Acne in Adolescence and Cause-specific Mortality: Lower Coronary Heart Disease but Higher Prostate Cancer Mortality

The Glasgow Alumni Cohort Study

B. Galobardes¹, G. Davey Smith¹, M. Jeffreys², S. Kinra¹, and P. McCarron³

¹ Department of Social Medicine, University of Bristol, Bristol, United Kingdom.
² Centre for Public Health Research, Massey University, Wellington, New Zealand.
³ Department of Epidemiology and Public Health, The Queen’s University of Belfast, Belfast, United Kingdom.

Received for publication August 16, 2004; accepted for publication January 27, 2005.

Androgen level or androgen activity is implicated in several health outcomes, but its independent role remains controversial. This study investigated the association between history of acne in young adulthood, a marker of hormone activity, and cause-specific mortality in the Glasgow Alumni Cohort Study. Male students who attended Glasgow University between 1948 and 1968 and participated in voluntary health checks reported history of acne (n = 11,232). Vital status has been traced, and risk factors in adulthood are known for about 50% of the participants. Those with a history of acne were more often nonsmokers while university students and tended to be from a lower socioeconomic position. The two groups did not differ in other adolescent (height, body mass index, blood pressure, and number of siblings) or in most adult risk factors. Students who reported a history of acne had a lower risk of all-cause (hazard ratio = 0.89, 95% confidence interval (CI): 0.76, 1.04) and coronary heart disease (hazard ratio = 0.67, 95% CI: 0.48, 0.94) mortality but had some evidence of a higher risk of prostate cancer mortality (hazard ratio = 1.67, 95% CI: 0.79, 3.55). This study shows that androgen activity during adolescence may protect against coronary heart disease but confer a higher risk of prostate cancer mortality.

acne vulgaris; androgens; coronary disease; hormones; mortality; prostatic neoplasms

Abbreviations: CI, confidence interval; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision.

Editor’s note: An invited commentary on this article appears on page 1102.

Testosterone has been implicated in prostate cancer development and, although once thought to explain the higher risk of coronary heart disease in men, its role in health outcomes is controversial (1). A recent review concluded that circulating androgens have a neutral or protective effect on coronary heart disease risk, while acknowledging that firm conclusions cannot be drawn from the currently available evidence (2). Observational studies have examined the association between markers of hormonal status and disease. Men who suffered myocardial infarction shaved less frequently, an indication of low androgen activity, than did a group of controls (3). In a recent prospective study, Ebrahim et al. (4) reported higher all-cause, coronary heart disease, and stroke mortality among men who shaved less frequently. On the other hand, hair loss,
a marker of greater androgen activity, has been associated with a higher risk of coronary heart disease.

Acne vulgaris first develops at the onset of puberty as a result of hormonal changes, although additional mechanisms are also involved (6). The initial lesion, the comedo, fills with lipids because of increased activity of the sebaceous gland and becomes visible under androgen stimulation. Inflammatory acne results from the action of Propionibacterium acnes, a pathogen present in normal skin flora which metabolizes sebaceous triglycerides, consuming glycerol and releasing free fatty acids, neutrophil, and complement attractants (7). Results from a twin study (8) and a study demonstrating increased risk of acne in first-degree relatives of adults with persistent acne (9) suggest that acne is partially inherited. No major environmental exposure has been consistently reported. Acne can be a marker of increased androgen activity during puberty and, if acne risk is related to health outcomes, this would support a potential role of hormones in disease etiology.

Androgens are the main hormones involved in the development of acne, although the specific mechanisms are not known. In addition, acne is rare in adulthood despite androgen levels remaining high. Other hormones, such as growth hormone and insulin-like growth factors, increase in puberty, raising the possibility that they contribute to acne development, and they are also considered to be linked to adult disease.

To our knowledge, the association between history of acne in young adulthood and mortality has not been studied. We investigated the hypothesis that a marker of greater androgen activity during adolescence may affect subsequent risk of chronic disease in a cohort of former students who underwent clinical examinations at Glasgow University between 1948 and 1968 and for whom a history of acne and information on cause-specific mortality and selected disease risk factors are available.

