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Original Article

Evaluation of Breast Cancer Incidence Trends in the Karaganda Region of Kazakhstan

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Abstract

Background: The study conducted a component analysis of the dynamics of the incidence of breast cancer (BC) in Karaganda region.

Methods: Primary data were for registered patients with BC (ICD 10–C50) in Kazakhstan, Karaganda region the period of 2009-2018. Evaluation of changes in BC incidence in the population of Karaganda was performed using component analysis according to the methodological recommendations.

Results: Overall, 4,391 new cases of BC and 1,202 deaths were recorded. The incidence rate increased from 44.4 (2009) to 72.7 in 2018 and the overall growth was 28.37 per 100,000 population of female, including due to the age structure – $\sum\Delta_A$=3.13, due to the risk of acquiring illness – $\sum\Delta_R$=22.69 and their combined effect – $\sum\Delta_{RA}$=2.56. The component analysis revealed that the increase in the number of patients with BC was mainly due to the growth of the population (Δ_P=+3.7%), changes in its age structure (Δ_A=+10.3%) and changes associated with the risk of acquiring illness (Δ_R=+75.0%). The mortality rate in the region changed from 18.6 (2009) to 10.9 (2018) and tended to decrease.

Conclusion: The role of the influence of demographic factors and the risk of acquiring illness on the formation of the number of patients and the incidence of BC was evaluated. In this region, these indicators were the highest. The implementation of the results of this study is recommended in management of anticancer activities for BC.

Keywords: Breast cancer; Incidence; Trends; Component analysis

Introduction

Breast cancer is the most common malignant disease among the female population of Kazakhstan like in many developed countries of the world (1). The incidence of BC is about 2.3 million new cases annually, the age-standardized incidence rate (ASR) is 47.8 per 100,000 population of female (2) and remains alarmingly high; these data make it clear that there is little progress in the prevention of this disease. (3-6). Breast cancer is the most common cause of cancer death in women worldwide. Every year, there are about 700 thousand deaths (2) and among the deaths from other types of cancer ranks fifth. Recently published epidemiological reports from various parts of the world indicate a significant increase in breast cancer deaths (7-10).

According to IARC, more than 2.5 million cases of BC are expected by 2025, about 1.2 million cases of which are among the Asian population, with an increase of 10.8% in this region and change in number of cases were due to population. Moreover, the increase in mortality from this pathology in the Asian population will be 13.8% (11,12). Given these data, the primary goal of health care is to reduce the ever-increasing morbidity, mortality, and economic costs of breast cancer (13-17).

Kazakhstan is making significant efforts to improve the health and life expectancy of its population, but even so, the incidence of cancer remains high. In Kazakhstan, there was a global trend in the incidence of BC. The results of our previous study (18-20) showed that Kazakhstan refers to regions with an average incidence rate (Eritrea–42.1 per 100,00, Djibouti – 42.4 per 100,000, the Republic of Moldova – 42.6 per 100,000 and Qatar – 42.7 per 100,000) (2). At the same time, the Karaganda region belongs to the regions with a very high incidence, compared with other regions of Kazakhstan.

The aim of the study was to analyze trends in the incidence of breast cancer in Karaganda, a region with a high quantity of breast cancer cases.

Materials and Methods

Cancer registration and patient recruitment

New cases of BC were extracted from the accounting and reporting forms of the Ministry of Health of the Republic of Kazakhstan – form 7 and form 35, formed from the register of oncological diseases based on the region from 2009 to 2018 using the International Disease Code 10, code C50.

Population denominators

The female population of Karaganda region as the 2018 census was 726,014. Population denominators for calculation of incidence rates were provided by the Bureau of National Statistics for 2009-2018. Data on the number of female population of the region are used, presented on the official website (21).

According to the data processing center of the Bureau of National Statistics (2018) 1202 women died from breast cancer in the study region.

Information about the region under study

Karagandy Province, also spelled Qaraghandy Province, is a region of Kazakhstan. The region's population is 1,376,882 (2020). Ethnic groups (2020): Kazakh: 52.36%; Russian: 35.07%; Ukrainian: 2.84%; German: 2.28%; Tatar: 2.21%; Others: 5.24%. Karaganda is the capital of Karaganda Region in the Republic of Kazakhstan. It is the fourth most populous city in Kazakhstan, behind Almaty (Alma-Ata), Nur-Sultan and Shymkent. Population: 497,777 (https://stat.gov.kz, 2020 Estimate). Karaganda is approximately 230 km south-east of Kazakhstan's capital Nur-Sultan (formerly known as Astana).

