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An analysis of cause-specific and sex-specific schedules of cancer mortality in an urban complex: Evidence from routine records in Ghana

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Abstract

Background: In countries without functioning cancer registries, population-based cancer estimates are problematic, and the burden of all-sites and site-specific cancer mortality is hard to gauge.

Objective: The study aimed to estimate cause-specific, age- and sex-specific cancer mortality burden using data from the Vital Registration System (VRS) in an urban complex with no cancer registry.

Methods: The Ghana Vital Registration System (GVRS) is designed to be coterminous with the national political-administrative units, allowing for mortality reporting at the household level. Death records are stored centrally at the National Office in Accra, the capital of Ghana. We collected and analysed, using Binomial/Poisson, Hazard and Cox regression models, mortality records from Ghana's VRS over a 14-year (1998-2011) period in order to estimate and study the relationship among sex, age, and the risk of dying of cancer.

Results: Overall, the results showed an increase in cause-specific hazard rates with increasing age. The results also showed strong evidence of a difference in all-cause relative hazard rate between males and females (1.12, 95% CI 1.07 - 1.19, $p < 0.001$). Finally, further cause-specific analyses showed that, while stomach cancers and lymphomas were more prevalent in males than females, the converse was true for bladder and pancreatic cancers (11.4% and 12.5%, respectively).

Conclusion: The consistency of the findings reported here with results from similar analyses using data from standard cancer registries supports the view that routine data from vital registration systems can be used validly to estimate the burden of cancer mortality in resource-poor settings where cancer registries are unavailable.

Keywords: Cause-specific mortality, Cox regression, Ghana, Vital Registration System

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INTRODUCTION

In developing countries, where rapid urban growth occurs with concomitant deterioration in urban environmental quality, there are reports of corresponding significant elevation in chronic disease outcomes, especially cancer mortalities. By reducing air pollution levels alone, countries can reduce the burden of disease from stroke, heart disease, lung cancer, and both chronic and acute respiratory diseases, including asthma. In addition, urban sprawl potentially influences cancer mortality via direct and indirect exposure to environmental carcinogens [1-4]. Chronic diseases, and especially malignancies, are an increasing problem in low- and

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middle-income countries (LMICs). For instance, a global cancer analysis dubbed "GLOBOCAN 2012" showed that there were 847,000 new cancer cases (6% of the global total) and 591,000 deaths (7.2% of the global total) in the 54 countries of Africa in 2012, with about three-quarters in the 47 countries of sub-Saharan Africa [5]. The analysis further indicated that, while cancer profiles often differed markedly across regions, the most common cancers in men were prostate (16.4% of new cancers) and liver cancers (10.7%), as well as Kaposi sarcoma (6.7%) with the most important ones in women being breast (27.6% of all cancers) and cervix cancers (20.4%).

Despite overwhelming evidence of a rapid increase in the burden of all cancers in LMICs and in Africa in particular, population-based tracking of cancer incidence is incomplete, and the systems of cancer tracking or cancer registries remain relatively weak or dysfunctional in most cases. Consequently, only very few or no published data on cancer mortality across age groups and gender exist. The paucity of data on cancer mortality in LMICs has largely been blamed on problems with collecting data on cancer mortality. However, while these problems are recognised and widely described [6-10], including numerous data quality issues that are associated with analysing data from hospital-based data sources, data from VRS still constitute an invaluable source of information on trends and patterns of cancer mortality in settings where incidence and mortality data are unavailable. In support of the latter argument, the overall objective of this analysis was to estimate and compare, with other studies, the cause-specific, age- and sex-specific cancer mortality burden using data from a Vital Registration System (VRS) in an urban complex, employing composite statistical models. The study, therefore, specifically sought to determine the association between cancer and sex, determine the time trend in cancer mortality, identify the most susceptible subgroups, identify the commonest cancer types over a 14-year span, and finally ascertain whether there was a relationship between cancer type and age group.

