Effects of Age, Time Period, and Birth Cohort on the Prevalence of Diabetes and Obesity in Korean Men.

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Running title: APC Effects on the Prevalence of Diabetes and Obesity

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ABSTRACT

Introduction: We examined changes in the prevalence of diabetes, obesity, and overweight in 412,881 Korean men in birth cohorts from 1933 to 1972 over 8 years from 1992 to 2000 and separately analyzed the effects of age, time period, and birth cohort.

Methods: The study included male employees of Korean government organizations and schools who were between 20 and 59 years of age in 1992. Diabetes was diagnosed on the basis of self-reports in 1992 or fasting blood glucose levels ($\geq 126$ mg/mL, 7.0 mmol/L). The age period cohort (APC) model was used to estimate the effects of age, time period, and birth cohort.

Results: In Korean male birth cohorts from 1933 to 1972, the age-specific prevalence of diabetes, obesity, and overweight in men 28-59 years of age increased annually by 0.41% (3.03 to 6.29%), 0.18% (0.70 to 2.16%), and 1.49% (23.48 to 35.41%), respectively from 1992 to 2000. The relative change in diabetes was largest among the younger cohorts (>400% increase over 8 years) and corresponded to the change in obesity. Apart from the contribution of age, clear cohort and period effects were evident for diabetes, although the magnitude of the effect was slightly less than that for obesity.

Conclusion: Prevention of diabetes through the control of obesity, particularly in young men, clearly needs to be emphasized.
The prevalence of diabetes has been increasing worldwide and is now epidemic in nature (1). The worldwide prevalence of diabetes in all age groups was estimated at 2.8% in 2000 and is predicted to be 4.4% by 2030 (2). The number of deaths from diabetes in 2000 was estimated at 2.9 million, equivalent to 5.2% of all deaths globally (3). In Korea, diabetes was the fifth leading cause of death and accounted for 4.8% of all deaths in 2004 (4).

This increase in the prevalence of diabetes is associated with various risk factors. These include modifiable or environmental factors, such as physical inactivity and obesity, and non-modifiable or biological factors, such as genetic factors, old age, race/ethnicity, and family history (5).

A study in Sweden reported a stable incidence rate, but an increasing prevalence of diabetes over time (6), and suggested that the increase in life expectancy was the main reason for the increasing prevalence (6,7). However, recent US studies have indicated an increase in both the prevalence and incidence of diabetes and suggested that the rapid increase in obesity was a major factor (8,9).

Short-term increases in weight and a high body mass index (BMI) are regarded as important factors in the increase in the prevalence of diabetes. Weight increases of 5 kg or more induced a population-attributable risk of 27% for type 2 diabetes, and the increase in BMI in the US during the 1980s may foreshadow a future large increase in the incidence of diabetes (10).

South Korea has seen remarkable economic growth over the past 30 years, with a 57-fold increase in the per capita gross national income (GNI) to $14,000 in 2004 (11). With economic growth, health indicators, such as life expectancy (from 63 years in 1973 to 76 years in 2001 (12)) and infant mortality (from 4.5% in 1970 to 0.62% in 2000 (13)), have also improved. However, there is concern that these demographic changes may increase the prevalence of diabetes, due both to an increase in obesity, especially among young people (14), and an increase in the number of elderly people, because of longer life expectancy.

We examined whether the prevalence of diabetes has increased recently in Korean men and whether any such increase involves changes across time and birth cohorts independent of population aging. It is meaningful to distinguish between the effect from environmental changes and that from biological aging, because of the difference in the implication for prevention. In addition, we also examined whether the prevalence of obesity and overweight show changes similar to the prevalence of diabetes, as they represent modifiable factors associated with the increased prevalence of diabetes in Korea.

**METHODS**

Our study population was employed in government organizations and schools throughout the country. The employees received biennial health examinations by the Korean National Health Insurance Corporation. Of the study population 60% lived in metropolitan areas or large cities and 40% lived in smaller provincial cities or rural towns. Details of the cohort selection method (Korean National Health Service Study, KNHS), the health examination, and the brief questionnaire used have been published previously (15,16). Women were excluded from this study because the number of female civil servants was too small, and their age distribution differed markedly from that of men. A trained nurse measured the height and weight of each subject, who wore light clothing and no shoes. A fasting blood sample was obtained at medical institutions equipped with standardized, high-quality laboratories authorized by the Korea Association of Clinical Pathology and Quality Control.
Diabetes was defined based on a history of physician-diagnosis or a fasting blood glucose (FBG) level of (126 mg/mL ((7.0 mmol/L), in accordance with the new American Diabetes Association (ADA) criteria (17). Information on physician-diagnosed diabetes was collected by asking the following question in a self-administered questionnaire, “Have you had a history of diabetes diagnosed by a doctor?” Body mass index (BMI) was calculated as body weight, in kilograms, divided by the square of the height, in meters. Obesity and overweight were defined as BMI ≥30 and BMI ≥25, respectively.

