ABSTRACT

Purpose: To examine the pattern of testicular cancer incidence by age, time period and birth cohort since 1969 in Canada. *Method:* In addition to analyses of the secular trends by age group and birth cohort separately, an age-period-cohort model and the submodels with standard Poisson assumptions were fitted to the data. *Results:* The overall age-adjusted incidence of testicular cancer increased in Canada, from 2.8 per 100,000 males in 1969-71 to 4.2 in 1991-93. The younger age groups showed much higher absolute incidence rates in the recent period compared with those in the early period. Age-period-cohort modelling of data restricted to males aged 20-84 years suggested that the observed increase in testicular cancer could be largely attributed to a birth cohort effect. A steady increase in risk was observed among men born since 1945; those born between 1959 and 1968 were 2.0 (95% CI, 1.5 - 2.6) times as likely to develop testicular cancer as those born between 1904 and 1913. *Conclusion:* The risk of testicular cancer has increased over time and changing exposure to environmental factors early in life may be responsible for this.

ABRÉGÉ

Objectif : examiner l'évolution de l'incidence du cancer des testicules par âge, période de temps et cohorte de naissance depuis 1969 au Canada. *Méthode :* outre les analyses des tendances générales par catégorie d'âge et cohorte de naissance séparément, on a appliqué aux données un modèle âge-période-cohorte et les sous-modèles avec les hypothèses habituelles de Poisson. *Résultats :* l'incidence générale, ajustée selon l'âge, du cancer des testicules a augmenté au Canada, passant de 2,8 pour 100 000 hommes en 1969-1971 à 4,2 en 1991-1993. Les catégories d'âge plus jeune sont apparues avoir des taux d'incidence absolus beaucoup plus élevés au cours de la période récente en comparaison avec la période antérieure. La modélisation âge-période de temps-cohorte des données limitée aux hommes âgés de 20 à 84 ans suggère que l'augmentation constatée du cancer des testicules pourrait être largement attribuable à un effet de cohorte de naissance. On a observé une augmentation régulière du risque chez les hommes nés après 1945; les individus nés entre 1959 et 1968 avaient 2,0 (95 % IC, 1.5 - 2,6) plus de probabilité de développer un cancer des testicules que ceux nés entre 1904 et 1913. *Conclusion :* le risque de cancer des testicules a augmenté et les changements de l'exposition aux facteurs environnementaux au début de la vie pourraient en être la cause.

Birth Cohort Effects Underlying the Increasing Testicular Cancer Incidence in Canada

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Testicular cancer is a relatively rare disease, accounting for only 1.1% of all malignant neoplasms in men, but it is the most common cancer in young and middle-aged males. More importantly, the age-adjusted incidence rate has been increasing by 1.6% per year between 1985 and 1992 in Canadian men.[1] Studies from other countries have also shown a dramatic increase in the incidence of testicular cancer during the past several decades.[2-6] The age-standardized incidence rate has doubled every 15 to 25 years in Northern European countries,[7] and the increasing trend in testicular cancer risk has been shown to follow a birth cohort pattern.[2] A recent study showed that the age-adjusted incidence rate of testicular cancer has increased 3.5-fold in Connecticut, USA during the last 60 years of cancer registration.[3] The cause of these trends is unknown.

Most of the previous studies have been carried out in European countries and the United States. No comparable analysis of testicular cancer trends has been reported from Canada. The purpose of the current study was to examine the pattern of testicular cancer incidence by age, time period and birth cohort in Canada.

METHODS

Data source

Data on the incidence of testicular cancer were obtained from the National Cancer Incidence Reporting System (NCIRS) of Statistics Canada, which began collecting data from provincial and territorial cancer registries in 1969. Data for 1992 and 1993 were obtained from the Canadian Cancer Registry (CCR) which replaced the NCIRS. Quebec data were excluded from this analysis, because comparison could not be made due to the fact that improved reporting procedures were not implemented in Quebec until 1981. Annual population estimates were obtained from the Demography Division of Statistics Canada. The incidence data included in this study cover the period from 1969 through 1993.