Statistical analysis

The main method used in the study of incidence was a retrospective study using descriptive and analytical methods of modern oncoepidemiology. Age-standardized incidence rates (ASRs) were calculated for eighteen different age groups (0-4, 5-9, …, 80-84, and 85+) and ten calendar periods from 2009 to 2018 (1-year intervals). ASRs standardized to the world population proposed by WHO (22) with recommendations from the National Cancer Institute (NCI, 2013) were estimated for each studied year.

The extensive, crude and age-specific incidence rates (ASIR) are determined according to the generally accepted methodology used in modern sanitary statistics. The annual averages (M, P), mean error (m), Student criterion, 95% confidence interval (95% CI), and average annual upward/downward rates (T%) were calculated. We did not justify the main calculation formulas in this paper, since they are detailed in the methodological recommendations and textbooks on medical and biological statistics (23-25).

The dynamics of incidence rates was studied for 10 years, while the trends of incidence were determined by the least squares method. To calculate the average annual growth rate and/or growth rate of the dynamic series, the geometric mean equal to the root of the power of n from the product of the annual growth rate indicators was used.

The dynamics of the incidence of BC was studied using a component analysis according to the methodological recommendations (26). The method of component analysis was used in this study to break down the growth of number of cases belonging to the same population, but in different time periods.

There are 7 components of the increase in the number of cases. The first 3 components are related to changes in the population number, its age structure, and the combined influence of these factors. The true increase in the number of patients with oncological pathology is due only to a change in the risk indicator of morbidity and is represented by the 4th component. The following 3 components are associated with the risk of developing a malignant neoplasm, with the growth of the population, changes in its age structure, and the influence of all three factors. Thus, the last 4 components are associated with an increase in the risk of developing the disease. The "risk of acquiring illness" refers to the whole range of reasons that can lead to an increase, decrease or stabilization of morbidity rates.

The method of components was applied to study the dynamics of the number of BC patients and has been performed on cases that occurred from 2009 to 2018 among the population of the region. Assessments of the component analysis of the dynamics of morbidity of BC in the population of Karaganda region are presented in the relevant tables.

Viewing and processing of the received materials was carried out using the Microsoft 365 software package (Excel, Word, PowerPoint), in addition, online statistical calculators were used (https://medstatistic.ru/calculators/averagestudent.html), where Student criterion was calculated when comparing the average values.

The following symbols and abbreviations were used in this article: AN – absolute number; ASIR – age specific incidence rate; ASP (Δ_A) − the age structure of the population; ASR – age-standardized rate; END − the expected number of diseases; NCRC − the number of BC cases; PN (Δ_P) − population number; RAI (Δ_R) − risk of acquiring illness; R^2 – the value of the approximation confidence; SI − structural indexes; P−the incidence of BC; $^0/_{0000}$ – prosantimille, designation per 100,000.

Ethics approval

Because this study involved the analysis of publicly available administrative data and did not involve contacting individuals, consideration and approval by an ethics review board was not required. At the same time, the submitted data is in accordance with the Law of the Republic of Kazakhstan No. 257-IV of March 19, 2010 "About State statistics" (http://adilet.zan.kz/rus/docs/Z100000257), the information in the summary report is confidential and can only be used for statistical purposes in accordance with the Principles of the World Medical Association (27).

Results

During the study period, 4,391 new cases of BC were registered in Karaganda region. The greatest proportion of patients falls on the age of 55-59 yr (15.3%), while among dead women it is 60-64 yr (15.0%) (Table 1).

