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*Original Article*

# Trends in the incidence and mortality of cutaneous melanoma in Hong Kong between 1983 and 2015

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**Abstract:** The rapid growth of cutaneous melanoma (CM) has been observed globally, especially in the White population. However, due to the low incidence and mortality rates, epidemiological analyses for the CM in the Chinese population was largely overlooked. Here, the quality-controlled public data of CM in Hong Kong were available to partly address this knowledge gap. Using the CM data registered from 1983 to 2015 in the Hong Kong Cancer Registry, Hospital Authority, a joinpoint regression method and an age-period-cohort model was implemented to analyze the trends in incidence and mortality rates in Hong Kong. A total of 1842 diagnosed cases and 853 deaths of CM was registered. The overall age standardized rates of incidence and mortality were 0.7 per 100000 person-years and 0.3 per 100000 person-years, respectively. Over the entire study period, significant growth in mortality were detected with the average annual percent changes (AAPC) of 1.4% (confidential interval [95% CI]: 0.1%-2.7%) per year, while no significant changes were found in the incidence rates for the total population. The incidence rates for people aged 65 years and over declined significantly (AAPC: -1.4% [95% CI: -2.5%--0.4%]). A full age-period-cohort model best explained changes in the incidence and mortality rates. Associating multi strategies in beating CM and continuous declines in the incidence of cohort effects, the incidence of CM in Hong Kong is estimated to decrease for the next generation.

**Keywords:** Age-period-cohort model, epidemiology, mortality, incidence

## Introduction

Cutaneous melanoma (CM) has been one of the rapid increase cancers worldly over the past four decades [1-5], especially for the White populations [6-8]. Despite the huge Asian population, trends in incidence and mortality rates have been overlooked because of low Asian incidence rates [9-11]. Specifically, the Chinese population exceeded 1.37 billion in 2015 [12], about 18.7% of the world population [13]. In 2015, there was about 8,000 newly diagnosed cases and 3,200 deaths by the CM [14]. Although the National Central Cancer Registry of China had established for collecting cancer data nationally since 2002, a continuous long-term report for CM covered the whole country is still deficient for further analysis, e.g. trends analysis, because of limited high quality available data [14, 15]. Fortunately, the Hong Kong Cancer Registry (http://www3.ha.org.hk/cancereg/datacollection.html) supported the quality-controlled data of CM from 1983.

According to an earlier study [16], the mean age standardized incidence rate between 1982 and 2002 was 0.8 (per 100,000 person-years, same as below), and 0.6 for men and women, respectively. In the same period, the mean age standardized mortality rate was 0.3 and 0.2 for men and women, respectively. Their results represent a decreased trend in incidence rates and a modest growth in mortality rates for the Hong Kong population using linear regression methods. For the CM, aging and ultraviolet radiation exposure are two of the main risk factors for development of CM [3, 17, 18]. In an aging era for Hong Kong, the incidence and mortality rates of CM are estimated to grow [17]. Moreover, according to the ultraviolet radiation index [19], sun protection for the Hong Kong population is required in 93% of days annually, when the maximum ultraviolet radiation index was greater than two (UV Radiation Information, Hong Kong Observatory, http://www.hko.gov.hk/wxinfo/uvindex/chinese/cfreq_dist.htm). Various activities to control the development of CM have been carried out in Hong Kong, e.g. enhancing educational circular [20] and updating medical management [21]. In addition, sufficient epidemiological studies on the incidence and mortality of CM are beneficial to improve to the management of CM. Except for the effects of aging [17], previous studies for Caucasians showed birth cohort plays roles in effecting the incidence and mortality of CM [22-24]. However, little is known about age, period, and birth cohort effects on the incidence and mortality of CM in Hong Kong.

Therefore, this study aimed to investigate the trends in incidence and mortality rates of CM in Hong Kong between 1983 and 2015 using the jointpoint regression method and the age-period-cohort models.