The quality of Canadian cancer incidence data has been discussed extensively elsewhere.[8,9] In general, the quality of testicular cancer registration is better than that for many other malignancies. Testicular cancer is an anatomically and clinically distinct entity, and it mostly strikes young men. The site is easily accessible and more likely to be biopsied. The patients usually receive surgical treatment. Testicular cancer thus is less likely to be misclassified by site or otherwise subject to underreporting.[10] Data on the histologic types of testicular cancer (i.e., seminoma and non-seminoma) were not included in this analysis, however, because such information was not consistently recorded by the NCIRS prior to 1983 across provincial/territorial cancer registries.[8]

Statistical analysis

The secular trends in age-adjusted incidence rates for all males as well as for those aged 15-49 years and 50-84 years, were modelled using log-linear regression first. The average annual percent change (AAPC) in testicular cancer incidence was

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derived from the expression [exp (β)-1]x100, where β is the regression coefficient. Age-specific incidence rates were estimated to compare the pattern of age at diagnosis in three 5-year periods: 1969-73, 1979-83 and 1989-93. All age-adjusted rates were calculated using direct standardization with the 1990 World Standard Population serving as the standard.

Analyses integrating age at diagnosis, period of diagnosis and birth cohort were then performed according to the groups defined below. The entire study period was grouped into five 5-year time periods based on the year of diagnosis: 1969 through 1973, 1974 through 1978, 1979 through 1983, 1984 through 1988, and 1989 through 1993. Age at diagnosis was also grouped into 5-year intervals, yielding 14 age groups from age 15 to 19 through 80 to 84 (in order to avoid unstable estimates due to the small number of incident cases occurring in very young and old ages). Corresponding to these age groups and time periods, a total of 18 overlapping, 10-year birth cohorts (beginning with birth years 1884-1893, and ending with birth years 1969-1978) were created. Each case occurring in any given 5-year age group and 5-year time period was assigned to only one 10-year birth cohort, though the cohort intervals overlap. Our analysis focused on 16 birth cohorts, as the first and the last cohorts were excluded due to small sample size and few incident cases.

To determine if the increase in testicular cancer risk follows a birth cohort pattern and if so, to quantify and compare any birth cohort effects, age-specific incidence rates of the cancer were plotted in the 16 birth cohorts. An age-period-cohort model and the submodels with standard Poisson assumptions were fitted to the incidence data.[11,12] An age-drift model was also fitted to summarize the linear effects unattributable specifically to period or cohort influences.[12] To test the effect of period and cohort individually after controlling for age effect, respective two-factor models were compared to the age-drift model. Parameter estimates were obtained using the maximum likelihood method through SAS procedure GENMOD.[13] Models were evaluated using the deviance, defined to be twice the difference between the maximum achievable log likelihood and the log likelihood at the maximum likelihood estimates of the regression parameters.[13] Specific effects, such as cohort and period effects, were tested by comparing the difference in deviance between the respective models. For example, comparing an age model and an age-cohort model means that an important factor has been added. In the assessment of the goodness of fit of a given