Table 1: Breast cancer rates in the Karaganda region of Kazakhstan, 2009-2018

Age	*AN (%)*	*Incidence* per 100,000 P±m	95% CI	T, %	R^2	*Death (%)*	*Mortality* per 100,000 P±m	95% CI	T, %	R^2
>30	34 (0.8)	1.1±0.2	0.7-1.5	−6.0	0.1344	2 (0.2)	0.1±0.0	0.0-0.2	−27.9	0.1208
30-34	66 (1.5)	12.2±1.5	9.2-15.3	+1.2	0.0098	16 (1.3)	3.0±1.0	1.1-5.0	−30.7	0.3979
35-39	176 (4.0)	34.5±3.0	28.7-40.3	+5.7	0.4057	35 (2.9)	6.8±1.4	4.1-9.5	−16.6	0.565
40-44	288 (6.6)	59.0±4.6	50.0-68.1	+3.7	0.2171	58 (4.8)	11.9±2.0	8.0-15.9	−8.3	0.2424
45-49	435 (9.9)	90.2±3.0	84.2-96.1	+2.0	0.3458	99 (8.2)	20.1±3.0	14.2-25.9	−11.4	0.5538
50-54	602 (13.7)	123.3±7.4	108.8-137.9	+3.3	0.2970	140 (11.6)	28.5±3.5	21.8-35.3	−7.7	0.4133
55-59	674 (15.3)	154.6±5.5	143.9-165.3	+1.3	0.1357	167 (13.9)	39.2±5.5	28.3-50.1	−12.6	0.741
60-64	646 (14.7)	181.1±6.9	167.6-194.7	+2.6	0.4473	180 (15.0)	51.4±5.9	39.9-62.9	−5.4	0.2345
65-69	537 (12.2)	205.2±4.7	162.7-247.8	+8.0	0.4978	139 (11.6)	55.5±7.3	41.3-69.7	−0.6	0.0025
70-74	440 (10.0)	190.0±11.4	167.7-212.4	+1.6	0.0756	168 (14.0)	71.1±4.4	62.6-79.7	−3.1	0.2692
75-79	298 (6.8)	162.9±9.1	145.0-180.8	+2.9	0.2630	103 (8.6)	61.5±6.9	48.1-75.0	−10.6	0.8797
80-84	138 (3.1)	144.3±14.3	116.3-172.3	+2.8	0.0781	65 (5.4)	69.4±9.9	50.0-88.9	−2.0	0.0202
85+	57 (1.3)	103.3±20.3	63.4-143.1	+6.6	0.1009	30 (2.5)	57.6±13.9	30.4-84.7	−7.6	0.1002
Total	4391 (100.0)	60.9±2.8	55.5-66.4	+4.1	0.7776	1202 (100.0)	16.7±1.3	14.2-19.2	−6.4	0.7272
ASR	–	47.9±1.83	44.3-51.5	+3.2	0.6787	–	13.0±1.09	10.8-15.1	−7.4	0.7792

Age-related indicators of BC incidence had a peak in 65-69 yr (205.2±4.7$^0/_{0000}$). Trends in age-related indicators of BC incidence tended to increase in almost all age groups, except for group of >30 yr (T=−6.0%), where there was a decrease. The value of the approximation confidence of the listed decreases is not significant (Table 1). Age-related indicators of BC death had a peak in 70-74 yr (71.1±4.4$^0/_{0000}$). Trends in age-related BC mortality rates tended to decrease in all age groups (Table 1).

Trends in age-related indicators affected the overall incidence rates, so the crude incidence rates of BC increased from 44.36 (2009) to 72.73 per 100,000 female population in 2018 (*P*=0.000), the total increase was 28.37$^0/_{0000}$ and depended on changes in the age structure of the population (Table 2).

Table 2: Component analysis of the BC incidence growth in Karaganda region, 2009-2018