MATERIALS AND METHODS

Detailed information on the Glasgow Alumni Cohort is available elsewhere (10). Briefly, between 1948 and 1968, students at Glasgow University were invited to attend a health examination carried out by physicians. Information on sociodemographic characteristics, health behaviors, and medical history, including history of acne, was obtained by means of questionnaire. Data collected during the physical examination included measurements of height, weight, and blood pressure. A total of 11,756 men, representing about 50 percent of the complete male student population, participated in the study. Since 1998, approximately 85 percent (n = 9,919) of the male cohort has been successfully traced through the National Health Service Central Register, which provides continuous updates on the date and cause of death for members of the cohort. There were 1,315 deaths up to February 2004. During 2001 and 2002, members of the cohort that were still alive were contacted through a postal questionnaire (n = 8,410) that sought to determine additional childhood information and adult sociodemographic characteristics and risk factors. About 50 percent of the male cohort (n = 4,191) responded to the adult postal follow-up. The authors obtained ethical approval for the study and informed consent from the participants.

Only men are included in this report because of the small number of women attending the university from 1948 to 1968 and the low number of female deaths. Participants with missing information on acne history were excluded (n = 39), as were students aged more than 30 years at the time of examination (n = 479) and those with unknown date of death (n = 6), resulting in a total of 11,232 men included in these analyses.

Variable description

History of acne was ascertained during the student’s visit to the health services of the university. It was noted in the medical history section of the questionnaire, but details were not available on how the history of acne was measured or on any treatment received. Given the prevalence of history of acne in this cohort, we hypothesize that mainly severe acne was recorded (11). Childhood socioeconomic position was assigned by coding the father’s occupation into social class, a five-point scale from I (most affluent) to V (least affluent), using the Registrar General’s classification (12, 13). Age (years), number of siblings, height (meters), body mass index (kg/m²), systolic and diastolic blood pressure (mmHg), current smoking habit, occasional and regular alcohol consumption, and history of acne were recorded while the student was at the university.

Among those who participated in the postal follow-up in 2001–2002, the following adult characteristics were obtained: adult socioeconomic position based on the main occupation held (from I to V, height (meters), body mass index (kg/m²), marital status, smoking (never, former, or current), physical activity (yes/no to a question about performing sufficient exercise to work up a sweat) (14), alcohol consumption in the last 12 months (≤1–2 days/week vs. ≥3 days per week), and physician’s diagnosis of hypertension (present/absent).

Cause-specific mortality

International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10), codes were used to group cause-specific mortality: coronary heart disease (ICD-9 codes 410–414 and 429.2; ICD-10 codes I20–I25 and I26.6); stroke (ICD-9 codes 431–438; ICD-10 codes I61–I69 and G45); lung cancer (ICD-9 code 162; ICD-10 code C34); prostate cancer (ICD-9 code 185; ICD-10 code C61); colon cancer (ICD-9 code 153; ICD-10 code C18); and external causes of death including accidents, suicide, and violence (ICD-9 codes 800–999 and E800–E999; ICD-10 codes S00–T98 and V01–Y89).

Statistical analysis

Cox proportional hazards models were used to estimate the risk of overall and cause-specific mortality associated with history of acne in young adulthood, adjusting for examination date, socioeconomic position, and several disease risk factors measured at the university, which are potential confounders of the association between acne and cause-specific mortality.
It was not possible to adjust for adult risk factors, because to date there have been few deaths in those who participated in the 2001–2002 follow-up and for whom adult characteristics are known, but we present a descriptive analysis of this subgroup of former students.

RESULTS

A history of acne was reported by 2,024 students (18.0 percent). Age, height, body mass index, systolic and diastolic blood pressure, and number of siblings at the university were similar among those with and those without a history of acne (table 1). Students with a history of acne were more often nonsmokers at the university (68.20 percent vs. 65.59 percent; \(p = 0.022\)) and from a lower socioeconomic background. In adulthood, those with a history of acne were more likely to have never smoked (47.74 percent vs. 43.34 percent; \(p = 0.027\)) (table 2). There were no differences in adult social class, marital status, height, body mass index, physical activity, alcohol consumption, fat consumption, or hypertension.