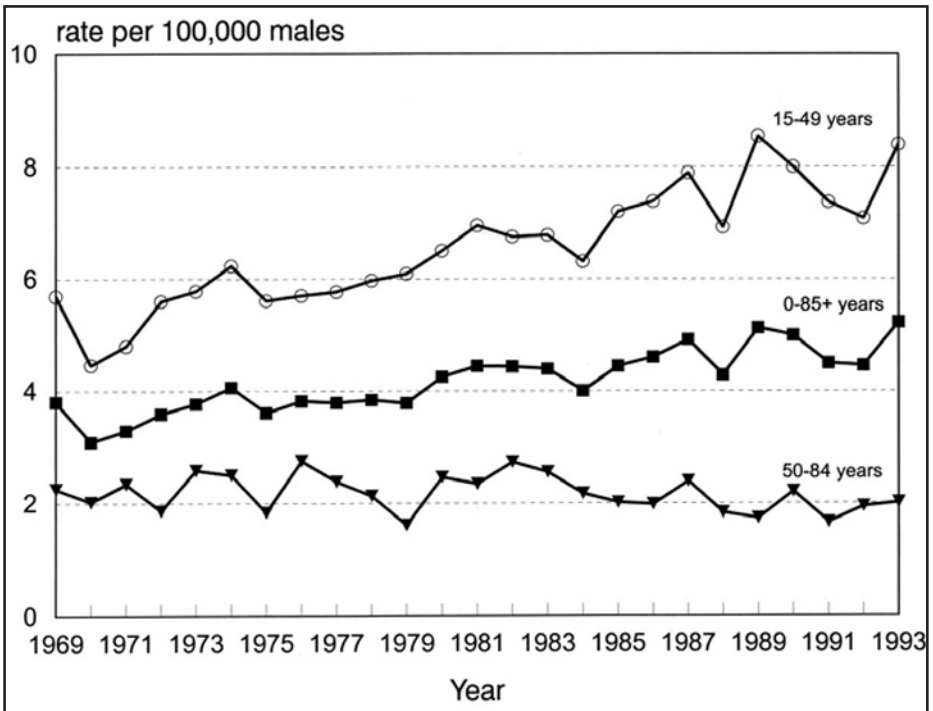

Figure 1. Age-adjusted incidence rates per 100,000 males for testicular cancer in all ages and truncated age groups in Canada, 1969-1993
* Rates were adjusted to the 1990 World Standard Population.

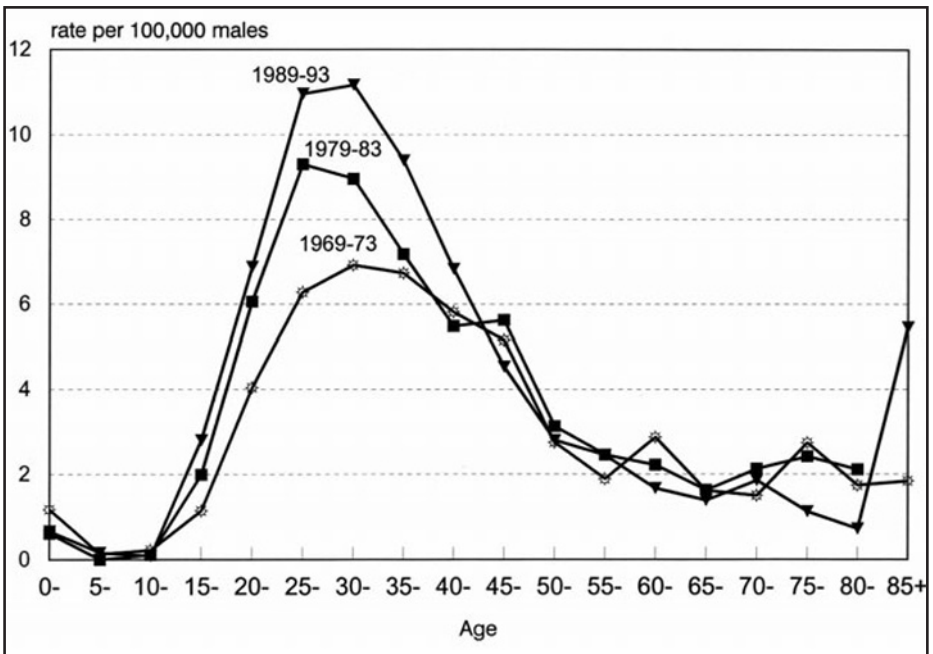

Figure 2. Age-specific rates of testicular cancer per 100,000 males in Canada, 1969-1973, 1979-1983 and 1989-1993

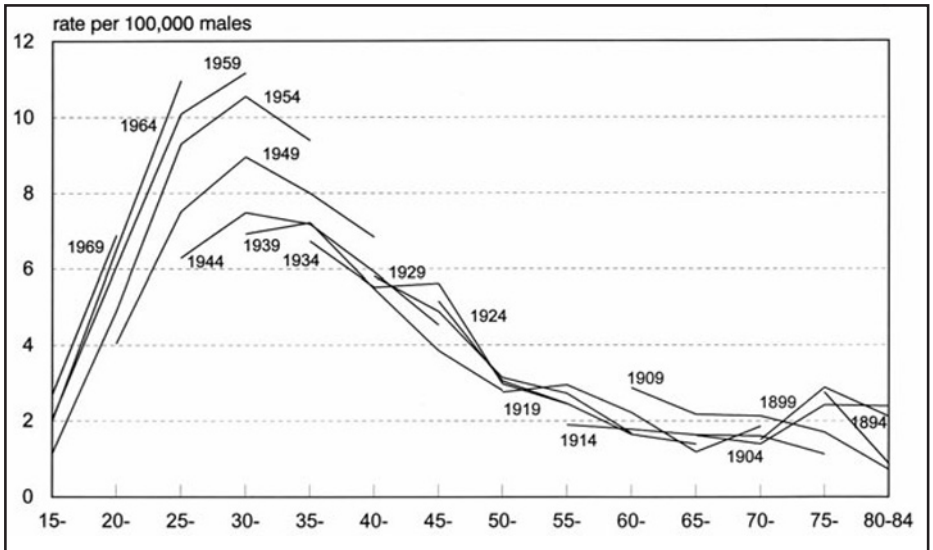

Figure 3. Age-specific incidence rates of testicular cancer per 100,000 males by birth cohort in Canada

* The numbers in the figure denote the median year of each selected 10-year birth cohort.