## Material and methods

### *Data sources*

The CM data (code C43, the International Classification of Diseases 10th revision) registered from 1983 to 2015 were derived from Hong Kong Cancer Registry, Hospital Authority (http://www3.ha.org.hk/cancereg/c_a1b.asp, accessed 10th, December, 2017). Briefly, the Hospital Authority manages the Hong Kong's public hospital services, and the Hong Kong Cancer Registry is a population-based cancer registry and a member of the International Association of Cancer Registries. All data registered were quality controlled. The morphologically verified cases have been over 85%, and the death certificated only percentage (DCO%) has been less than 1% in recent years (see the official website for detail about data quality, http://www3.ha.org.hk/cancereg/quality.html). The data contain the following categories: sex, five-year age groups, diagnosed cases, deaths, and age standardized rates (ASR, per 100,000 person-years) of the incidence and mortality of CM. The ASR was calculated as the number of incidences and deaths per 100,000 person-years, based on the World Standard population (World 2000) [25].

### *Joinpoint regression method*

The joinpoint regression method [26] has been widely used in the trend analysis of cancer data. The method starts with zero jointpoint for the dataset, which indicates there is a linear trend over the full study period, and then, adds more significant statistical joinpoints to the trend model using a Monte Carlo permutation method. To avoid the likelihood of spurious trend occurrence [27], a maximum of three joinpoints are added over the entire period. Finally, the annual percentage change (APC) with each joinpoint and the average annual percentage change (AAPC) are outputted. We conducted these analyses using a desktop joinpoint software version (Version 4.5.0.1-June 12, 2017), downloaded from the Surveillance Research Program of the US National Cancer Institute (http://surveillance.cancer.gov/joinpoint/). The trends in the rates in all age groups and the truncated age groups (25-44, 45-64, and 65-85+) were analyzed for the total, the males, and the females.

### *Age-period-cohort model*

The age-period-cohort model is a class of Poisson regression models to describe the incidence and mortality rates as a sum of age effect, calendar period effect and birth cohort (birth cohort = period-age) effect [24, 28]. To deal with the non-identifiable problem in this model, five sub-models were arranged in the sequence with all relevant test: age, age-drift, age-cohort, age-period-cohort, and age-period. The age sub-model represents changes in the age-specific rates over the study period after controlling the period and cohort effects; the age-drift sub-model represents the overall linear trend in the CM, reflecting the sum of the linear period and cohort effect [29]; the age-cohort and age-period sub-models represent the non-linear cohort and period effect, respectively. The age-period-cohort sub-model, a full model, reflect all three terms impact the trends in the CM. The likelihood-ratio test derived from the deviance statistic was used to choose the best fitting model [29, 30] by assessing likelihood-based deviance statistics and penalizing additional degrees of freedom starting from an age parameter only. In short, the smaller the residual deviance of the sub-model, the better the model [31]. The effects of age, period, and cohort were calculated as the age-specific

**Table 1.** Cases and trends in incidence and mortality rates of cutaneous melanoma for the total, female and male in Hong Kong between 1983 and 2015