MATERIALS AND METHODS

Certified records of cancer deaths by autopsies and death certificates spanning the 14 years from 1998 to 2011 were extracted from the Ghana VRS. Cases were entered into a database using EpiData version 3.0 (EpiData Association, Odense, Denmark) and then transferred to Stata version 17.0 (StataCorp, College Station, TX, USA) for analysis. Variables collected were the date of diagnosis, age, sex, date of death, nationality and cancer sites. Underlying causes of cancer deaths were coded according to the International Classification of Diseases: 9th revision (ICD-10) [11,12]. The ages were grouped according to the format used by the International Agency for Research on Cancer (IARC) for cancer reporting; i.e., 0 - 14, 15 - 24, 25 - 34, 35 - 44, 45 - 54, 55 - 64, and ≥ 65 years [11,12]. A modified Cox proportional hazards model was applied to account for grouped mortality data and age-specific hazards. This model has been used in similar analyses of vital statistics data and has demonstrated validity in estimating hazard ratios [13]. Its adaptation to our dataset allowed for robust estimation of hazard differentials across age and sex groups. The estimated risk/hazard of dying from cancer is presented as follows:

$$x_i = \begin{cases} 0 & if\ in\ divdidual\ i\ is\ a\ female \\ 1 & if\ individual\ i\ is\ a\ male \end{cases}$$

$$\lambda_i(t) = \lambda \cdot (t)\, exp(\beta X_i)$$

With X_i defined as above we get

$$\lambda_i(t) = \begin{cases} \lambda_{male(t)} = \lambda_0(t) \text{if individual } i \text{is a female} \\ \lambda_{female(t)} = \lambda_0(t)\, exp(\beta) \text{ if individual } i \text{is a male} \end{cases}$$

The mortality rate ratio on hazard ratio (HR) between males and females is

$$HR = \frac{\lambda_{male(t)}}{\lambda_{female(t)}} = \frac{\lambda_o(t)\, exp(\beta)}{\lambda_0(t)} = exp(B) \text{If } HR < 1,$$

Then males die less than females

If $HR = 1$, then males and females have the same mortality ratio

If $HR > 1$, then males die more than females

In this study, the effect of age was tightly controlled because the incidence of most diseases, especially chronic diseases, is known to be strongly associated with age [14-16].

To estimate the incidence rate ratio (IRR), we let y have a Poisson distribution with parameter, which then means that

$$P\left|y = k\right| = \frac{e^{-\lambda}\lambda^k}{k!} \quad k = 0,1,2,5 \qquad (1)$$

Since both $E(y) = \text{var}(y)$

Taking the $\log$ of $E(y)$ we get

$$\log E(y) = \beta_o + \beta_1 x_1 + \cdots + \beta_e x_e \qquad (2)$$

The Poisson regression fits a linear model to the log counts of the number of events. In fitting linear models, we look for group differences and interaction, adjusting for covariates and confounders. In this analysis, the event of interest was death events due to cancer, and so in fitting our rates, we applied the term:

$$r = \frac{count\ events}{population\ size}$$

Where count event = death events due to site-specific cancer
Population size = all cancer deaths
Taking the log of the above, we get:

$$\log (r) = \beta_1 + \beta_1 x_1 + \ldots.. + \beta_e x_c$$

$$\log \ = \frac{(\text{Cancer death})}{(\text{all cause of death})} = \beta_0 + \beta_1 x_1 + \ldots.. + \beta_e x_e \qquad (3)$$

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= log (cancer death = $\beta_0 + \beta_1 x_1 + ... + \beta_e x_e$ + log (all cause of death) (4)

Data quality issues and analytic strategies

Fundamentally, different populations differ in their age structure, and a comparison of health outcomes associated with age across these populations would potentially create confounding as a consequence of differences in age structure. In addition, VRS in developing countries are often weak and incomplete. Biases therefore arise as a result of incomplete cancer mortality reporting and by dint of differences in age structures across the temporal scale. The relative frequency of different types of cancer varies in relation to age. Thus, the proportion of different cancers in a particular series is strongly influenced by the age composition of the series. This poses a problem when comparing summary statistics derived from populations of different age structures [17]. To overcome this problem and allow comparison across sub-populations and age-groups, mortality counts were modelled using a Poisson distribution, which assumes independence of events and equality of the mean and variance.