TABLE I
Characteristics of Different Age-Period-Cohort Models for Testicular Cancer Incidence, Canada, 1969-1993

Terms in Model	df	Deviance	Change in Deviance	p-value
Age	49	221.48		
Age-drift	48	171.92	49.56	0.0000
Age-period*	45	117.81	54.11	0.0000
Age-cohort*	35	34.88	137.04	0.0000
Age-period-cohort†	32	27.62	90.19	0.0000
			7.26	0.0640

* p-values refer to comparisons of the age-period and age-cohort models with the age-drift model, respectively.
† p-values refer to comparisons of the age-period-cohort model with age-period and age-cohort models, respectively.

model, the deviance was also used.[11,12] Preliminary analyses suggested that testicular cancer in adolescent men (i.e., 15-19 years of age) was unique which made the interpretation of modelling results difficult. Consequently, the subjects aged 15-19 years were not included in the final age-period-cohort analysis.

RESULTS

A total of 9,216 incident cases of testicular cancer were registered in Canada (excluding Quebec) by NCIRS and CCR between 1969 and 1993. The age-adjusted incidence rates for all males as well as for the age groups 15-49 years and 50-84 years are presented in Figure 1. The overall age-adjusted incidence rate has been increasing by 50% in Canada, from 2.8 per 100,000 in 1969-71 to 4.2 per 100,000 in 1991-93 (AAPC = 1.9, $p < 0.01$). However, the increase in the incidence can be almost entirely attributed to younger men (15-49 years), who showed an increase in testicular cancer incidence from 4.6 per 100,000 in 1969-71 to 7.2 in 1991-93 (AAPC = 2.1, $p < 0.01$). The incidence rate among adolescents (age 15-19 years) almost tripled during the period, increasing from 0.98 per 100,000 in 1969-71 to 2.76 in 1991-93 (AAPC = 4.5, $p < 0.01$). A slight decrease in the incidence of testicular cancer was evident in the older men (50-84 years), from 2.3 per 100,000 in 1969-71 to 2.0 in 1991-93 (AAPC = - 0.6, $p > 0.05$); however, this decrease was not statistically significant.

TABLE II
Relative Risk (RR) with Confidence Interval (95% CI) of Developing Testicular Cancer for Birth Cohorts in Canada*

Median Year of Birth	RR	95% CI
1894	1.60	1.06 - 2.42
1899	1.42	0.92 - 1.86
1904	1.51	1.14 - 1.97
1909†	1.00	1.00 - 1.00
1914	1.17	0.92 - 1.48
1919	1.10	0.87 - 1.40
1924	1.10	0.87 - 1.40
1929	1.09	0.85 - 1.39
1934	1.01	0.79 - 1.29
1939	1.07	0.83 - 1.37
1944	1.24	0.97 - 1.60
1949	1.48	1.15 - 1.91
1954	1.65	1.27 - 2.13
1959	1.83	1.41 - 2.38
1964	1.97	1.48 - 2.62

* The results in the table are obtained from age-cohort model.
† Reference birth cohort.

Figure 2 shows age-specific rates of testicular cancer incidence in three periods (1969-73, 1979-83 and 1989-93). The highest incidence of testicular cancer was observed between the ages of 15 and 44 years in all the three periods. However, absolute rates of the incidence in the three periods were markedly different with the more recent periods (1979-83 and 1989-93) showing higher peak rates of testicular cancer compared with the earlier period (1969-73). The incidence rates increased noticeably among those aged 15 to 39. The figure also suggests that in recent periods, younger age groups were showing the highest rates of testicular cancer incidence. Analysis by birth cohort (Figure 3) showed that the rates of testicular cancer incidence between 15-44 years of age among males increased with each successive birth cohort.