### TABLE 1. Age-adjusted means and prevalence of childhood and young adulthood characteristics,* by history of acne, Glasgow Alumni Cohort Study, 1948–1968 (baseline)

<table>
<thead>
<tr>
<th></th>
<th>History of acne (mean (SD))</th>
<th>No history of acne (mean (SD))</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) ((n = 11,232))</td>
<td>20.0 (2.40)</td>
<td>20.7 (2.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm) ((n = 11,196))</td>
<td>174.96 (6.37)</td>
<td>174.78 (6.35)</td>
<td>0.255</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2)) ((n = 11,189))</td>
<td>21.57 (2.23)</td>
<td>21.60 (2.23)</td>
<td>0.549</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg) ((n = 11,182))</td>
<td>131.06 (13.01)</td>
<td>130.58 (12.97)</td>
<td>0.135</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg) ((n = 11,159))</td>
<td>77.02 (8.52)</td>
<td>77.36 (8.49)</td>
<td>0.114</td>
</tr>
<tr>
<td>No. of siblings ((n = 11,229))</td>
<td>1.71 (1.56)</td>
<td>1.72 (1.56)</td>
<td>0.723</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No. %</th>
<th>No. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father’s social class I–II ((n = 10,830))</td>
<td>1,948</td>
<td>53.25</td>
</tr>
<tr>
<td>No smoking ((n = 10,703))</td>
<td>1,943</td>
<td>68.20</td>
</tr>
<tr>
<td>Occasional or regular alcohol consumption ((n = 9,584))</td>
<td>1,798</td>
<td>55.30</td>
</tr>
</tbody>
</table>

* Age-adjusted values for all variables except age.
† SD, standard deviation.

### TABLE 2. Age-adjusted means and prevalence of descriptive adulthood characteristics in the subgroup of participants that responded to a postal follow-up, by history of acne, Glasgow Alumni Cohort Study, 2001–2002

<table>
<thead>
<tr>
<th></th>
<th>History of acne (mean (SD*))</th>
<th>No history of acne (mean (SD))</th>
<th>(p) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm) ((n = 4,031))</td>
<td>176.41 (6.52)</td>
<td>176.47 (6.50)</td>
<td>0.809</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2)) ((n = 3,961))</td>
<td>25.50 (3.14)</td>
<td>25.52 (3.13)</td>
<td>0.883</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>No. %</th>
<th>No. %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married or living together ((n = 4,044))</td>
<td>770</td>
<td>90.56</td>
</tr>
<tr>
<td>Adult social class I ((n = 2,971))</td>
<td>578</td>
<td>51.28</td>
</tr>
<tr>
<td>Never smoked ((n = 4,058))</td>
<td>774</td>
<td>47.74</td>
</tr>
<tr>
<td>No physical activity ((n = 4,044))</td>
<td>774</td>
<td>33.82</td>
</tr>
<tr>
<td>Hypertension ((n = 4,010))</td>
<td>765</td>
<td>30.54</td>
</tr>
<tr>
<td>Alcohol consumption on 1–2 days/week or less ((n = 4,018))</td>
<td>763</td>
<td>38.92</td>
</tr>
</tbody>
</table>

* SD, standard deviation.
Men with a history of acne measured at the university had lower overall (hazard ratio (HR) = 0.89, 95 percent confidence interval (CI): 0.76, 1.04), cardiovascular (HR = 0.74, 95 percent CI: 0.57, 0.95), and coronary heart disease (HR = 0.72, 95 percent CI: 0.55, 0.94) mortality (table 3). There was some evidence that these men had a higher risk of death from prostate cancer (HR = 1.27, 95 percent CI: 0.75, 2.15). The history of acne was not associated with mortality due to stroke, lung cancer, colon cancer, or external causes. Adjustment for childhood socioeconomic circumstances and for behavioral and biologic risk factors present while the student attended the university did not affect these estimates. Excluding people with missing confounders did not change the estimates in models 1 and 2.