In total, 412,881 men from birth cohorts from 1933 to 1972 with available health examination data on weight, height, and FBG in 1992, 1996, and 2000 were included in this study.

The age-standardized prevalence was calculated using standard population data for Korea in 2000. The relative change was defined as the difference from 1992 to 2000, divided by the baseline level, and expressed as a percentage.

To estimate the effects of age, time period, and birth cohort on the prevalence of diabetes, we developed an age-period-cohort (APC) model with Poisson regression analysis. This statistical model is generally used in epidemiology studies (18,19) and distinguishes among the effects from age, period, and cohort, which are time-related variables. Age effects are associated with different age groups, period effects affect all ages simultaneously over time, and cohort effects involve changes across groups with the same birth year. Age effects reflect biological changes and are important in the development of chronic diseases. Period and cohort effects reflect environmental changes. In particular, cohort effects represent early exposures to environmental factors that have different health risks in specific cohorts. The APC model assumes a linear dependency among age, period, and cohort. To solve the non-identifiability problem of the full APC model, we used the general method by setting constraints on the parameters to be estimated (20). The dependent variables (the prevalence of diabetes and obesity) were log transformed. The estimates were obtained from the model

$$\phi_{ijk} = \mu + \alpha_i \text{Age} + \beta_j \text{Period} + \gamma_k \text{Cohort} + \epsilon_{ijk},$$

where $\phi_{ijk}$ represents the natural logarithm of prevalence of diabetes or obesity, $\mu$ the intercept term, $\alpha_i$ the effect of age $i$, $\beta_j$ the effect of period $j$, $\gamma_k$ the effect of cohort $k$, and $\epsilon_{ijk}$ the error term, respectively.

We did not analyze the prevalence of overweight using the APC model, because it seemed too high for a Poisson regression. The Genmod function in SAS was used to analyze the APC model.

RESULTS

For the birth cohorts from 1933 to 1972, the prevalence of diabetes, obesity, and overweight in Korean men increased annually by 0.61% (2.46 to 7.33%), 0.18% (0.65 to 2.09 %), and 1.89% (20.31 to 35.43%) respectively over the 8-year period. In Korean men aged 28-59 years, the age-standardized prevalence of diabetes, obesity, and overweight also increased annually by 0.41% (3.03 to 6.29%), 0.18% (0.70 to 2.16%), and 1.49% (23.48 to 35.41 %), respectively, over the same 8-year period. The relative change in the prevalence of diabetes, obesity, and overweight over the 8 years from 1992 to 2000 was determined for the birth cohort from 1933 to 1972. The relative increase in diabetes was higher in the younger birth cohorts (>400% increase over 8years) and corresponded to the change in obesity (Table 1).

The age-specific prevalence in the group at intervals of 4 years of age for diabetes, obesity, and overweight were plotted against birth cohort and time period for Korean men between 28 and 59 years of age (Fig. 1). Each line connects the values for the same age group in different birth cohort and time period.
For example, line 5 represents the group aged 44-47 in all graphs. At this age, the birth cohort of 53-56 had a higher prevalence of diabetes compared to the older birth cohort of 45-48. Likewise, men aged 44-47 had a higher prevalence in year 2000 compared to those in year 1992. The younger birth cohort (those born more recently) and the most recent year had higher age-specific prevalence.

Figure 2 shows the prevalence ratios for age, time period, and birth cohort, estimated by the APC model. Each graph indicates the independent effect of age, time period, or birth cohort on the prevalence of diabetes (DM) or obesity (OB), adjusting for the other factors. The leftmost group in the X axis serves as the baseline and thus has the ratio of 1 (=e^0). The Y axes were shown in the scale of natural logarithm.

Although age was a relatively important predictor for the prevalence of diabetes, we also observed an increasing trend for the prevalence of diabetes in younger birth cohorts and the latest period after adjusting for the age effect through the full APC model, although the magnitude of the effect was slightly less than that for obesity.