We acknowledge that in routine mortality data, underreporting and misclassification may lead to overdispersion. To control for variability in risk estimation, we used Bayesian models, specifically the model proposed by Besag, York, and Mollié [16,18,19], which account for two types of random effects: spatiality and heterogeneity. Prior distributions are assigned to the random effects, and a hyperprior distribution is assigned to the parameter of the prior distribution. In this paper, the spatial effect was analysed using conditional autoregression. Again, following the suggestion of several authors, a uniform distribution of $U(0,5)$ is usually assigned to the standard deviation of the random effects [9,15,20-25]. Moreover, it is argued that when the population has a different age structure, it is best to calculate the Age Standardised Cancer Ratio (ASCAR), which can serve as a basis for comparison [8].

RESULTS

An increasing rate of all-age cancer mortality for both sexes was observed over a 14-year span in urban Accra (Figure 1). From 1998 to 1999, the mortality rate ratio was the same for both sexes. However, from 2000 onward, the rate for females slowly declined, while that of their male counterparts continued to rise. An overtime increase in cancer mortality rate ratio in both males and females described an intriguing wave-like trajectory. The overall trend for both sexes showed an initial steady increase until 2002, when the rate ratio began to decline in females, while that in males tapered gently from 2005 to 2011. With respect to site-specific cancer mortality, the most common cancers in descending order were prostate (12.5%), larynx (11.4%), breast (11.4%), stomach (7.3%), cervix (5.6%), lung (4.9%), bladder (4.7%) and ovary (3.2%) (Table 1). In all, cancers of unknown origin had the highest relative proportion (26.2%). During the period 1998 to 2011, ovary (1.27) and cervical (1.26) cancers had the highest rate ratio. This was followed by breast (1.25), lung (0.97), and bladder (0.95) cancer.

Table 2 shows that, while prostate cancer was the commonest cause of death (ASCAR, 12.9%), cancer of the larynx was the second commonest cause of death (ASCAR, 10.9%) in the urban complex studied. Deaths due to colon, throat and ovary cancers were among the least with ASCAR of 1.3%, 2.0% and 3.8% respectively. The burden of cancers of unknown sites was 27.1% suggesting a rather weak diagnostic infrastructure in settings without cancer registries. Cancer mortality hazard rate for both sexes increased with age (Table 2). The age group with the lowest