The age-drift model reduced the deviance of the basic age model significantly. The age-period model resulted in a marginal improvement on the age-drift model, but did not fit the data (deviance = 117.8, df = 45, $p < 0.0001$). The age-cohort model improved on the age-drift model considerably, and it fit the data well (deviance = 34.9, df = 35, $p = 0.47$). The full age-period-cohort model also fit the data well (deviance = 27.6, df = 32, $p = 0.69$), but produced little improvement compared with the age-cohort model when degrees of freedom were taken into consid-

eration. A comparison of the age-period model with the full age-period-cohort model showed substantial improvement, indicating that the birth cohort effects were much stronger than the period effects. The age-cohort model was therefore chosen to represent the observed testicular cancer incidence pattern (Table I).

Relative risks for developing testicular cancer were calculated based on the age-cohort model with the 1909 cohort (i.e., the men born between 1904 and 1913) used as the reference group. The risk of testicular cancer among Canadian males born subsequently was higher than that of males born in earlier periods. The increase in the risk achieved statistical significance with the 1949 cohort (i.e., those born since 1945). Men born between 1959 and 1968 (the 1964 cohort) were 2.0 (95% CI, 1.5-2.6) times more likely to develop testicular cancer as those born between 1904 and 1913 (Table II).

DISCUSSION

Our study shows a 50% increase in the incidence of testicular cancer in Canada over the last 25 years. The increasing risk of developing testicular cancer follows a birth cohort pattern; sequentially increasing risks are observed among those born since the Second World War. Also, higher incidence rates are observed in younger age groups in more recent time periods. Testicular cancer is now increasingly a disease of young men. These findings confirm observations made in previous studies.[2-4]

The age-period-cohort model has considerable advantages over the simple descriptive methods of examining secular trends, although it requires cautious interpretations.[11,12,14] This method allows for a simultaneous evaluation of the effects of age, year of diagnosis (period), and year of birth (cohort). However, in the full age-period-cohort model, the individual effects cannot be uniquely identified (i.e., the nonidentifiability problem).[12] In our analysis, the age-cohort model was found to be superior to the age-period model and therefore was considered to adequately represent the observed testicular cancer incidence pattern among Canadian men from 1969 to 1993.

The increase in testicular cancer incidence among adolescents (age 15-19 years) has also been observed in other populations.[5,6] Several studies have shown that the increase in this age group is largely attributable to an increased incidence of nonseminoma.[3,4] It has also been suggested that the increase is caused mainly by a trend towards earlier age at puberty.[3-5] Including this age group in our age-period-cohort model resulted in a statistically significant period effect, implying that the age group 15-19 years experienced mixed cohort and period effects.[3,5] To avoid the nonidentifiability problem, we excluded this age group from our age-period-cohort analysis. However, analysis examining trends in each of the two histologic subtypes of testicular cancer (seminoma vs nonseminoma) is likely to be more informative.

The finding that birth cohort is a much more important determinant of testicular cancer risk than time period suggests that the observed increase in testicular cancer incidence mainly results from changes in risk factors affecting entire birth cohorts.[14] As mentioned previously, improvements in diagnosis and reporting of testicular cancer are unlikely to have been responsible for the observed trends. Testicular cancer is a distinct clinical and histopathologic entity, and the proportion of morphologically confirmed lesions was very high. If such a bias was operating, it would have contributed to period rather than cohort effects.[13]

Many etiologic hypotheses have been proposed to explain the observed increase in testicular cancer. These include increases in exposure to diethylstilboestrol (DES) in utero, early lifetime exposure to viruses, trauma to the testis, and parental occupational exposures.[2-8] Some analytic studies have focused on the association between testicular cancer and perinatal exposures.[15-18] The results of these studies suggest that prenatal and perinatal exposures are probably important in the development of testicular cancer, although the hypothesis needs to be confirmed by larger and more comprehensive studies.

The finding that cohort effects are important in testicular cancer trends provides some support to the hypothesis that the exposure to etiologic factors occurs very early in life. Although exposures occurring in any period of life could result in a cohort effect, testicular cancer occurs predominantly in young men. Furthermore, the absolute incidence rate in younger age groups has been increasing steadily. Hypotheses regarding testicular carcinogenesis should therefore consider etiologic factors operating early in life, perhaps even in utero. Our study as well as a study by Bergstrom et al.[2] found an apparent post-war increase in testicular cancer in Canada and in Scandinavian countries. We speculate that these increases may be due to increased exposures to carcinogens since World War II or due to new carcinogens introduced around the early post-war period.