Age group (i)	***Age structure*** $(Sij = \frac{N_{ij}}{N_j})$		***Growth of structural indicators*** ***($S_{i2}-S_{i1}$) (3)−(2)***	***BC incidence, ⁰/₀₀₀₀***		***Incidence growth***			
	2009 (S_{i1})	2018 (S_{i2})		2009 (P_{i1})	2018 (P_{i2})	General ($P_{i2}-P_{i1}$) (6)−(5)	Including due to changes of Δ_A (4)×(5)	Δ_R (2)×(7)	Δ_{RA} (4)×(7)
1	2	3	4	5	6	7	8	9	10
<30	0.4393	0.4133	−0.0260	1.93	1.33	−0.6	−0.050	−0.262	+0.015
30-34	0.0750	0.0784	+0.0034	18.82	17.57	−1.3	+0.063	−0.094	−0.004
35-39	0.0718	0.0690	−0.0028	33.43	49.88	+16.4	−0.093	+1.181	−0.046
40-44	0.0678	0.0678	+0.0000	50.01	75.20	+25.2	−0.001	+1.708	−0.001
45-49	0.0754	0.0645	−0.0109	82.47	98.25	+15.8	−0.897	+1.189	−0.172
50-54	0.0648	0.0624	−0.0024	76.33	119.16	+42.8	−0.179	+2.774	−0.101
55-59	0.0573	0.0667	+0.0094	128.29	140.41	+12.1	+1.212	+0.694	+0.115
60-64	0.0366	0.0538	+0.0172	154.24	199.60	+45.4	+2.652	+1.662	+0.780
65-69	0.0389	0.0460	+0.0071	94.50	344.45	+249.9	+0.673	+9.714	+1.780
70-74	0.0354	0.0240	−0.0114	151.49	206.35	+54.9	−1.728	+1.944	−0.626
75-79	0.0182	0.0296	+0.0114	108.51	148.92	+40.4	+1.234	+0.736	+0.460
80-84	0.0139	0.0160	+0.0021	71.21	155.24	+84.0	+0.148	+1.167	+0.175
85+	0.0056	0.0085	+0.0028	25.05	81.27	+56.2	+0.071	+0.317	+0.159
Total	$\sum S_{i1}$=1.0	$\sum S_{i2}$=1.0		P_1=44.36	P_2=72.73	+28.37	$\sum\Delta_A$=+3.13	$\sum\Delta_R$=+22.69	$\sum\Delta_{AR}$=+2.56

At the same time, the average annual growth rate of the aligned indicator was T=+4.1%, and the value of the approximation confidence was close to 1 (R^2=0.778) (Table 1).

Then, we will consider the component analysis results of the dynamics of the number of patients with BC in this region as a whole. The growth in the number of patients with BC in the republic was 68.2% (Table 3) and was associated with the influence of the following factors (Table 4):

1. Growth of population number Δ_P=+3.7%.
2. Changes in the age structure of the population Δ_A=+10.3%.
3. Combined effect of changes in population number and its age structure Δ_{PA}=+0.3%.
4. Risk of acquiring illness Δ_R=+75.0%.
5. Combined effect of changes in the risk of acquiring illness and population number Δ_{PR}=+1.9%.
6. Combined effect of changes in the risk of acquiring illness and age structure of the population Δ_{RA}=+8.5%.
7. Combined effect of the changes in the risk of acquiring illness of the population and its age structure Δ_{RAP}=+0.2%.

The total increase in the absolute number of patients overall equals the sum of components: n_2-n_1=8+22+1+161+4+18+0=214 or +68.2% in comparison with the primary number of patients (214÷314×100=68.2%).

At the same time, the components of the increasing in the percentage at the primary level are equal for the women population:

$$\underbrace{2.6\%+7.1\%+0.2\%}_{9.8\%}\ \underbrace{+51.1\%+}_{51.1\%}\ \underbrace{1.3\%+5.8\%+0.1\%}_{7.2\%}\ =68.2\%$$

Thus, BC is characterized by an increase in the number of cases as a result of changes in the total number and structure of the female population (9.8% of the total increase of 68.2%). The real increase in the number of cases (risk of acquiring illness) was Δ_R =+51.1% (Table 4).

Table 3: Component Analysis of the BC Incidence in Dynamics in Karaganda region from 2009 till 2018