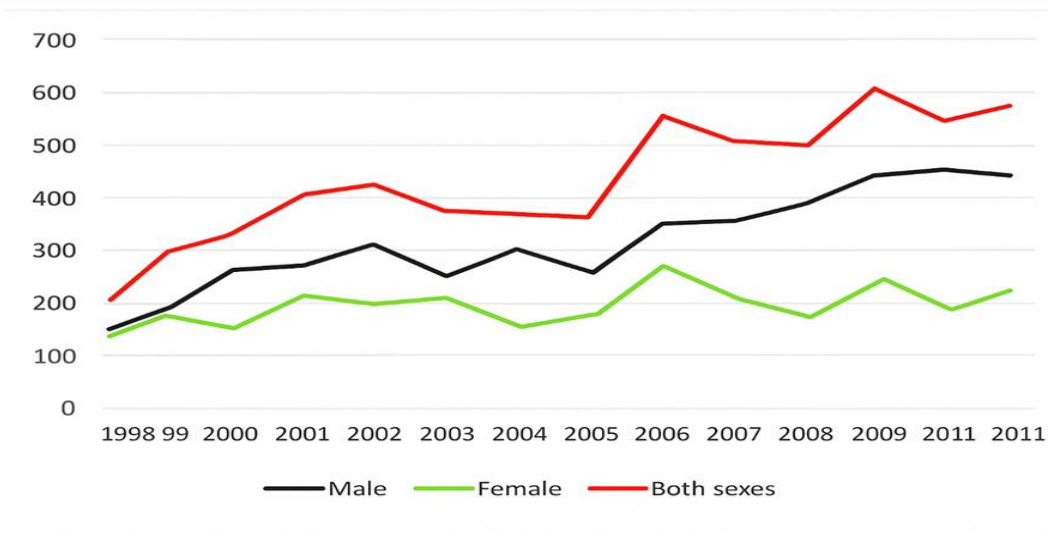

Figure 1. Trends of sex-specific cancer mortality

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hazard rate was 15-24, with (HR = 1.47; 95% CI = -1.23-1.74, p = 0.200) for females and (HR = 1.51; 95% CI = 1.27-1.80, p = 0.022) for males. The age group 55-64 was associated with the highest hazard (HR = 4.23, 95% CI = 3.72 - 4.79, p = 0.050) for females and (HR = 4.66, 95% CI = 3.22 - 4.15, p = 0.042) for males, respectively. Age group 65+ was associated with HR = 3.26, 95% CI = 2.90 - 3.67, p < 0.001 for females and (HR = 3.76, 95% CI = 2.45 - 3.11, p = 0.010) for males. There was strong evidence of differences across both sex and age.

Malignancies of the breast (breast cancer) accounted for 22.98% of deaths that occurred among members of the age group 45 – 54 years. This was followed by those in the age group 25 - 34, where breast cancer accounted for 14.51% of deaths. Prostate (21.31%) and stomach (10.56%) malignancies were more common among the age 65+ group, while lymphomas remained the most frequent cancers among the age group 15 - 24, making up to 20.33% of cancer deaths within this group. Most deaths that occurred among the group 65+ were carcinomas of unknown origin. There were, however, no deaths recorded for cancer of the throat for the age group 0 - 14. The results in Table 4 show strong evidence of differences between tumour sites and age groups (chi = 86.69, 95% CI 1.28 - 2.35, p = 0.0001).

Table1. Relative frequency (RF) and incidence rate ratio (IRR) of cancer cases

Tumor site	ICD-10 Code	RF	IRR
Pancreas	C25	5.2	0.81
Bladder	C67	4.7	0.95
Breast	C50	11.4	1.25
Cervix	C53	5.6	1.26
Colon	C18	1.8	0.99
Liver	C22	4.3	0.88
Lung	C33.C34	4.9	0.97
Larynx	C32	11.4	0.89
Ovary	C56	3.2	1.27
Prostate	C61	12.5	0.70
Stomach	C16	7.3	0.88
Throat	C11	1.4	0.85
Unknown	-	26.2	0.92
All Site	-	100.0	0.99

Table 2. Proportion of cancer deaths by age group

Site	All Ages	0-14	15-24	25-34	35-44	45-54	55-64	65+	ASCAR
Pancreas	0.05	0.02	0.00	0.02	0.04	0.06	0.06	0.07	5.3
Bladder	0.05	0.01	0.01	0.03	0.07	0.03	0.06	0.05	4.9
Breast	0.11	0.04	0.06	0.11	0.19	0.21	0.12	0.05	10
Cervix	0.06	0.01	0.04	0.03	0.06	0.06	0.06	0.07	5.8
Colon	0.02	0.00	0.02	0.02	0.01	0.02	0.02	0.02	1.3
Liver	0.04	0.03	0.07	0.06	0.05	0.05	0.04	0.03	4.6
Lung	0.05	0.03	0.06	0.06	0.03	0.05	0.07	0.04	5.1
Larynx	0.11	0.56	0.27	0.16	0.12	0.06	0.05	0.05	10.9
Ovary	0.03	0.02	0.03	0.02	0.04	0.05	0.04	0.02	3.8
Prostate	0.13	0.02	0.03	0.03	0.03	0.05	0.13	0.26	12.9
Stomach	0.07	0.02	0.01	0.03	0.05	0.07	0.08	0.11	6.3
Throat	0.01	0.00	0.01	0.01	0.02	0.01	0.02	0.02	2
Unknown	0.26	0.26	0.39	0.42	0.29	0.27	0.23	0.20	27.1
All Site	0.32	0.12	0.021	0.05	0.11	0.02	0.09	0.25	100

Table 3. Hazard rates for the various age categories stratified by sex for all-cause cancers