DISCUSSION

Our study showed that the prevalence of diabetes in Korean men aged 28-59 years increased over the 8-year period from 1992 to 2000, and the relative change was greater in the younger birth cohorts. To our knowledge, there are few existing data on time-related trends in the prevalence of diabetes in adult Asian populations that have used repeated measurements of the same individuals to analyze the age, period, and cohort effects.

Limited number of serial cross-sectional studies has reported the change of the prevalence of diabetes in Asia. In a representative population in Chennai (representing urban India), the prevalence of diabetes was 8.3%, 11.6%, 13.5%, and 14.3% in 1989, 1995, 2000, and 2004 respectively.

The age of onset of diabetes seemed to become younger over time. The authors stated that increased diabetes prevalence with an earlier onset would have a great impact on the national health and economy (21). In a national survey of the population in Singapore aged 18-69 years, the prevalence of diabetes increased from 4.7% in 1984 to 8.4% in 1992 (22). In a study of the Chinese population aged 25-64 years, the prevalence of diabetes was 2.5% in 1994 (23) and another study of the Chinese population aged 35-74 years reported a prevalence of diabetes of 5.5% in 2000-2001 (24). In Bangladesh, the prevalence of diabetes rose from 2.23% in 1990 (25) to 3.8% in 1999-2000 (26).

In our study, the increase in the age-standardized overall prevalence of diabetes and obesity for ages 28 to 59 years from 1992 to 2000 might have resulted from environmental effects, such as changes in diet and physical activity. However, limited data are available for this study period. The total number of registered private cars from 1992 to 2000 increased 2.4 fold (from 4,810,000 to 11,390,000) (27) and the daily calorie intake per person increased from 1875 Kcal in 1992 to 1976 Kcal in 2001 and the major preferred nutrient source shifted from carbohydrates to fat and meats (28).

In general, changes in the prevalence of diabetes and obesity over time may arise from the combination of population aging and environmental effects, such as changes in diet and physical activity across time and birth cohorts. To assess the magnitude of environmental effects on diabetes and obesity apart from aging, we used the APC model. The full APC model (Fig. 2) separates age, period, and birth cohort effects. The effect of age on diabetes is well-known and may be related to increasingly impaired β-cell function with age (29). Apart from the age effect, we also found a time period effect for all ages and birth cohort effects in younger birth cohorts. These patterns in the prevalence
of diabetes closely follow those of obesity in this study, suggesting that the increase in obesity is the major cause of the diabetes epidemic. Obesity can be particularly important in triggering genetic elements that cause diabetes (30).

Our analysis by birth cohort indicated that the age of onset of diabetes in Korean men is decreasing. This is an important public health issue, because early-onset diabetes can produce more aggressive complications, such as macro- and microvascular disease, diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy, over extended periods. Hillier and Pedula (31) found that compared to typical adult-onset diabetes diagnosed at ≥ 45 years of age, early-onset adults with diabetes, diagnosed at 18-44 years of age, had an 80% increased risk of requiring insulin therapy; they were also 20% more likely to develop micro-albuminuria and had a much higher relative risk of cardiovascular disease. In addition, this study by Hillier and Pedula demonstrated that a higher BMI was a major factor for early-onset diabetes (BMI in early-onset and usual-to-late-onset was 37.2 versus 33.3). We found that the prevalence of obesity and overweight was increased greatly in the younger generation and birth cohorts. This rapid increase in weight in the younger generation and cohorts may be major cause of the early onset of diabetes.

Several factors may explain the rapid increase in the prevalence of obesity and overweight in younger generations and birth cohorts. Older generations may be less accepting of obesogenic environments and may be slower to adopt new lifestyles than younger generations and be more likely to maintain their old habits of diet and physical activity. According to Korean national data, shifting from carbohydrates to fat and meats as the major preferred nutrient source and higher consumption of snacks, fast food, and soft drinks were especially remarkable in younger Koreans (28). Furthermore, the time spent using computers was markedly higher in the younger generation (24.3% in 20 year-olds versus 1.7% in 50 year-olds) (32). As a consequence of the rapid economic growth in Korea and the ready acceptance of obesogenic environments, younger generations may be more seriously affected by obesity than older generations.

Although our findings suggest that the increase in diabetes resulted from the increase in obesity, the prevalence of obesity (BMI≥30) was still very low (2%) in our study, compared to the US population (30%) (9). It appears puzzling that, even at such a relatively low level of obesity, the prevalence of diabetes is approaching a level (7.3% at age 28-67 years in 2001) similar to that in the US population (8.2% at age 20 - 74 years in 1999-2000) (9).

