An evaluation of the 25 by 25 goal for premature cardiovascular disease mortality in Taiwan: an age-period-cohort analysis, population attributable fraction and national population-based study

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ABSTRACT

Objectives The aim of the 25 by 25 goal is to reduce mortality from premature non-communicable diseases by 25% before 2025. Studies have evaluated the 25 by 25 goal in many countries, but not in Taiwan. The aim of this study was to estimate the 25 by 25 goal for premature mortality from cardiovascular diseases in Taiwan.

Methods We applied the age-period-cohort model to project the incidence of premature death from cardiovascular disease from 2015 to 2024 and used the population attributable fraction to estimate the contributions of targeted risk factors. The probability of death was used to estimate the percent change.

Results The percent change in business-as-usual trend during 2010-2024 was only a 6% (range 1.7-10.7%) lower risk of premature mortality from cardiovascular disease among men. The greatest reduction in the risk of mortality occurred with a 30% reduction in the prevalence of smoking; however, there was only a 14.5% (10.6-18.3%) decrease in percent change and in the corresponding number of men (3706: range 3543-3868) who were prevented from dying. More than a 25% reduction in the percent change of premature cardiovascular disease mortality among women was achieved without control of any risk factor. To reach a 25% reduction in men before 2025, there needs to be a 70% reduction in the prevalence of smoking to reduce mortality by 26.2% (22.9-29.3%).

Conclusions Cigarette smoking is the primary target in the prevention of cardiovascular disease. Through the stringent control of smoking, the goal of a 25% reduction in premature mortality from cardiovascular disease may be achieved before 2025 in Taiwan.

INTRODUCTION

Non-communicable diseases (NCDs) have become an issue in global health, resulting in health and economic burdens in the 21st century. More than 36 million people die from NCDs every year; almost half of the deaths from NCDs occur between the ages of 30 and 70 years, the so-called 'premature' deaths, and almost three quarters of NCD deaths occur in low and middle income countries.1 The four main types of NCDs are cardiovascular disease, cancer, chronic respiratory disease, and diabetes.2 Among these, cardiovascular disease is the primary cause of premature deaths and accounts for almost half of all deaths from NCDs.3

Many health programmes have addressed the prevention and treatment of NCDs over the past decade. In 2011, the United Nations (UN) General Assembly promulgated a political declaration and asked their member states to achieve the goal of a 25% reduction in premature mortality due to NCDs before 2025 (abbreviated as the '25 by 25 goal').4 In response to the 25 by 25 goal, WHO not only developed a global monitoring framework but also published a 2013–2020 Action Plan with several targets, such as the control of alcohol, physical inactivity, salt/sodium, tobacco, high blood pressure and diabetes/obesity, as well as improvements in medical treatment.5 In 2013, the World Heart Federation (WHF) proposed a Global Cardiovascular Disease Taskforce with the specific goal of achieving the 25 by 25 goal, but with a focus on only cardiovascular disease by addressing the major risk factors of tobacco use and hypertension.6

In response to these health initiatives, studies have evaluated the 25 by 25 goal in many countries but none has addressed the risk factors, especially those for cardiovascular disease, in Taiwan.7–15 Among the 10 leading causes of death in Taiwan in 2015, cardiovascular diseases, including heart disease and cerebrovascular disease, were the second and third leading causes of death16; 19% of the total deaths were caused by cardiovascular disease, and 44% of these were premature deaths.16

The aims of this study were to project the premature cardiovascular disease mortality rates to 2025 by age, period, and cohort analysis, and to estimate the 25 by 25 goal in Taiwan in order to answer the critical questions as to how many people could be saved from death by achieving the targets for risk factors, and how much the prevalence of risk factor targets needed to change in order to reach the 25 by 25 goal.