Age Group	Female			Males		
	Hazard rate	*P*-value	95% CI	Hazard rate	95% CI	*P*-value
15-24	1.47	0.200	-1.23- 1.74	1.51	1.27- 1.80	0.022
25-34	1.58	0.010	1.54- 2.06	1.73	1.50- 2.00	0.002
35-44	2.34	0.030	2.05- 2.67	2.37	2.07- 2.70	0.011
45-54	3.20	0.020	2.81- 3.64	3.95	2.60- 3.36	0.030
55-64	4.23	0.050	3.72- 4.79	4.66	3.22- 4.15	0.042
>65	3.26	0.000	2.90- 3.67	3.76	2.45- 3.11	0.010

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Table 4. Relationship between specific and all-other cancer cause mortalities

Tumor site	0-14	15-24	25-34	35-44	45-54	55-64	65 above	Total	Chi
Pancreas	4.07	0.55	2.27	4.76	5.43	6.07	8.03	5.83	86.69**
Bladder	1.63	2.2	4.08	6.14	2.54	6.87	5.13	4.87	
Breast	6.5	8.79	14.51**	21.51	22.98**	13.53	7.78	14.1	
Cervix	0.81	5.49	3.4	6.91	6.00	8.66	9.02	7.28	
Colon	1.63	1.65	2.27	2.15	3.12	2.79	2.47	2.54	
Liver	6.5	6.59	4.99	5.99	5.08	4.08	3.34	4.5	
Lung	6.5	7.14	6.12	3.23	4.85	5.87	4.08	4.83	
Lymphoma	2.44	20.33	14.74	11.98	12.47	9.95	5.68	9.88	
Ovary	1.63	2.75	3.17	4.92	6.24	4.58	2.84	4.07	
Prostate	2.44	3.3	1.81	2.15	3.35	9.95	21.31**	10.33	
Stomach	4.07	2.75	4.31	4.92	6.35	7.36	10.56**	7.39	
Throat	0	1.1	0.91	1.38	0.92	1.49	0.93	1.08	
Unknown	61.79	37.36	37.41	23.96	20.67	18.81	18.84	23.29**	
Total	100	100	100	100	100	100	100	100	

DISCUSSION

Previous Ghanaian mortality series indicated that liver and prostate are the leading male cancer mortalities, while breast, followed by haematopoietic malignancies, dominate among females [17]. Some cancers, especially stomach and liver cancers, however, are comparatively prevalent in both sexes. Cancer has been reported to be associated with age [7,8,11,17], and the probability of acquiring it, including the risk factors associated with the disease, has been reported to increase with age [26]. Similarly, our data showed that mortality hazards increased with age, peaked at 55–64 years, and declined at ≥ 65 years in both sexes. This pattern may be influenced by biological, diagnostic, and demographic factors, and may vary by cancer type and country [27]. Moreover, this peak-and-decline profile has been described in other settings [28] and underscores the need to target prevention and care to adults approaching late midlife while maintaining supportive care for older adults. Altogether, the observed differences were probably due of individual genetic and physiological constitutions, including differential lifestyles, occupations, and exposures, as reported in previous studies [22,29,30].

With respect to temporal patterns, over the period 1998-2011, it was noted that the trend of cancer mortality among the sexes continued to increase steadily. A decrease was, however, recorded in 2005, after which the increasing trend continued again. The observed decline in 2005, followed by a return to an upward trend, may reflect contemporaneous health system changes, urbanisation dynamics, and shifts in healthcare-seeking behaviours in Accra during that period, rather than purely biological or random variation. Regarding specific cancer types, the topmost malignancies in urban Accra were prostate, larynx, breast and stomach cancers. Given the urban focus of our study, it is plausible that environmental and occupational exposures contributed to the observed cancer mortality patterns. For instance, urban Accra is characterised by high levels of air pollution, vehicular emissions, industrial activity [31,32], and occupational hazards [33], all of which may influence site-specific cancer risks. When compared regionally, these patterns show partial consistency with GLOBOCAN 2012 estimates for sub-Saharan Africa, where breast, cervical, prostate, and liver cancers were the leading causes of cancer mortality [34,35]. While prostate and breast cancers were common to both datasets, our series identified laryngeal and stomach cancers as prominent, whereas GLOBOCAN emphasised cervical and liver cancers. This contrast underscores potential regional variations in diagnostic capacity, exposure patterns, and reporting systems. Prostate cancer emerged as the leading cause of cancer mortality among men in our study. Given that prostate cancer is a male-specific malignancy that predominantly affects older men, its high frequency in the 65+ age group is consistent with established epidemiological patterns. In addition, the high proportion of cancers of unknown origin warrants attention. This may reflect diagnostic delays, limited access to pathology and imaging facilities, and possible coding issues within the VRS. Such gaps highlight the urgent need to strengthen diagnostic infrastructure and mortality coding systems to reduce the burden of cancers classified as “unknown”.

