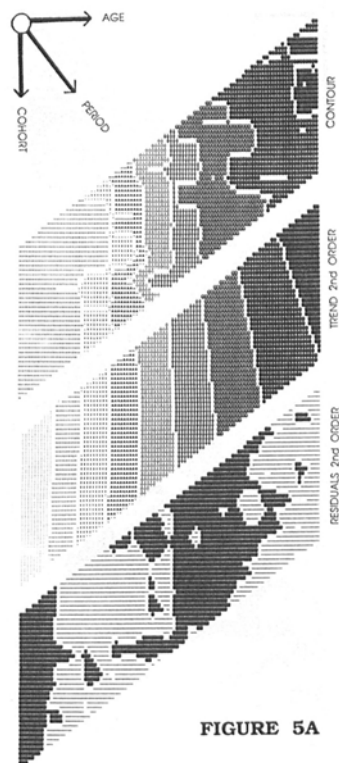


FIGURE 5A

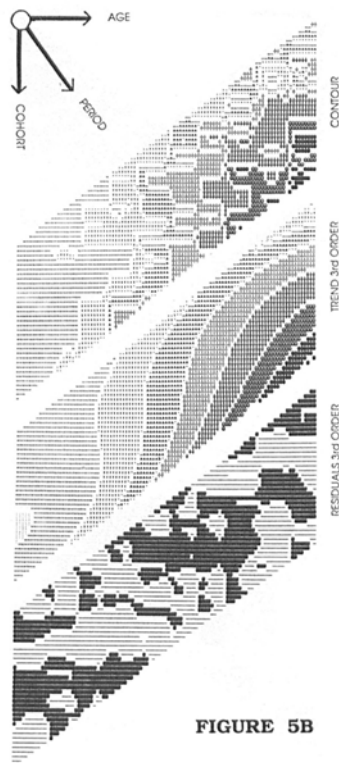


FIGURE 5B

Fig. 5. Age, period and cohort surfaces for a) laryngeal and b) pleural cancer in males aged 30–79. Switzerland, 1950–84.

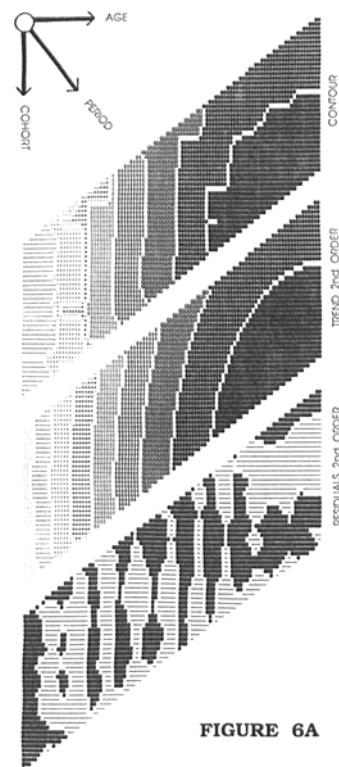


FIGURE 6A

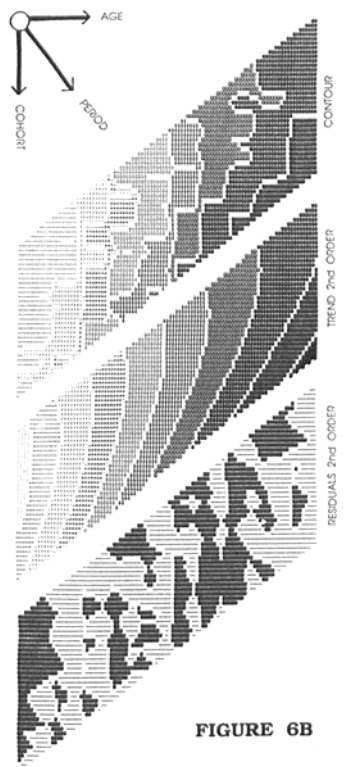


FIGURE 6B

Fig. 6. Age, period and cohort surfaces for lung cancer in a) males and b) females aged 30–79. Switzerland, 1950–84.