| Overall | N | AAPC[a] | Trend 1 | | Trend 2 | | Trend 3 | |
|---|---|---|---|---|---|---|---|---|
| | 1983-2015 | | Years | APC[b] | Years | APC | Years | APC |
| Incidence | | | | | | | | |
| Overall | 1842 | -0.1 (-3.4, 3.4) | 1983-1986 | 28.4 (-5.0, 73.5) | 1986-1994 | **-10.8 (-17.7, -3.3)** | 1994-2015 | 0.7 (-0.8, 2.2) |
| 25-44 | 321 | -0.6 (10.2, 10.0) | 1983-1991 | 1.6 (-9.6, 14.3) | 1991-1994 | -33.1 (-77.2, 96.6) | 1994-2015 | **4.2 (1.4, 7.1)** |
| 45-64 | 659 | 0.7 (-3.3, 4.9) | 1983-1986 | 27.6 (-12.2, 85.4) | 1986-1996 | **-9.2 (-15.2, -2.8)** | 1996-2015 | **2.5 (0.2, 4.7)** |
| 65-85+ | 807 | **-1.4 (-2.5, -0.4)** | 1983-2015 | **-1.4 (-2.5, -0.4)** | | | | |
| Mortality | | | | | | | | |
| Overall | 853 | **1.4 (0.1, 2.7)** | 1983-2015 | **1.4 (0.1, 2.7)** | | | | |
| 25-44 | 83 | **21.7 (6.2, 39.6)** | 1983-2015 | **21.7 (6.2, 39.6)** | | | | |
| 45-64 | 291 | **1.6 (0.2, 2.9)** | 1983-2015 | **1.6 (0.2, 2.9)** | | | | |
| 65-85+ | 471 | **1.9 (0.4, 3.4)** | 1983-2015 | **1.9 (0.4, 3.4)** | | | | |
| Males | | | | | | | | |
| Incidence | | | | | | | | |
| Overall | 945 | 1.4 (-3.1, 6.2) | 1983-1986 | 48.2 (-0.8, 121.2) | 1986-1994 | **-11.3 (-20.3, -1.3)** | 1994-2015 | 1.1 (-0.9, 3.2) |
| 25-44 | 156 | 0.8 (-0.9, 11.7) | 1983-2015 | 0.8 (-0.9, 11.7) | | | | |
| 45-64 | 368 | 1.3 (-4.5, 7.4) | 1983-1988 | 18.5 (-9.4, 55.0) | 1988-1996 | -14.6 (-27.3, 0.2) | 1996-2015 | **4.4 (0.8, 8.2)** |
| 65-85+ | 395 | -0.5 (-2.0, 1.0) | 1983-2015 | -0.5 (-2.0, 1.0) | | | | |
| Mortality | | | | | | | | |
| Overall | 459 | **1.7 (0.3, 3.2)** | 1983-2015 | **1.7 (0.3, 3.2)** | | | | |
| 25-44 | 43 | -0.6 (-23.2, 28.7) | 1983-2015 | -0.6 (-23.2, 28.7) | | | | |
| 45-64 | 164 | **1.6 (-0.0, 3.2)** | 1983-2015 | **1.6 (-0.0, 3.2)** | | | | |
| 65-85+ | 246 | 1.6 (-0.2, 3.3) | 1983-2015 | 1.6 (-0.2, 3.3) | | | | |
| Female | | | | | | | | |
| Incidence | | | | | | | | |
| Overall | 888 | **-2.0 (-3.8, -0.1)** | 1983-1996 | **-6.1 (-9.6, -2.4)** | 1996-2015 | 0.9 (-1.2, 3.1) | | |
| 25-44 | 165 | -1.6 (-4.0, 0.9) | 1983-2015 | -1.6 (-4.0, 0.9) | | | | |
| 45-64 | 291 | -1.2 (-2.7, 0.3) | 1983-2015 | -1.2 (-2.7, 0.3) | | | | |
| 65-85+ | 412 | -2.6 (-5.2, 0.1) | 1983-1995 | -8.6 (-13.9, -3.0) | 1995-2015 | 1.3 (-1.5, 4.1) | | |
| Mortality | | | | | | | | |
| Overall | 394 | **2.1 (0.6, 3.5)** | 1983-2015 | **2.1 (0.6, 3.5)** | | | | |
| 25-44 | 40 | **46.6 (18.7, 81.2)** | 1983-2015 | **46.6 (18.7, 81.2)** | | | | |
| 45-64 | 127 | 12.3 (-2.0, 28.7) | 1983-2015 | 12.3 (-2.0, 28.7) | | | | |
| 65-85+ | 225 | **2.4 (0.5, 4.3)** | 1983-2015 | **2.4 (0.5, 4.3)** | | | | |

Notes: [a]: APC: Annual percentage changes; [b]: AAPC: Average annual percentage changes; Bold asterisk represents significant changes at P<0.05 levels.

rates for reference period, rate ratio relative to the reference period year (1983), and rate ratio relative to the reference cohort year 1940, respectively. All of the above was implemented with the "*apc.fit*" function in the "*Epi*" package [32] in the R software [33].

## Results

### *Descriptive data of cutaneous melanoma in Hong Kong (1983-2015)*

A total of 853 deaths and 1842 cases of incidence were registered between 1983 and 2015 in Hong Kong (**Table 1**). The deaths were with a male:female ratio of 1.16:1, while the incidences were with the ratio of 1.06:1 (**Table 1**). The overall ASR of incidence between 1983 and 2015 was 0.8 for the male, 0.6 for the female, and 0.7 for the total, respectively. The overall ASR of mortality was 0.4 for the male, 0.3 for the female, and 0.3 for the total, respectively. The ASR of incidence and mortality increased with age. The overall ASR was 0.38 for incidence and 0.10 for mortality aged 25-44, then increased to 1.27 and 0.54 aged 45-64, 3.32 and 1.80 aged 65 years and over (**Figure 1**).