There are several possible explanations. First, BMI may not have the same implications for Asians and Caucasians, because Asians have a lower BMI for a given percentage of body fat (33). Second, Asians may have more visceral adipose tissue, after adjusting for age and total body fat (34). Third, a rapid increase in BMI over a relatively short time, even for people of average weight, may be a major factor in the development of diabetes (35). As discussed above, the larger relative changes in the prevalence of diabetes among younger men in our study may reflect the pressure of the obesogenic environment in modern Korean society. This high environmental demand may be causing obesity to increase at a rate above the level of adaptability, leading to the higher prevalence of diabetes, relative to the current prevalence of obesity. This suggestion is also consistent with the findings of an earlier Korean study, showing that in younger men, those in whom obesity increased faster had higher cardiovascular mortality (36).

Our study has several limitations. First, we defined diabetes as having a FBG level ≥126mg/dL, following the new ADA criteria.
Although using FBG gives a slightly lower estimate of the prevalence of diabetes than does the oral glucose tolerance test (OGTT), according to the World Health Organization (WHO) (37,38), FBG has been recommended for epidemiological studies because of time and cost considerations (39). Second, our 2000 data showed a lower level of diabetes prevalence in men than was reported in national data in 2001 (8.1% in men (40) versus 7.3% for age-standardized prevalence). Diabetes may be associated more with a lower than higher socioeconomic status (5). Our study population was employed in government organizations and schools, where employment security and socioeconomic position were higher than in the average working population in Korea, and most of them (60%) lived in metropolitan area or large cities. In addition, the age range differed somewhat between the national data and this study. Specifically, the national data included more elderly people (the age range was 20-99 in the national data versus 28-67 in this study). Furthermore, use of antidiabetic medications was not utilized for diabetes definition in our study due to lack of data. It could also underestimate diabetes prevalence in our study.

In conclusion, the information obtained from our study provides a better understanding of the effect of age, time period, and cohort on the prevalence of diabetes and obesity. Apart from the contribution of age, clear cohort and period effects were present for diabetes, although the magnitude of the effect was less than that for obesity. Prevention of diabetes through the control of obesity, such as by promoting physical activity and balanced healthy diet, clearly needs to be emphasized particularly in young men. In addition, further studies to address the causes of the increase in obesity and diabetes are needed.

ACKNOWLEDGMENTS
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REFERENCES

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TABLE 1. Number of participants in each birth cohort in three surveys; and the prevalence of diabetes, obesity and overweight in Korean men by birth cohort and survey year.