FIGURE 7A

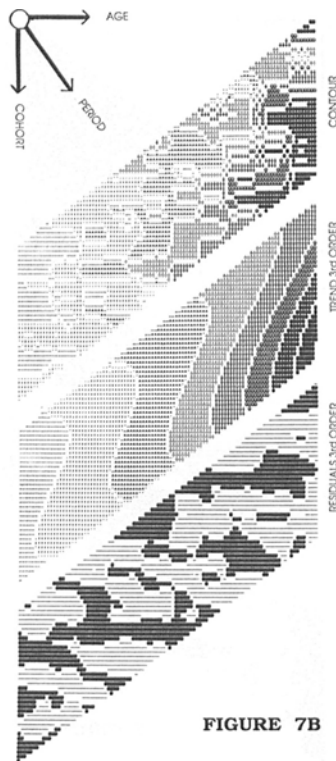


FIGURE 7B

Fig. 7. Age, period and cohort surfaces for a) bone and b) connective and soft tissue sarcomas in males aged 30–79. Switzerland, 1950–84.



FIGURE 8A

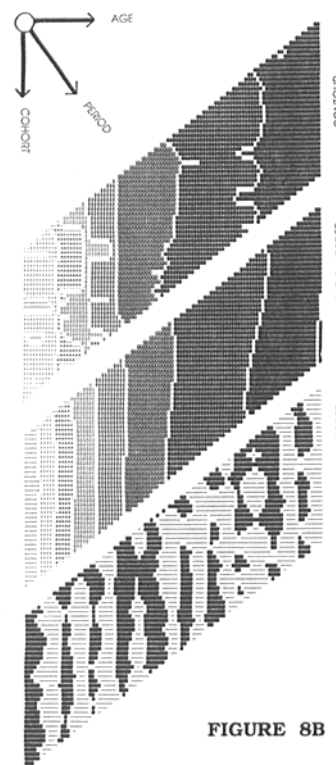


FIGURE 8B

Fig. 8. Age, period and cohort surfaces for a) skin (including melanoma) and b) breast cancers in females aged 30–79. Switzerland, 1950–84.

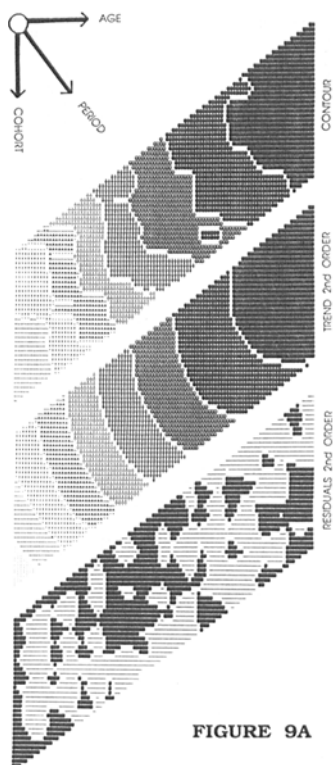


FIGURE 9A

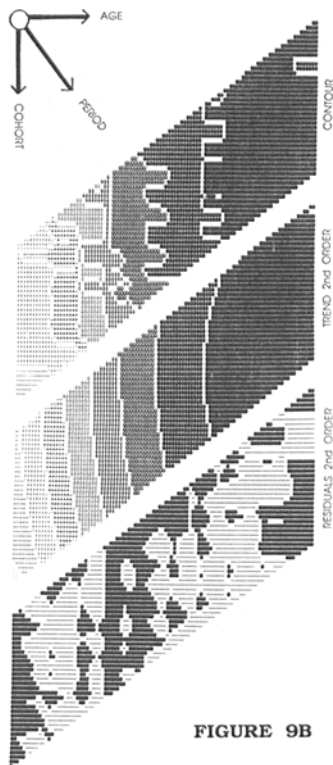


FIGURE 9B

Fig. 9. Age, period and cohort surfaces for a) uterine and b) ovarian cancer in females aged 30–79. Switzerland, 1950–84.