### *Annual percentage changes in incidence and mortality of cutaneous melanoma in Hong Kong (1983-2015)*

**Table 1** shows the results of the joinpoint regression analysis for the total, female, and male in Hong Kong between 1983 and 2015.

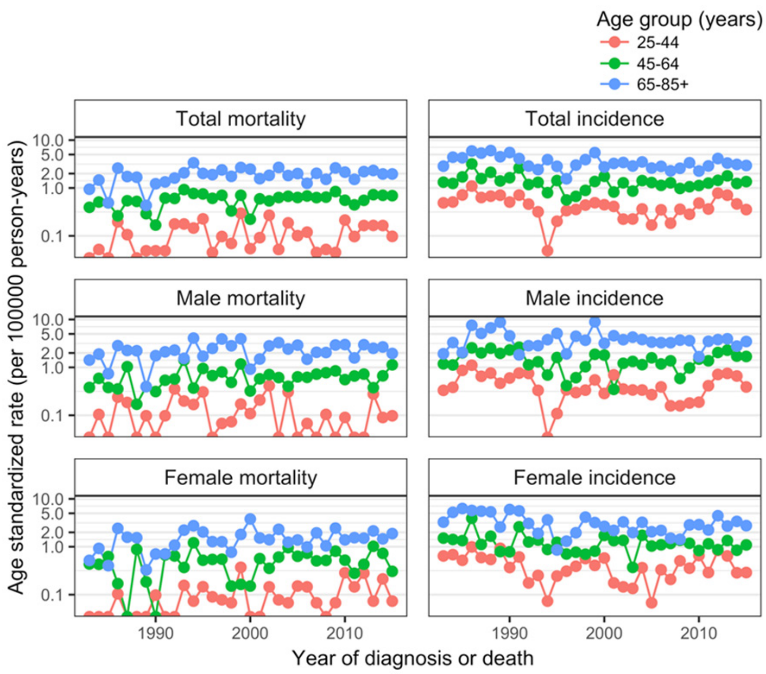


**Figure 1.** Temporal changes in the age-specific rates of incidence and mortality of CM in the groups aged 25-44 years, 45-64 years, and 65 years and over, 1983 to 2015.

For the overall trends, the mortality rates in the total increased significantly by 1.4% (95% CI: 0.1%, 2.7%) per year (**Table 1**). In addition, significant growth in mortality rates in the male and female groups were found by 1.7% (95% CI: 0.3%, 3.2%) per year and by 2.1% (95% CI: 0.6%, 3.5%) per year, respectively. For the overall trend in the incidence rates, females had significant declines by -2.0% (95% CI: -0.1%, -3.8%) per year, while no significant changes were detected in the total and the males. For age-specific trends, people in all main age groups (25-44, 45-64, and 65-85+) were found to have significant increases in mortality rates (**Table 1**) by 21.7% (95% CI: 6.2%, 39.6%), 1.6% (95% CI: 0.2%, 2.9%), and 1.9% (95% CI: 0.4%, 3.4%) per year, respectively. Furthermore, the incidence rates for people in the group aged 25-44 and aged 45-64 increased significantly by 4.2% (95% CI: 1.4%, 7.1%), 2.5% (95% CI: 0.2%, 4.1%) since 1996. The incidence rates for people aged 65 years and more declined significantly (-1.4%, [95% CI: -2.5%, -0.4%]) over the entire study period.

*Age-period-cohort analysis of cutaneous melanoma in Hong Kong*

**Table 2** shows the goodness of fit for the age-period-cohort models including each term in the model. According to the deviance analysis, a full age-period-cohort model best explained the relationships between the changes in the ASR and the explanatory variables (age, period, and cohort) for the total, male, and female (**Table 2**). Strong age effects of CM on the incidence and mortality rates in Hong Kong are illustrated (**Figure 2**). The period and cohort effects were estimated by the rate ratio with the year 1940 as the cohort reference effect and the year 1983 as the period reference effect (**Figure 3**). The cohort effect on the incidence reached the maximum around the 1910 for female. Then, the effects declined from 1940 for the total, females, and males. The period effects on the incidence increased from 1983 to 1990, and then decreased until to 1996 for females and males. After 1996, the period effects on male incidence leveled off, while the effects on females continued to increase. The cohort effects on the mortality for males and females increased since the 1940s. The period effects on the mortality climbed from 1983 to the end of the 1990s, and then the period effects on female leveled off, while on males increased from 2007.