METHODS

Data sources

according to the 9th and 10th versions of the International Classification of Diseases (ICD-9 from 1990 to 2008; and ICD-10 after 2009) codes for heart disease: 391, 392.0, 393–398, 410–414, 415.19, 416, and 420–429 (ICD-9), and I01-I02.0, I05-I09, I20-I25, I27, and I30-I32 (ICD-10). For cerebrovascular disease, the codes 430–438 and I60-I69 (for both ICD-9 and ICD-10) were selected. Population numbers from 1990 to 2014 were abstracted from the online database provided by the Department of Statistics of the Ministry of the Interior in Taiwan. Age and calendar year were similarly categorised. Data for the age-specific prevalence of hypertension and diabetes were taken from the database, Taiwan Behavioural Risk Factor Surveillance System, provided by the Health Promotion Administration in Taiwan. A total of 34 406 hypertensive and 57 574 diabetic premature deaths from 2010 to 2014 were identified. Data for the age-specific prevalence of hyperlipidaemia were taken from the database, National Health Interview Survey, provided by the Health Promotion Administration in Taiwan. A total of 21 940 premature deaths in 2009 were identified. Data for the age-specific prevalence of smoking were taken from the database, Taiwanese Adult Smoking Behaviour Surveillance System, provided by the Health Promotion Administration in Taiwan. A total of 84 171 premature deaths from 2010 to 2014 were available for analysis. The age-specific prevalence of smoking, diabetes, hypertension and hyperlipidaemia are presented in the online supplementary table S1. The relative risks of high blood pressure, high total cholesterol and high blood glucose for cardiovascular disease were used to determine the conservative estimates for hypertension, hyperlipidaemia and diabetes, and were taken from the study by Singh and colleagues. The relative risk for smoking in cardiovascular disease was taken from the study by Kontis and colleagues. The relative risks of smoking, high blood pressure, high total cholesterol and high blood glucose are presented in the online supplementary table S2. We excluded body mass index (BMI) in our study design because of its potential invalidity in diagnosing obesity in Asians. The association between BMI and obesity in Asians had shown that those with a lower BMI were fatter than comparable whites. Previous studies have also indicated that the accuracy of BMI in predicting overweight or obesity is limited.

Statistical analysis
The world standard (WHO 2000) population proportions were used to calculate the age-adjusted mortality rates. The age-period-cohort (APC) method proposed by Tzeng and Lee was used to forecast cardiovascular mortality. The non-identifiability problem (of parameter estimation) arises because the three temporal variables used in the APC model have an exact linear relationship: cohort + age = period; that is, given a person’s birth year and his/her age of death, the calendar year in which the person died is then known.

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However, this problem did not hamper the present mortality forecasting, because the fitted values in the non-identifiable APC model were the same for all possible sets of parameter estimates.

In accordance with the WHO action plan, we calculated the population attributable fractions (PAF) and the probability of death in the absence of other causes of death for a partial elimination of exposure using the formulas presented in the online supplementary appendix 1. Specifically, we considered a 30% reduction in the prevalence of smoking, a 25% reduction in the prevalence of hypertension, a 30% reduction in the prevalence of diabetes, and a 30% reduction in the prevalence of hyperlipidaemia. All statistical analyses were performed using SAS software (9.4 version, SAS).

RESULTS
Figure 1 shows the age-adjusted mortality rates for heart disease, cerebrovascular disease and cardiovascular disease from 1990 to 2014 and the projections for 2015 to 2024 for men and women. For heart disease in men, 285 deaths per 100 000 population occurred from 2010 to 2014—a 1.12-fold

![Figure 1](image)

Figure 1  Age-adjusted mortality rates for heart disease, cerebrovascular disease and cardiovascular disease from 1990 to 2014 and the projections for 2015 to 2024 for men and women.

![Figure 2](image)

Figure 2  Age, period, and cohort effects and their projected effects on heart disease (panel A) and cerebrovascular disease (panel B) among men (blue line) and women (red line).
Table 1 Percent change from probability of death from cerebrovascular disease, heart disease, and cardiovascular disease by gender and four risk factors