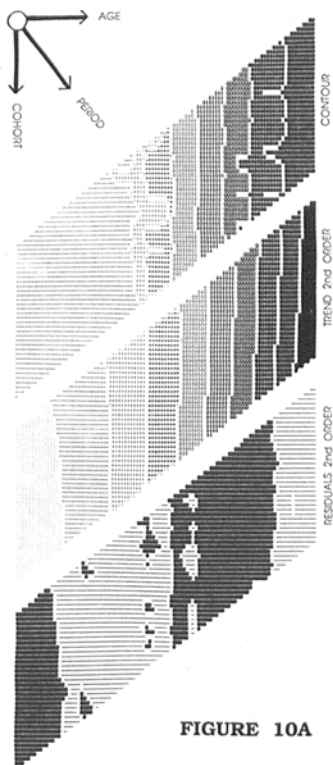


FIGURE 10A

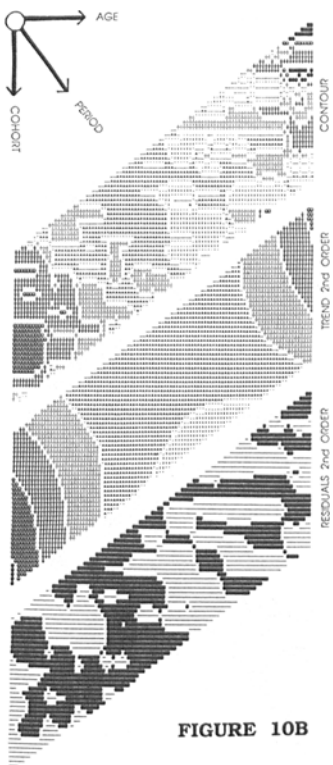


FIGURE 10B

Fig. 10. Age, period and cohort surfaces for a) prostatic and b) testicular cancer in males aged 30–79. Switzerland, 1950–84.

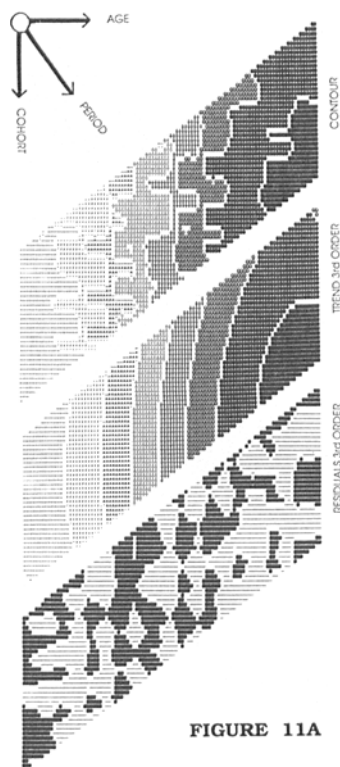


FIGURE 11A

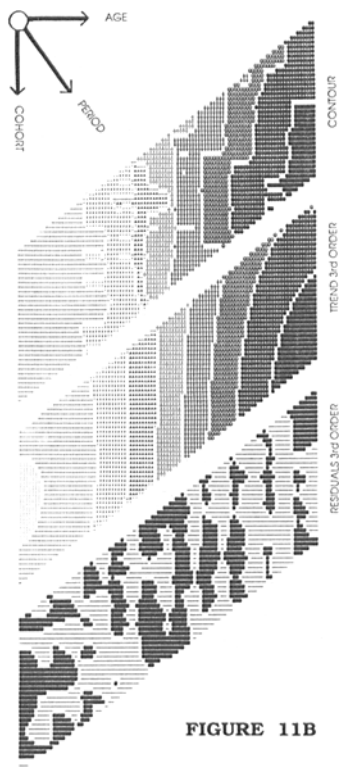


FIGURE 11B

Fig. 11. Age, period and cohort surfaces for a) bladder and b) kidney cancer in males aged 30–79. Switzerland, 1950–84.