## Discussion

This study reports the trends in incidence and mortality rates of CM in Hong Kong between 1983 and 2015 using the jointpoint regression method and the age-period-cohort method. The main epidemiology results included, over the entire period, 1) 853 deaths and 1842 diagnosed cases reported; 2) the overall incidence and mortality ASR over the entire period were 0.7, and 0.3, respectively; 3) significant growth in the mortality for the total were detected; 4) a full age-period-cohort model explained best for changes in the incidence and mortality rates.

Two possible improvements should be carried out for this study future. The first is that explicit cases of CM for the Chinese population need to

**Table 2.** Goodness of fit for age-period-cohort model for incidence and mortality rates of the total, female, and male in Hong Kong

| Terms in model | Total | | Male | | Female | |
|---|---|---|---|---|---|---|
| | Res. Df[a] | Res. Deviance[b] | Res. Df | Res. Deviance | Res. Df | Res. Deviance |
| Incidence | | | | | | |
| Age | 424 | 327.43 | 424 | 855.91 | 424 | 574.01 |
| Age-drift | 423 | 310.19 | 423 | 843.13 | 423 | 547.13 |
| Age-Cohort | 420 | 310.08 | 420 | 842.48 | 420 | 545.39 |
| Age-Period | 420 | 295.46 | 420 | 834.32 | 420 | 516.98 |
| Age-Period-Cohort | 417 | 294.69 | 417 | 833.58 | 417 | 511.69 |
| Mortality | | | | | | |
| Age | 425 | 248.18 | 425 | 641.42 | 425 | 515.38 |
| Age-drift | 424 | 243.23 | 424 | 632.87 | 424 | 410.9 |
| Age-Cohort | 421 | 240.8 | 421 | 620.08 | 421 | 406.41 |
| Age-Period | 421 | 241.21 | 421 | 627.49 | 421 | 409.98 |
| Age-Period-Cohort | 418 | 235.94 | 418 | 616.08 | 418 | 400.69 |

Notes: [a]: Res. Df: Residual degree; [b]: Res. Deviance: the residual deviance of the model performance.

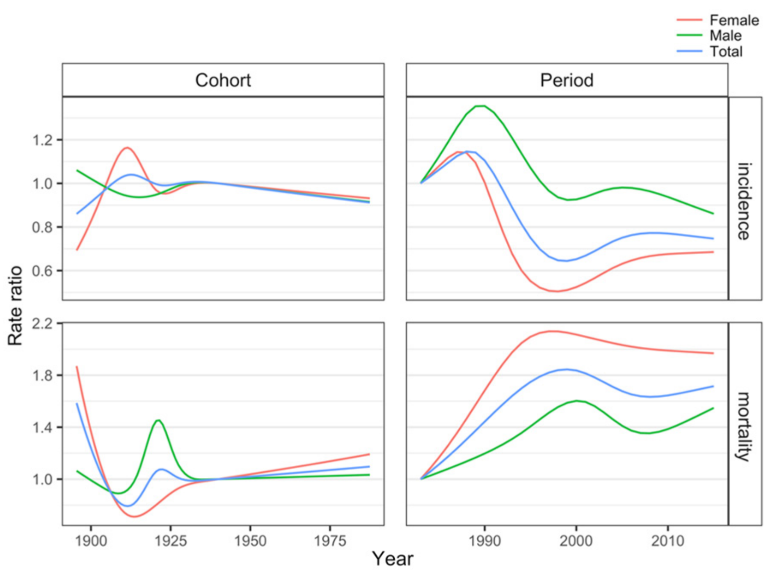


**Figure 2.** Age effects on the incidence and mortality rates of the total, females and males in Hong Kong from 1983 to 2015.