Age group (i)	***NTC (n_{ij})***		***PN (N_{ij})***		***Crude (P_{ij})***		***Standardized (P^c_{ij}) (***		***END in 2018***
	2009 (j=1)	2018 (j=2)	2009 (j=1)	2018 (j=2)	2009 (j=1)	2018 (j=2)	2009 (j=1)	2018 (j=2)	($P_{ij}N_{i2}10^{-5}$) (6)×(5)×10^-5
1	2	3	4	5	6	7	8	9	10
<30	6	4	310964	300052	1.93	1.33		0.586	5.8
30-34	10	10	53125	56930	18.82	17.57		1.318	10.7
35-39	17	25	50849	50122	33.43	49.88		3.583	16.8
40-44	24	37	47990	49199	50.01	75.20		5.098	24.6
45-49	44	46	53355	46820	82.47	98.25		7.405	38.6
50-54	35	54	45851	45316	76.33	119.16		7.718	34.6
55-59	52	68	40534	48428	128.29	140.41		8.040	62.1
60-64	40	78	25934	39079	154.24	199.60		7.312	60.3
65-69	26	115	27513	33387	94.50	344.45		13.387	31.6
70-74	38	36	25084	17446	151.49	206.35		7.312	26.4
75-79	14	32	12902	21488	108.51	148.92		2.714	23.3
80-84	7	18	9830	11595	71.21	155.24		2.156	8.3
85+	1	5	3992	6152	25.05	81.27		0.458	1.5
Total	n_1=314	n_2=528	N_1=707923	N_2=726014	P_1=44.36	P_2=72.73	$P^c_1 = 44.36$	$P^c_2 = 67.04$	$E(n_2)$=345
Growth	$\frac{n_1 - n_2}{n_1}100 = 68.2$		$\frac{N_1 - N_2}{N_1}100 = 2.56$		$\frac{P_1 - P_2}{P_1}100 = 64.0$		$\frac{P^c_1 - P^c_2}{P^c_1}100 = 51.1$		

Table 4: Influencing components on the number of cases of breast cancer in Karaganda region

Components of growth in the number of cases due to:	***AN***	***% growth***	
		to (n_2-n_1)	to n_1
1. Growth PN $\Delta_P = \frac{N_1 - N_2}{N_1} n_1$	8	+3.7	+2.6
2. Changes ASP $\Delta_A = \frac{N_1}{N_2}(E(n_2) - n_2 - \Delta_H$	22	+10.3	+7.1
3. Combined effect of changes in PN and ASP $\Delta_{PA} = \frac{N_2 - N_1}{N_1}\Delta_A$	1	+0.3	+0.2
		$\sum_{1-3}$=+14.4	$\sum_{1-3}$=+9.8
4. Change of RP $\Delta_R = N_1(P^c_2 - P^c_1) \times 10^{-5}$	161	+75.0	+51.1
5. Combined effect of changes of RP and PN $\Delta_{RP} = \frac{N_2 - N_1}{N_1}\Delta_R$	4	+1.9	+1.3
6. Combined effect of changes of RP and ASP $\Delta_{RA} = \frac{N_2 - N_1}{N_1}\Delta_R$	18	+8.5	+5.8
7. Combined effect of the changes RP. PN and ASP $\Delta_{PAR} = \frac{N_1}{N_2}(n_2 - n_1 - \sum_{x=1}^{5})$	0	+0.2	+0.1
		$\sum_{1-3}$=+85.6	$\sum_{1-3}$=+58.4
Total $\sum_{1-7}$	214	100.0	68.2

Next, we will review incidence of BC, taking into account the age of women to be screened. Thus, the incidence in the age group 40-69 yr increased from 91.6±6.2 (2009) to 151.8±7.6 (*P*=0.000) per 100,000 female population, and the overall increase (+60.14$^{0}/_{0000}$) was mainly due to the risk of acquiring illness ($\sum\Delta_R$=+52.08$^{0}/_{0000}$), and the average annual growth rate of the aligned indicator was T_g=+4.1% and the value of the approximation confidence is R^2=0.7875.

In order to exclude the influence of the age structure of the female population of the region, standardized indicators of incidence and mortality were calculated. Thus, the ASR in this region was 47.9±1.8 (95% CI=44.3-51.5) per 100,000 female population, the dynamics of the indicators tended to grow (*P*=0.000) and the average annual growth rate of the aligned indicator was T_g=+3.2, and the value of the approximation confidence R^2=0.6787 (Table 3).

In dynamics, the standardized mortality rate from BC in Karaganda region tended to decrease from 15.2±1.3 (2009) to 7.8±0.9 per 100,000 female population in 2018 (*P*=0.000), and the average annual incidence rate for the studied years was 13.0±1.1 (95% CI=10.8-15.1). The average annual rate of decline of the aligned indicator was T_d=−7.4% (R^2=0.7792) (Fig. 1).