In summary, our study shows an increasing secular trend in testicular cancer in Canada and suggests a birth cohort phenomenon as underlying this increase. These findings confirm those of epidemiologic investigations in other countries and help to focus etiologic hypotheses on factors that are likely responsible for the observed trends.

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1) Des normes et des protocoles communs pour l'accès, l'interprétation et la publication de données, ainsi que pour la protection des renseignements personnels.
2) De l'amélioration de l'accès aux renseignements existants – inventaires des bases de données existantes, métadonnées et expertise, ainsi qu'un moyen d'accès de type « guichet unique » se servant des nouvelles technologies pour notamment accélérer l'accès aux données.
3) Du développement et de l'adoption de normes – pour la classification des maladies, des expositions et autres phénomènes de santé, des éléments des bases de données, ainsi que pour l'informatique.
4) De la mise au point et du partage de moyens électroniques innovateurs pour avoir accès, intégrer, analyser, présenter et disséminer l'information.
5) Du renforcement des ressources et des compétences humaines disponibles pour effectuer la surveillance partout au Canada.

On pense que les partenaires fédéraux, provinciaux, locaux et régionaux, les ONG et les établissements d'enseignement peuvent renforcer leurs moyens de surveillance en faisant partie du réseau de surveillance de la santé envisagé pour le Canada.

D'aucuns ont dit que « ce qui est mesurable est réalisable. » Si l'on accepte cette hypothèse, alors les carences et les déficiences de la surveillance que l'on vient de présenter ci-dessus signifient qu'il est fort probable que les Canadiens ne reçoivent pas les meilleures interventions pouvant réduire les risques qu'ils courent de contracter une maladie évitable ou de mourir prématurément. Toutefois, on constate des signes de progrès. La **Canadian Coalition on Cancer Surveillance** a été créée à la suite d'un atelier organisé par le **National Cancer Institute of Canada** à Kananaskis en novembre 1996. La coopération entre des organismes bénévoles, professionnels, provinciaux et fédéraux a débouché sur la reconnaissance des besoins et des priorités en ce qui concerne la surveillance du cancer au Canada et les mesures de suivi devraient se traduire par des améliorations de l'information comme les données de stadification de base pour les nouveaux cas diagnostiqués de cancer. Des activités analogues ont été lancées pour les maladies cardiovasculaires et pour le diabète.

Santé Canada a entrepris plusieurs projets de surveillance innovateurs de validation conceptuelle pour voir s'il est possible d'avoir des systèmes de surveillance en temps réel ainsi que pour tester le renforcement des systèmes de surveillance locaux, régionaux, nationaux et mondiaux. Le projet Roadmap en phase de développement par Santé Canada, Statistique Canada et l'Institut canadien d'information sur la santé est conçu de sorte à fournir de meilleures données sur le rendement du système de soins de santé ainsi que sur l'état de santé des Canadiens. Le projet Roadmap a pour principal objectif de créer des dossiers médicaux personnalisés, d'étendre l'Enquête nationale sur la santé de la population aux régions de santé infraprovinciales, d'améliorer ou de concevoir différentes mesures du recours aux soins de santé (y compris aux produits pharmaceutiques, aux soins à domicile, aux soins de santé mentale, aux soins de la toxicomanie, aux soins de rééducation et aux soins primaires), d'améliorer les normes des données et le partage de ces dernières, de perfectionner les registres des maladies, et de faciliter le calcul des coûts des soins de santé en mettant au point des mécanismes et des méthodes de détermination des coûts.

Les propos ci-dessus portaient essentiellement sur la nécessité pour la surveillance de satisfaire à l'une des principales fonctions de la santé publique, à savoir l'évaluation. La surveillance est également importante pour assurer d'autres fonctions essentielles, à savoir l'élaboration de politiques et la promotion des intérêts. Des données de surveillance exactes et disponibles au moment requis sont essentielles pour évaluer les besoins de santé et pour justifier les ressources nécessaires pour garantir des programmes efficaces de protection et de promotion de la santé ainsi que de lutte contre la maladie. Pareilles données sont

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