<table>
<thead>
<tr>
<th>Gender</th>
<th>Outcome</th>
<th>Cerebrovascular disease</th>
<th>Heart disease</th>
<th>Cardiovascular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>Heart disease</td>
<td>−26.3% (−22.1 to −30.2)</td>
<td>−27.5% (−23.3 to −30.7)</td>
<td>−29.2% (−25.1 to −33.0)</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease</td>
<td>−26.7% (−22.5 to −30.7)</td>
<td>−27.5% (−23.3 to −30.7)</td>
<td>−29.2% (−25.1 to −33.0)</td>
</tr>
<tr>
<td>Women</td>
<td>Heart disease</td>
<td>−21.5% (−15.0 to −27.4)</td>
<td>−22.2% (−15.8 to −28.5)</td>
<td>−23.5% (−17.9 to −29.2)</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease</td>
<td>−22.2% (−15.8 to −28.5)</td>
<td>−23.5% (−17.9 to −29.2)</td>
<td>−24.2% (−17.9 to −29.2)</td>
</tr>
</tbody>
</table>

Figure 2 shows the APC analysis and the forecasting effects of heart disease (upper panel) and cerebrovascular disease (lower panel). For age effects in males, the mortality rate of the oldest 65–69 year age group was 28-fold that of the youngest 30–34 year age group for heart disease, and 49-fold for cerebrovascular disease. In comparison, the ratios of age effects for females were a little stronger. On the other hand, the trends in the period effect of heart disease and cerebrovascular disease in both sexes were similar to the age-adjusted mortality rates (figure 1) and the basic descriptive graphs by age and calendar year (see online supplementary figure S1). The forecasting periods of 2015–2019 and 2020–2024 were all smaller than 2010–2014 for both sexes in terms of heart disease and cerebrovascular disease. In terms of cohort effects, heart disease and cerebrovascular disease in both sexes showed a falling trend from 1925 to 1950, and a rising trend thereafter. These trends were consistent with the association between westernisation and CVD at the developing stage after the 1970s. At this stage, those people born after the 1950s faced the impact of westernisation, resulting in metabolic syndrome and obesity. The forecasting cohorts in 1985 and 1990 were all larger than that in 1980 for heart disease and cerebrovascular disease in both sexes.

Through the analysis and forecast by APC modelling, we combined heart disease and cerebrovascular disease as cardiovascular disease and used the probability of death to estimate the percent change between 2010–2014 and 2020–2024 (table 1). A total of 30 103 deaths from cardiovascular diseases (19 100 from heart disease and 11 003 from cerebrovascular disease) occurred from 2010 to 2014. The percent change in the business-as-usual trend between 2010–2014 and 2020–2024 would be a 6% (range 1.7–10.1%) lower risk of premature cardiovascular disease mortality among men. Even if each risk factor target were achieved, the percent change would still be far below the 25 by 25 goal for cardiovascular disease in men. Among men, the percent change in the smoking target was larger than that in the other risk factor targets, in that a 14.5% (range 10.6–18.3%) reduction would save 3706 (3543–3868) men from premature death. The results for cerebrovascular disease in men were inconsistent, in that they showed a 26.3% (22.1–30.2%) reduction in the business-as-usual trend and a 33.5% (29.8–37.0%) reduction in the trend where the smoking target was achieved. A total of 1077 (1006–1135) men would be saved from death from cerebrovascular disease if the smoking target were reached. In contrast, the results for heart disease in men showed a 5% (9.7–0.5%) increment in the business-as-usual trend and a 4.8% (0.6–8.8%) reduction in the trend where the smoking target was achieved. A total of 2628 (2485–2782) men
would be saved from death from heart disease if the smoking target were reached. Even if no risk factor targets were achieved, the results for cardiovascular disease in women all showed more than a 25% reduction before 2025. Among women, achieving the smoking target could help reduce deaths by 29.9% (23.9–35.3%). That was a little larger than the other risk factors, and would save 159 (145–173) women from premature death. The probability of death from cerebrovascular disease could be reduced by 37.5% (31.4–43.0%) in the business-as-usual trend and by 39.7% (33.8–44.9%) in the trend where the smoking target was achieved. In terms of heart disease among women, the percent change was only a 21.5% (15.0–27.4%) lower risk in the business-as-usual trend.