FIGURE 12A

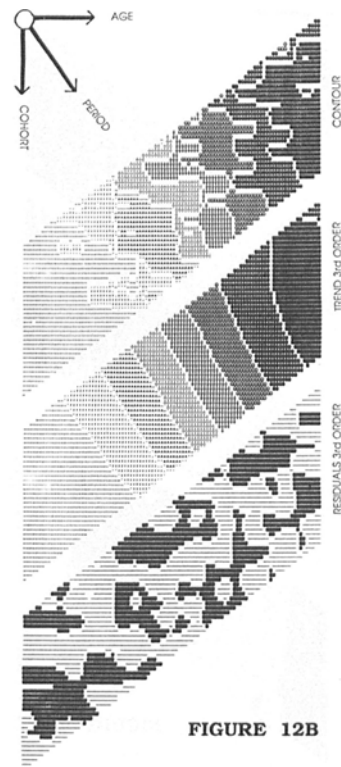


FIGURE 12B

Fig. 12. Age, period and cohort surfaces for a) brain or nerves (benign and malignant) and b) thyroid cancer in females aged 30–79. Switzerland, 1950–84.

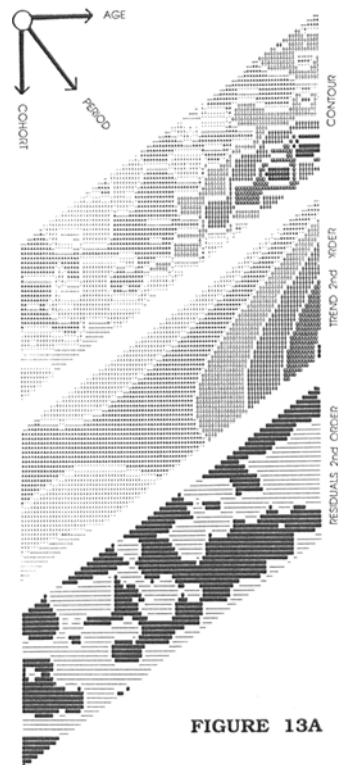


FIGURE 13A



FIGURE 13B

Fig. 13. Age, period and cohort surfaces for a) Hodgkin's disease and b) all other lymphomas in males aged 30–79. Switzerland, 1950–84.

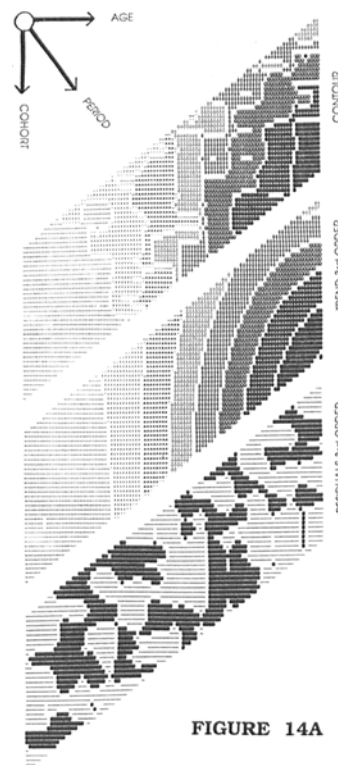


FIGURE 14A



FIGURE 14B

Fig. 14. Age, period and cohort surfaces for a) multiple myeloma and b) leukaemias in males aged 30–79. Switzerland, 1950–84.