With regards to breast cancer, mortality peaked at ages 45 – 54, with a secondary peak at 25 – 34. This pattern aligns with reports that breast cancer risk factors are relatively common in younger women, contributing to an earlier age of onset in some populations [2,17,36,37]. In contrast, studies from Caucasian populations typically report peak mortality at older ages, highlighting possible differences in genetic susceptibility, reproductive factors, and healthcare access [38]. In addition, in terms of regional consistency, our findings are consistent with broader African patterns, where breast cancer is the leading cause of cancer death among women and prostate cancer is the leading cause among men [39]. With respect to sex differences, the observed steeper hazard rate slope for males than for females probably indicates that males were more temporally susceptible to all-cause cancers than females between 2008 and 2011 in the urban complex. Mortality

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hazards increased with age in both sexes; we refrain from direct cross-sex comparisons within age strata, given model parameterisation and available outputs. Considering mortality hazards, both females and males showed a decline from 55 – 64 to ≥ 65 years, aligning with the overall peak-and-decline pattern observed.

Comparison and validation of our findings with the results of other studies

Consistent with our findings, studies employing Cox proportional hazards on registry and vital records have similarly shown strong age-graded increases in cancer mortality risk and sex differences in overall hazard. For example, analyses using Cox models on registry or vital statistics data reported monotonic age-related increases in mortality hazards with a late-life attenuation, and higher overall hazards in males, trends that are consistent with our results [40]. These findings have important policy implications; In the absence of a national cancer registry, VRS data can serve as a crucial resource for monitoring cancer mortality and informing national cancer control strategies. Such data can support priority-setting, guide the allocation of limited resources, and strengthen evidence-based planning for cancer prevention and care in Ghana.

Regarding limitations, we acknowledge that the study period (1998–2011) may not necessarily reflect contemporary trends. However, in the absence of a continuous national cancer registry in Ghana, this dataset represents one of the few comprehensive mortality records available for cancer. As such, it provides a valuable historical baseline against which future data can be compared and helps to highlight long-term patterns of cancer mortality in an urban Ghanaian setting. Another limitation is that our data are based partly on autopsy records, which may introduce specific biases. Autopsy-based data may overrepresent hospital deaths and may differ in diagnostic accuracy compared to hospital-based or registry-based datasets. These factors should be taken into account when interpreting our findings.

Conclusion

In conclusion, our results compare well with studies that have used data from standard cancer registries. Specifically, findings from the cancer registry at the Korle-Bu Teaching Hospital [41] similarly identified breast and cervical cancers as the leading causes of cancer deaths among women and prostate cancer as the leading cause among men, consistent with our analysis. This consistency supports our view that routine data from vital registration systems can be used validly to estimate the burden of cancer mortality in resource-poor settings where cancer registries are unavailable. We therefore argue that cancer studies in such contexts should not be delayed while cancer registries remain non-existent or weak, especially when routinely reported mortality data are available and can provide valuable insights into cancer patterns. Beyond their methodological value, our findings underscore the potential of routinely collected mortality data to contribute directly to national cancer control strategies and resource allocation in Ghana and similar resource-limited settings.

DECLARATIONS

Ethical consideration

Ethical approval for the study was obtained from the University of Ghana Review Board at the Noguchi Memorial Institute for Medical Research (NMIMR-IRB CPN 058/14-15)

Consent to publish

All authors agreed on the content of the final paper.

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Competing Interest

The authors declare no conflict of interest

Author contribution

II and JD conceived and designed the study. JM and JNF gave conceptual advice. DD and JD did the statistical analysis and drafted the manuscript. II, SAB, SVS and JAM reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

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Availability of data

Data is available upon request to the corresponding author.

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