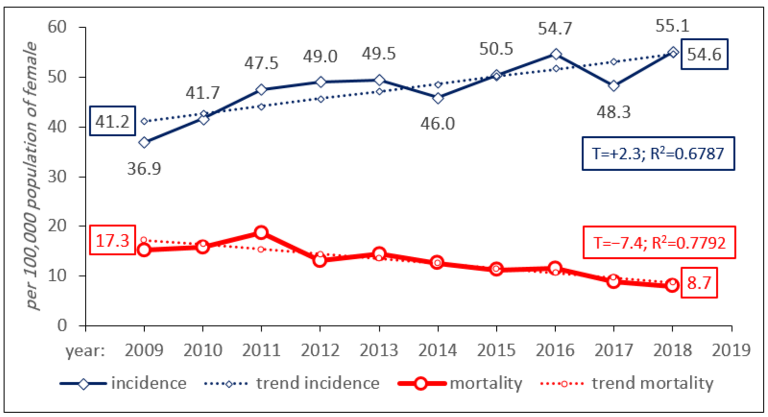

Fig. 1: Dynamics of standardized incidence and mortality rates of breast cancer in Karaganda, 2009-2018

Discussion

Generally, during the study period, the number of patients with BC increased by 68.2% from 314 to 528 cases, which turned out to be higher than predicted according to the component analysis – 345. Herewith, the proportion of patients under 50 yr of age was 22.8% and 77.2% in women over 50 yr and older.

Age-related indicators of incidence show a unimodal increase, with a peak of incidence in 65-69 yr – 205.2$^{0}/_{0000}$. The peak incidence of BC occurs at the end of postmenopausal age.

In our study, we provided information on the target group of screening considering the age group of 40-69 yr, since the accounting, registration and formation of reporting forms takes into account the age groups 0-4, 5-9, 10-14...65-69, 70-74 yr, etc. (described in the materials and methods). During the study period, 72.5% of the total number of new cases of BC were registered in the target group, and the incidence in this age group increased over time.

A similar pattern was observed in the study of Kamińska and co-authors (28), where BC was most common in women during menopause, 80% of cases of detection of the disease among women aged 50 yr and older.

The results of the component analysis indicate that in this region, the incidence of BC in the entire female population is increasing mainly due to the influence of such a factor as the risk of acquiring illness ($\sum\Delta_R$=+22.69$^{0}/_{0000}$), and the increase in patients due to this criterion was also significant in this region (Δ_R=+75.0%). Herewith, in the target group, the impact of the risk of acquiring illness on the incidence of BC was more pronounced ($\sum\Delta_R$=+52.08$^0/_{0000}$), and also the increase in the number of patients in this group (40-69 yr) was more affected by this criterion (Δ_R=+71.0%). The above is assessed as a positive result of anti-cancer measures in breast cancer, including screening.

An important criterion for evaluating anti-cancer measures is the analysis of mortality rates. Thus, standardized mortality rate decreased in Karaganda region.

Thus, the conducted component analysis indicates that there are positive results of the influence of mammalogical screening in Karaganda region, while the influence of other exogenous and endogenous factors is not excluded. Changes in epidemiological indicators are undoubtedly the results of the impact of anticancer measures – the implementation of breast screening. The obtained results can be used to improve anti-cancer activity. Further study of screening efficiency is a priority for our continued research. The changes were related to the ethnic composition of the region's population (29), the average age of breast cancer patients in the Karaganda region in Kazakh women was 51,7±0,5 yr, while in Russian women 58,9±0,2 yr and until 2018, the contingent of people for screening was 50 yr and thus screening was more effective in the last group (Order No. 995 of Dec 25, 2017 "On Amendments and Additions to the Order of the Acting Minister of Health of the Republic of Kazakhstan of Nov 10, 2009 No. 685 "On Approval of the Rules for Conducting Preventive Medical Examinations of Target Population Groups»).

Conclusion

Thus, as a result of the component analysis, the role of the influence of demographic factors and the risk of acquiring illness on the formation of the number of patients and the incidence of BC was evaluated. In this region, these indicators were the highest. The implementation of the results of this study is recommended in management of anticancer activities for BC.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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