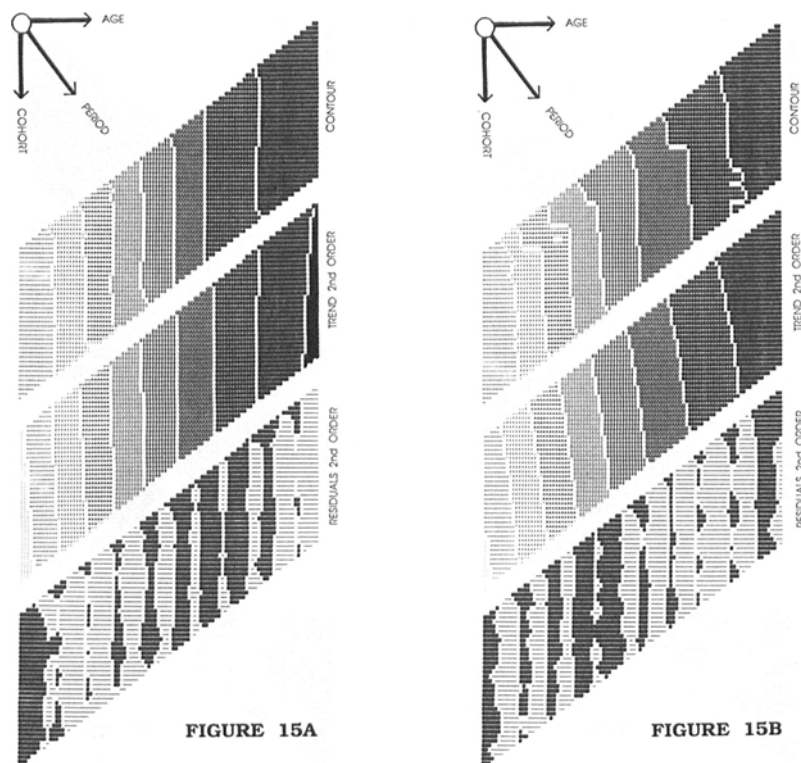


Fig. 15. Age, period and cohort surfaces for all cancer sites in a) males and b) females aged 30–79. Switzerland, 1950–84.

References

[1] Moolgavkar S.H., Steven R.G., Lee J.A.H. Effect of age on incidence of breast cancer in females. *JNCI* 62, 493–501, 1979.

[2] Cislaghi C. Le variabili temporali negli studi di mortalità. In: *Atti preliminari del terzo Convegno Nazionale sugli Studi di Mortalità*. Firenze, October 21–24, 1986. Firenze, Lega Italiana per la Lotta contro i Tumori, 1986, 151–159.

[3] Osmond C., Gardner M.J. Age, period and cohort models applied to cancer mortality rates. *Stat. Med.* 1, 245–259, 1982.

[4] Levi F., La Vecchia C., Decarli A., Randriamiharisoa A. Effects of age, birth cohort and period of death on Swiss cancer mortality, 1951–1984. *Int. J. Cancer* 40, 439–449, 1987.

[5] Hobcraft J., Menken J., Prestore S. Age, period and cohort effects in demography: a review. *Popul. Index* 48, 4–43, 1982.

[6] Pullum T.W. Separating age, period and cohort effects in white U.S. fertility, 1920–1970. *Soc. Sci. Res.* 9, 225–244, 1980.

[7] Kupper L.L., Janis J.M., Karmous A., Greenberg B.G. Statistical age-period-cohort analysis: a review and critique. *J. Chron. Dis.* 38, 811–830, 1985.

[8] Decarli A., La Vecchia C. Age, period and cohort models: review of knowledge and implementation in GLIM. *Riv. Stat. Appl.* 20, 397–410, 1987.

[9] Office Fédéral de la Statistique: *Nomenclature Suisse des Causes de Décès*, 1951. Berne, Office Fédéral de la Statistique, 1952.

[10] Office Fédéral de la Statistique: *Classification Internationale des maladies et causes de décès*. Adaptée aux conditions suisses et utilisée dès 1969 (8e révision). Berne, Office Fédéral de la Statistique, 1970.

[11] Doll R., Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *JNCI* 66, 1191–1308, 1981.