The PAF values of the four risk factors for both genders are shown in table 2. The PAF values for the smoking target were larger than the other risk factors in men. A 10.4% (8.2–12.4%) reduction in cardiovascular disease mortality would occur if the smoking prevalence decreased by 30%. Similarly, 10.4% (6.3–14.0%) and 10.4% (9.0–11.7%) reductions in cerebrovascular disease and heart disease, respectively, would occur if the smoking prevalence decreased by 30%. The PAF values for the other risk factors in men were all <4%. On the other hand, the PAF values were all <4% in women.

To understand more clearly why the premature cardiovascular disease mortality could not be reduced by 25% before 2025 among men by simply reaching the risk factor targets, we determined the PAF values by different age groups with the corresponding number of persons who would be saved from death if the risk factor targets were achieved (figure 3). For the smoking target, we found that the PAF values decreased from the youngest age group (17%) to the oldest age group (5%), but the corresponding number of persons who would be saved from deaths was inconsistent with the PAF values. A total of 108 people would be saved from death in the 30–34 year age group, and 740 in the 60–64 year age group. This result might be reasonable because the disease rates between 30 and 44 were smaller than the rates in the older age groups. Furthermore, this result might also help us to find out which age group was more effective for the control of cardiovascular disease. Despite the PAF values between 30- and 44-year-olds being higher, the number of persons who would be saved from deaths were still small. It might indicate that the contribution in the younger people would be limited even if the department of health promoted the stringent control of smoking. The same situation also happened in the 65–69 year age group because the PAF value was smaller.

We used the stringent control of smoking to estimate the percent change and the corresponding number of men who would be saved from death from cardiovascular disease (table 3). A 50% reduction in the prevalence of smoking would decrease deaths by 20.3% (16.7–23.8%) and save 6176 (5906–6444) men from death due to cardiovascular disease, and would decrease deaths by 11.4% (7.5–15.1%) and save 4381 (4141–4637) men from premature death caused by heart disease. The more stringent control of a 70% reduction in the prevalence of smoking would decrease deaths by 26.2% (22.9–29.3%) and save 8646 (8271–9025) men from death due to cardiovascular disease, and would decrease deaths by 18.1% (14.5–21.4%) and save 6133 (5798–6492) men from premature death caused by heart disease.

**DISCUSSION**

Our study showed that the reduction of premature mortality in females with cardiovascular disease may reach or exceed 25% before 2025 even if no targeted risk factors (smoking, hypertension, diabetes and hyperlipidaemia) were achieved. For males with cardiovascular disease, the inhibition of smoking behaviour would be more effective and important than the control of hypertension, diabetes, and hyperlipidaemia, but the 25 by 25 goal would still not be reached. To achieve the 25 by 25 goal, the stringent control of smoking, such as a 70% reduction in prevalence, would be necessary. Controlling smoking in the 45–64 year age group may be the most effective way to prevent cardiovascular disease.

Although the number of deaths from premature cardiovascular disease in women can probably reach the 25 by 25 goal without any control of the risk factors, the same is not true for men. This result was not similar to that of Sacco and colleagues who estimated the 25 by 25 goals for mortality from premature cardiovascular diseases in specific regions of the world. They showed that the probability cannot decrease by 25% before 2025 in specific regions of Eastern Europe and Central Asia, sub-Saharan Africa, North Africa and the Middle East, South Asia, East Asia and the Pacific, and Latin America and the Caribbean; however, the estimates of future trends in premature cardiovascular diseases show substantial variation across countries. Although their results across all regions were not similar to our results for both sexes, the pattern in high-income countries was consistent only among women. This indicated that comprehensive public health, medical care and treatment are effective in preventing future premature deaths from cardiovascular diseases in high-income countries. For example, the government of Taiwan implemented a National Health Insurance programme in 1995, and almost every person now has access to preventive healthcare and medical treatment. From 1982 to 1995 life expectancy increased by 2.43 years and mortality decreased by 17.2%; these figures improved to 4.01 years and 25.2%, respectively, from 1995 to 2008.