<table>
<thead>
<tr>
<th>Birth cohort (year)</th>
<th>N</th>
<th>Age (years)</th>
<th>Diagnosed diabetes</th>
<th>FBG * ≥126 (1)</th>
<th>FBG ≥126 (2)</th>
<th>Obesity †</th>
<th>Overweight ‡</th>
<th>Age (years)</th>
<th>FBG * ≥126 (3)</th>
<th>FBG ≥126 (4)</th>
<th>Obesity †</th>
<th>Overweight ‡</th>
<th>Relative change by birth cohort from 1992 to 2000**</th>
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</thead>
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<tr>
<td>1969~72</td>
<td>2,499</td>
<td>20-23</td>
<td>0.04</td>
<td>0.44</td>
<td>0.48</td>
<td>0.56</td>
<td>7.88</td>
<td>24-27</td>
<td>1.32</td>
<td>1.80</td>
<td>1.88</td>
<td>21.29</td>
<td>28-31 1.04 2.84 3.40 32.81 492 507 316</td>
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<tr>
<td>1965~68</td>
<td>22,313</td>
<td>24-27</td>
<td>0.04</td>
<td>0.58</td>
<td>0.62</td>
<td>0.38</td>
<td>11.50</td>
<td>28-31</td>
<td>1.03</td>
<td>1.65</td>
<td>1.29</td>
<td>24.83</td>
<td>32-35 1.86 3.51 2.40 34.87 466 532 203</td>
</tr>
<tr>
<td>1961~64</td>
<td>52,560</td>
<td>28-31</td>
<td>0.08</td>
<td>0.78</td>
<td>0.87</td>
<td>0.57</td>
<td>17.23</td>
<td>32-35</td>
<td>1.22</td>
<td>2.08</td>
<td>1.21</td>
<td>26.31</td>
<td>36-39 2.01 4.09 1.93 34.29 370 239 99</td>
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<tr>
<td>1957~60</td>
<td>86,097</td>
<td>32-35</td>
<td>0.18</td>
<td>1.10</td>
<td>1.28</td>
<td>0.64</td>
<td>20.56</td>
<td>36-39</td>
<td>1.70</td>
<td>2.98</td>
<td>1.12</td>
<td>27.89</td>
<td>40-43 2.53 5.51 1.79 35.36 330 180 72</td>
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<tr>
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<td>36-39</td>
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<td>1.60</td>
<td>1.99</td>
<td>0.70</td>
<td>23.93</td>
<td>40-43</td>
<td>2.25</td>
<td>4.24</td>
<td>1.20</td>
<td>30.48</td>
<td>44-47 3.22 7.47 1.87 37.51 275 167 57</td>
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<tr>
<td>1949~52</td>
<td>65,222</td>
<td>40-43</td>
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<td>3.03</td>
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<td>25.37</td>
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<td>3.03</td>
<td>6.06</td>
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<td>2.96</td>
<td>4.03</td>
<td>0.78</td>
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<td>3.61</td>
<td>7.63</td>
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<td>48-51</td>
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<td>30.39</td>
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<td>52-55</td>
<td>1.81</td>
<td>3.96</td>
<td>5.77</td>
<td>0.77</td>
<td>27.38</td>
<td>56-59</td>
<td>3.80</td>
<td>9.57</td>
<td>1.15</td>
<td>31.11</td>
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<td>56-59</td>
<td>2.00</td>
<td>5.01</td>
<td>7.01</td>
<td>0.87</td>
<td>26.77</td>
<td>60-63</td>
<td>5.27</td>
<td>12.28</td>
<td>1.20</td>
<td>30.44</td>
<td>64-67 6.21 18.49 1.20 34.58 164 38 29</td>
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<tr>
<td>1929~32</td>
<td>412,881</td>
<td>Mean</td>
<td>0.77</td>
<td>2.23</td>
<td>2.99</td>
<td>0.67</td>
<td>21.29</td>
<td>2.86</td>
<td>5.70</td>
<td>1.3</td>
<td>28.62</td>
<td>3.80</td>
<td>9.22 1.94 35.72</td>
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<tr>
<td></td>
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<td>Age standardized prevalence§ for birth cohort of 1972-1933</td>
<td>2.46</td>
<td>0.65</td>
<td>20.31</td>
<td>4.61</td>
<td>1.27</td>
<td>27.92</td>
<td>7.33</td>
<td>2.09</td>
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<tr>
<td></td>
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<td>Age standardized prevalence§ for age of 28-59</td>
<td>3.03</td>
<td>0.70</td>
<td>23.48</td>
<td>4.55</td>
<td>1.18</td>
<td>28.79</td>
<td>6.29</td>
<td>2.16</td>
<td>35.41</td>
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</tr>
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</table>

(1) : self reporting on physician diagnosed diabetes in 1992
(2) : FBG ≥ 126 mg/dl in 1992 without diagnosed diabetes
(3) : FBG ≥ 126 mg/dl in 1996 without diagnosed diabetes or FBG≥126 mg/dl in 1992
(4) : FBG ≥ 126 mg/dl in 2000 without diagnosed diabetes or FBG≥126 mg/dl in 1992 or 1996
*FBG : Fasting Blood Glucose, † Obesity : Body Mass Index of 30 or more, ‡Overweight : Body Mass Index of 25 or more
§The age-standardized prevalence was calculated using the standard population data for Korea in 2000
** The relative change was defined as the difference from 1992 to 2000, divided by the baseline level, and expressed as a percentage
**FIGURE 1.** The age-specific prevalence for diabetes, obesity, and overweight against birth cohort and time period for Korean men between 28 and 59 years of age

Age group: 1=28-31, 2=32-35, 3=36-39, 4=40-43, 5=44-47, 6=48-51, 7=52-55, 8=56-59 (years)

Each line connects the values for the same age group in different birth cohort and time period.
FIGURE 2. Estimated prevalence ratio of diabetes (DM) and obesity (OB) by age, period and cohort model in Korean men

The Y axis represents the prevalence ratio, $e^{\alpha_i}$, $e^{\beta_j}$, or $e^{\gamma_k}$, in the scale of natural logarithm, for the given group in the X axis compared to the leftmost group whose Y value is $e^0=1$. Other tick marks in the y axis represent $e^1=2.7$, $e^2=7.4$, $e^5=148.4$, etc. See text for more details.