[12] Draper N.R., Smith H. *Applied regression analysis*. New York, Wiley, 1966.

[13] Cislaghi C. Modelli di rappresentazione grafica di andamenti temporali di tassi. *Riv. Stat. Appl.* 20, 381–396, 1987.

[14] Dougenik G.C., Sheehan D.E. *SYMAP User's Reference Manual*. Harvard University, Bedford, Mass., 1975.

[15] Levi F., Decarli A., La Vecchia C., Randriamiharisoa A. La mortalité par cancer en Suisse, 1950–1984. Office Fédéral de la Statistique, Berne, 1988 (Statistique officielle de la Suisse, No 165).

[16] Gubéran E. Tendances de la mortalité en Suisse. 3. Tumeurs: 1921–1978. *Schweiz. med. Wochenschr. Suppl.* 11:110, 1–18, 1980.

[17] Welti F. La consommation des boissons alcooliques en Suisse de 1966 à 1970 et durant les périodes antérieures. Berne, Régie Fédérale des alcools, 1973.

[18] WHO: *World Health Statistics Annual*. WHO, Geneva, various issues.

[19] U.S. Office on Smoking and Health: *The Health Consequences of Smoking: Cancer. A Report of the Surgeon General of the Public Health Service*. Washington, U.S. Office on Smoking and Health, G.P.O., 1982.

[20] La Vecchia C., Levi F., Gutzwiller F. Fumée et santé: une épidémie évitable. *Méd. Hyg.* 45, 3453–3462, 1987.

[21] Hoar S.K., Blair A., Holmes F.F., Boysen C.D., Robel R.J., Hoover R., Fraumeni J.F. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. *J. Amer. med. Ass.* 256, 1141–1147, 1986.

[22] Lee J.A. Melanoma and exposure to sunlight. *Epidemiol. Rev.* 4, 110–136, 1982.

[23] Lyon J.L., Gardner J.W. The rising frequency of hysterectomy: its effect on uterine cancer rates. *Am J. Epidemiol.* 105, 439–443, 1977.

[24] La Vecchia C., Decarli A., Fasoli M., Franceschi S., Gentile A., Negri E., Parazzini F., Tognoni G. Oral contraceptives and

- cancers of the breast and of the female genital tract. Interim results from a case-control study. *Br. J. Cancer* 54, 311–317, 1986.
- [25] *Breslow N.E., Chan C.W., Dhom G., Drury R.A., Franks L.M., Gellei B., Lee Y.S., Lundberg S., Sparke B., Sternby N.H., Tulinius H.*, Latent carcinoma of prostate at autopsy in seven areas. *Int. J. Cancer* 20, 680–688, 1977.
- [26] *Davies J.M.* Testicular cancer in England and Wales: some epidemiological aspects. *Lancet* i, 928–932, 1981.
- [27] *Bubenhofen R., Hedinger C.* Schilddrüsenmalignome vor und nach Einführung der Jodsalzprophylaxe. *Schweiz. med. Wochenschr.* 107, 733–741, 1977.
- [28] Subcommittee for the Study of Endemic Goitre and Iodine Deficiency of the European Thyroid Association. Goitre and iodine deficiency in Europe Report. *Lancet* i, 1279–1282, 1985.
- [29] *Levi F., Wietlisbach V., Randriamiharisoa A.* Registre Vaudois des Tumeurs et statistiques des causes de décès: une analyse comparative des diagnostics après connexion informatique. In: *Mortalité cancéreuse: qualité des données en Suisse: pp. 31–43.* (Contributions à la Statistique Suisse, 125ème fasc.) Office Fédéral de la Statistique, Berne, 1984.
- [30] *Levi F., Decarli A., La Vecchia C.* Trends in cancer mortality in Switzerland. *Rev. Epidém. Santé Publique* 36, 15–25, 1988.

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Address for correspondence:

Prof. Carlo La Vecchia
Institut universitaire de médecine sociale et préventive
Bugnon 17
CH-1005 Lausanne