**Table 2** Values of the population attributable fraction (PAF) for heart disease, cerebrovascular disease, and cardiovascular disease by gender and four risk factors in 2020–2024

<table>
<thead>
<tr>
<th>Gender</th>
<th>Outcome</th>
<th>30% reduction in smoking prevalence</th>
<th>25% reduction in hypertension prevalence</th>
<th>30% reduction in diabetes prevalence</th>
<th>30% reduction in hyperlipidaemia prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>Heart disease</td>
<td>10.4% (9.0 to 11.7)</td>
<td>3.0% (2.1 to 3.9)</td>
<td>0.7% (0.4 to 1.1)</td>
<td>3.5% (2.8 to 4.2)</td>
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<tr>
<td></td>
<td>Cerebrovascular disease</td>
<td>10.4% (6.3 to 14.0)</td>
<td>4.0% (3.6 to 4.4)</td>
<td>0.6% (0.1 to 1.1)</td>
<td>1.7% (1.3 to 2.2)</td>
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<td>Cardiovascular disease</td>
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<td>3.0% (2.4 to 3.7)</td>
</tr>
<tr>
<td>Women</td>
<td>Heart disease</td>
<td>1.6% (1.2 to 2.0)</td>
<td>2.8% (2.1 to 3.5)</td>
<td>0.7% (0.4 to 1.0)</td>
<td>3.2% (2.7 to 3.8)</td>
</tr>
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<td>Cerebrovascular disease</td>
<td>1.6% (1.1 to 2.3)</td>
<td>3.5% (3.2 to 3.9)</td>
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</table>
Epidemiological transition might explain the mortality pattern in premature cardiovascular diseases in Taiwan and may be a possible reason for the difficulty in reaching the 25 by 25 goal for men. In general, epidemiological transition describes the changing process of demographic and health-related factors such as population growth, ageing, morbidity, and mortality. Although the mortality pattern of cardiovascular diseases in most countries cannot be fully explained by epidemiological transition, the dramatic decreasing trend of cardiovascular diseases in high-income countries can still be largely explained by it. For example, a study by Santosa and colleagues indicated that the 25 by 25 goal will be difficult...
to reach in Sweden because they are in a late stage of epidemiological transition, and the probability of premature death from cardiovascular disease decreased by 48.3% from 1991 to 2006. In our findings, mortality from premature cardiovascular disease in women and men decreased by 66% and 42%, respectively, from 1990 to 2014, and the mortality pattern was stable after 2014. This is consistent with the pattern in the late stage of epidemiological transition.

Following the disease guidelines of the Ministry of Health and Welfare in Taiwan, cardiovascular disease can be categorised as heart disease, cerebrovascular disease and hypertensive disease. Nevertheless, we excluded hypertensive disease in this study design in order to avoid biased results. Based on the definition of this disease, hypertensive disease includes hypertension and its complications, and the risk factors targeted in the 25 by 25 goal included the control of hypertension. If we included hypertensive disease in the statistical analysis, the target hypertension (a 25% reduction in prevalence) would lead to a 25% reduction in hypertensive disease mortality.

We excluded physical activity in our study design because previous investigations in Taiwan were not appropriate. Most used self-assessment questionnaires and the levels and frequency of physical activity were subjective. They were also too limited by recall bias to reflect the long-term distribution of physical activity in the population. Therefore, we turned to an investigation of blood lipids because the criteria for hyperlipidaemia were objective and more comparable than the criteria for the amount of exercise. We also excluded alcohol and salt/sodium because previous studies were inadequate. The online database of long-term surveillance by the Nutrition and Health Survey in Taiwan was a possible choice for the population distributions of alcohol and salt/sodium intake. This surveillance included seven investigations since 1980, but the last two were not national in scope (one involving junior high school students in 2010 and the other of senior high school students in 2011). The most recent investigation of national scope was from 2005 to 2008. Nevertheless, this investigation was inadequate and did not reflect the population distribution after 2009 because of the large variations in the population distribution, dietary patterns, and nutritional intake.

We estimated the contributions of the four risk factors by the PAF method as was done in previous studies. Kontis and colleagues used a time-based population impact fraction (PIF), which is an extension of the PAF method, but they let the prevalence and relative risk of risk factors depend on the calendar year; Lim and colleagues used an ordinary PAF. Despite these differences, the results were similar, especially for the estimation of NCDs attributable to risk factors in men. The control of smoking was an effective way to prevent NCDs and cardiovascular disease.