To further control for potential residual confounding due to a higher proportion of nonsmokers among those with a history of acne, we investigated the mortality pattern among the students who reported being nonsmokers at the university. For those reporting a history of acne compared with those who did not, the fully adjusted hazard ratio was 0.82 (95 percent CI: 0.66, 1.02) for all causes of death, 0.68 (95 percent CI: 0.46, 0.99) for cardiovascular disease, 0.65 (95 percent CI: 0.41, 1.02) for coronary heart disease, and 2.17 (95 percent CI: 0.94, 5.01) for prostate cancer mortality.

**Androgen activity**

Several hormones are implicated in the development of acne and, although androgens play a key role in this process, the specific mechanisms involved are not well understood. Administering androgens produces acne, and castrated men or men with genetic mutations that affect androgen metabolism or receptor function do not develop acne (15). Women with acne benefit from antiandrogen therapy (16) and from oral contraceptive therapy, which is believed to reduce androgen metabolites (17). However, it is not clear why acne spontaneously improves and disappears in most people. While acne recedes in late adolescence, androgen levels remain high until late adulthood, indicating that androgens alone cannot be responsible for the presence of acne (18, 19). Given the prevalence of history of acne among the Glasgow Alumni Cohort, we hypothesized that mainly severe cases of acne were recorded. However, androgen levels do not always correlate with acne severity (20) and, in studies reporting higher hormonal levels in acne patients, these are nevertheless within the normal physiologic range (21). In addition, many men do not develop noticeable levels of acne despite their high levels of androgens compared with women. Thus, whether it is only severe acne that relates to adult mortality risk cannot be assessed in our study.

Other markers of androgen activity have been previously related to health outcomes. Infrequent shaving, indicative of low androgen levels or of low androgen activity, is related to higher coronary heart disease and stroke risk (4). The sensitivity of sexual hair follicles to androgens depends on their distribution. Tenfold higher androgen concentrations are needed for the beard to appear compared with pubic hair, although there is great individual variability in the actual level of androgens (19). Greater sexual activity, another marker of higher androgen concentrations, was found to protect from coronary heart disease and, less clearly, from stroke in the Caerphilly Study (22). These sex-related characteristics—development of facial hair and frequency

**DISCUSSION**

A history of acne in young adulthood was associated with lower overall, cardiovascular disease, and coronary heart disease mortality but with higher prostate cancer mortality. This mortality pattern was also observed when analyses were restricted to nonsmokers. Adjustment for several socioeconomic and disease risk factors measured at the university did not affect the associations. In addition, the observed pattern of cause-specific mortality suggests that confounding is unlikely to explain these results.

---

**TABLE 3.** Hazard ratio and 95% confidence interval of all-cause and cause-specific mortality among men with a history of acne compared with those who did not have acne, Glasgow Alumni Cohort Study, 1948–2004

<table>
<thead>
<tr>
<th>Causes of death</th>
<th>No. of deaths</th>
<th>Hazard ratio Model 1*</th>
<th>95% confidence interval</th>
<th>No. of deaths</th>
<th>Hazard ratio Model 2†</th>
<th>95% confidence interval</th>
<th>No. of deaths</th>
<th>Hazard ratio Model 3‡</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>1,315</td>
<td>0.89 (0.76, 1.03)</td>
<td></td>
<td>1,286</td>
<td>0.87 (0.74, 1.01)</td>
<td></td>
<td>1,213</td>
<td>0.89 (0.76, 1.04)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>527</td>
<td>0.74 (0.57, 0.95)</td>
<td></td>
<td>518</td>
<td>0.72 (0.55, 0.94)</td>
<td></td>
<td>482</td>
<td>0.74 (0.56, 0.96)</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>369</td>
<td>0.67 (0.49, 0.93)</td>
<td></td>
<td>362</td>
<td>0.65 (0.47, 0.90)</td>
<td></td>
<td>336</td>
<td>0.67 (0.48, 0.94)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>88</td>
<td>1.27 (0.75, 2.15)</td>
<td></td>
<td>88</td>
<td>1.26 (0.74, 2.14)</td>
<td></td>
<td>81</td>
<td>1.24 (0.71, 2.17)</td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>87</td>
<td>1.25 (0.73, 2.13)</td>
<td></td>
<td>83</td>
<td>1.22 (0.71, 2.11)</td>
<td></td>
<td>80</td>
<td>1.27 (0.72, 2.24)</td>
<td></td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>43</td>
<td>1.58 (0.78, 3.20)</td>
<td></td>
<td>41</td>
<td>1.48 (0.71, 3.12)</td>
<td></td>
<td>37</td>
<td>1.67 (0.79, 3.55)</td>
<td></td>
</tr>
<tr>
<td>Colon cancer</td>
<td>47</td>
<td>1.03 (0.48, 2.21)</td>
<td></td>
<td>47</td>
<td>1.02 (0.48, 2.19)</td>
<td></td>
<td>43</td>
<td>1.01 (0.45, 2.27)</td>
<td></td>
</tr>
<tr>
<td>External causes</td>
<td>79</td>
<td>1.05 (0.60, 1.85)</td>
<td></td>
<td>76</td>
<td>1.02 (0.57, 1.82)</td>
<td></td>
<td>72</td>
<td>1.08 (0.60, 1.94)</td>
<td></td>
</tr>
</tbody>
</table>