The age effects show that the incidence and mortality rates are highly associated with advanced age. This supports epidemiological evidence with advanced age as one main risk factor of CM for Chinese population [3, 17]. Although the incidence and mortality rates in Hong Kong were less than the rates in the Caucasian population, the rapid growth in the deaths and new cases in Hong Kong still implies that more attention is needed for protecting against CM. In Hong Kong, the average age of onset of CM was 65.5 years [35]. The increasing aging ratio (> 65 years old) which increased from 7.1% in 1983 to 14.2% in 2013, and increasing number of older persons which increased two times over the past three decades can partially explain the rapid growth in death and new cases [14].

be expressed with clear epidemiological analysis. The second one is associated with more clinical data to explain the epidemiological results as the mechanical level.

Although there was increasing incidence and stable mortality rates among the White population [3], stable incidence and increasing mortality rates were found for the total population in Hong Kong [34]. The age-period-cohort model implied all these explanatory variables played overall roles in explaining the changes in these rates.

The period effects can impact all age groups equally. For the incidence, Hong Kong has taken various actions to protect the CM via multi-level publicities, e.g. education for students [20] as well as awareness and prevention campaigns for the general public [20]. These actions could moderate the effects of aging, and thus play roles in stabling incidence rates

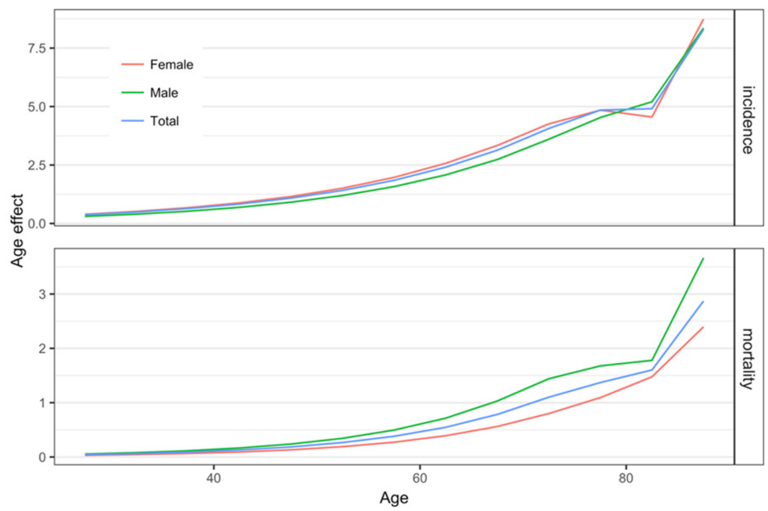


**Figure 3.** Period and cohort effects on the incidence and mortality rates of the total, females and males in Hong Kong. The reference year is 1983 for the period, and 1940 for the cohort.

of period effects. Specifically, females in East Asia tend to cover their skin to avoid sun exposure [36]. All combined activities can explain the significantly decreased incidence rate for females (**Table 1**). While for the mortality, the leveled mortality rate of period effects can be explained by the early detection, because the early stage of the CM is curable [37]. Meanwhile, the main outcome of early detection is the declining/stabling the mortality [5].

The cohort effects on the incidence of the total people decreased since 1910. It can partly explain that the recent declines in the incidence for older people. If these effects continue and the age effects are kept stable, with other periodic actions, the incidence rates of CM in the Hong Kong can be expected to decline or level off in the coming decades. By contrast, cohort studies for the White population showed will continue to raise in incidence rate in the next two or three decades [1, 38-40]. We are confused to explain why the cohort effects on mortality continued to increase since the 1930s, because the rate ratio of incidence was declining at the same period. Therefore, more effective evidence for this is needed.

The declining incidence rate is an encouraging result to promote more activities in the future, and this is the first step to reduce the mortality. Meanwhile, improvement in management of CM is the parallel way to cure this cancer [21]. Following the advice from previous studies [18, 21, 34, 35, 37, 41], three main approaches will be concluded: 1) initiative effective protection, 2) early detection, 3) updating managements of CM. So far, the first two have been advised broadly [20]. Associating these efforts with the continuing decline rate ratio of birth cohort, will facilitate further decrease in the incidence through the next generation.

In conclusion, for the Hong Kong population, the mortality increased significantly and the incidence rate kept stable between 1983 and 2015. A full age-period-cohort effects can explain the changes in incidence and mortality rates. Combing current multi-level prevention and declining rate ratio of birth cohort, the incidence rate can be expected to decrease in the coming decades.


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## Disclosure of conflict of interest

None.

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