Our study demonstrated the contributions of targeted risk factors, but there were limitations. First, we used the prevalence of hyperlipidaemia in 2009 to represent the population distribution in Taiwan. This assumed that the prevalence for each age group in 2009 would not be much different from the prevalence after 2009. This assumption is inappropriate, but the consequences are allowable because of the limited database. The investigation by the National Health Interview Survey in 2009 was the latest database which measured the prevalence of hyperlipidaemia. An earlier investigation was the Taiwan Nationwide Population-based Prevalence Survey of High Blood Pressure, Hyperglycemia, and High Blood Lipid Profile (usually abbreviated as Triple-H high-status) in 2002, and its follow-up survey in 2007. From the reports about Triple-H high-status in 2002 and 2007, the 5-year change in high blood lipids was not very different.

Second, we evaluated the contributions of single risk factors without further analysis of the contribution of multiple risk factors. Unfortunately, there was no available database which could be used. It might also be noted that middle and low income countries may be limited in terms of databases. Therefore, the analysis of single risk factors makes more sense for these countries. Finally, we chose a 5-year calculation for APC analysis in forecasting mortality to replace the single year calculation, and this was different from previous studies. This avoided a potential problem of forecasting error. The more points in time that are forecast, the greater the likelihood of errors. A total of 11 points in time are needed to forecast from 2014 to 2025 by single year calculations, but only two points by 5-year calculations. Therefore, the APC forecasting analysis was an appropriate method.

Although we believe that our study design and analysis were appropriate, there are some points worth considering in order to improve further research. Lloyd-Sherlock and colleagues argued that the 25 by 25 goal proposed by WHO and the UN is incompatible with the present needs of an ageing population, and indicated that because of institutional ageism, the survival of younger groups is more important than survival after age 70. According to cancer statistics in 2015 for Taiwan, 21,397 people who were more than 70 years old died of cardiovascular disease; that was 70% of the total deaths from cardiovascular disease. Therefore, we suggest that older people should be included in further research. Additionally, Bonita and Beaglehole argued that the 25 by 25 goal is insufficient for Asian women because secondhand smoke may be a factor for them, and the effect of a 30% reduction in tobacco use may be limited. Prevention of exposure to secondhand smoking should be considered as a component of the smoking target for women.

**CONCLUSIONS**

Our study developed a process to evaluate the contribution of risk factors related to NCDs, and the results provided an important reference to improve the rates of mortality from...
NCDs in the future. Our results suggested that smoking was the primary risk factor in the prevention of cardiovascular disease, and stringent control of cigarette smoking can help to achieve the 25 by 25 goal.

**Key messages**

What is already known about this subject? Cardiovascular diseases (heart disease plus cerebrovascular disease) have been the second and third leading causes of death in Taiwan since 1997. The 25 by 25 goal proposed by WHO was important in establishing relevant healthy policy, but no previous study provided relevant data in Taiwan.

What might this study add? We added the risk factor of hyperlipidaemia as a target in estimating the 25 by 25 goal in Taiwan. The trend of premature mortality in female cardiovascular disease can reach or exceed a 25% reduction before 2025 without any control of this risk factor. Smoking is the primary risk factor for premature cardiovascular mortality among men rather than the other risk factors of hypertension, diabetes, and hyperlipidaemia.

What might this impact clinical practice? Smoking cessation in the 45–64 year age group may lessen the risk of cardiovascular disease. The stringent control of cigarette smoking such as a 70% reduction in its prevalence can help Taiwan reach the 25% reduction in premature cardiovascular mortality in males before 2025.

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**Contributors** SYS was in charge of data collection, analysis, and wrote the first draft and the revision of the manuscript. WCL and KLC contributed to study design and wrote the part of first draft of the manuscript. TTC was in charge of data collection. All authors approved the final version of the manuscript.

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**Competing interests** None declared.

**Ethics approval** The proposal was approved by the IRB, National Taiwan University, and no consent from participants was needed because of anonymity.

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