* Model 1: adjusted for date of examination at Glasgow University Health Service.
† Model 2: adjusted for date of examination, father’s socioeconomic position, and number of siblings.
‡ Model 3: adjusted for date of examination, father’s socioeconomic position, number of siblings, height, body mass index, cigarette consumption, and systolic blood pressure.
of intercourse—and acne have a common androgen-related basis initiated at puberty.

Baldness, in particular of the male pattern (i.e., vertex but not frontal baldness) (23), baldness occurring at a younger age (24), and progression of baldness (25) are markers of higher androgen activity but, unlike other markers of androgen activity, are associated with higher risk of coronary heart disease (5, 23–25). The paradoxical effects of higher androgen activity in the form of hair loss (baldness) and of higher facial hair (beard growth) point to local or tissue-specific differences in androgen effects, which could also be relevant for the association of androgens with health outcomes.

The role of androgens with regard to health is not established, but debate about the potential benefits and risks of androgen replacement therapy in aging men is increasingly found in the medical literature. Clinical trials, particularly of long exposure to androgens, are rare (26). The Committee on Assessing the Need for Clinical Trials of Testosterone Replacement Therapy concluded that there is no sufficient evidence that testosterone treatment is beneficial in elderly men with symptoms that might be caused by hypogonadism (27). In a recent review, the authors reported conflicting results within studies and found that most epidemiologic studies lacked control for potential confounders (2). Among the studies that attempted to control for confounders, testosterone and dihydrotestosterone appeared to have a protective effect on cardiovascular disease (2). Another review found a potential coronary heart disease benefit from high levels of androgens (28). A case-control study reported lower levels of androgens among cases of coronary artery disease compared with controls, although there was no dose relation between androgen levels and severity of coronary disease (29). The Rotterdam Study reported an inverse association between free testosterone levels and aortic atherosclerosis among men who were nonsmokers (30). Low levels of testosterone seem to correlate with higher levels of atheroma, mediated by coronary artery vasodilatation and vascular inflammation (31), and with a lower ejection fraction of the left ventricle in males (32). However, in a twin study, no correlation was found between endogenous sex hormones and future coronary heart disease risk (33). The cardioprotection conferred by testosterone could be through effects on coronary heart disease risk factors (26, 30), but there is conflicting evidence on its role in the etiology of insulin resistance and hypertension (2). On the other hand, a genetic polymorphism, shorter polyglutamine stretches in exon 1 of the androgen receptor gene (CAG repeats) determining higher androgen activity, was associated with more severe coronary artery stenosis (34). In some studies, androgen exposure has been associated with higher, not lower, risk. High levels of exogenous androgens, such as found in some transsexual females and both male and female athletes, are associated with impaired endothelial vasodilatation and premature myocardial infarction and stroke (2, 35), although most of this evidence is from case series.

There was some evidence in our study that students with acne history have a higher risk of prostate cancer mortality. A case-control study in Australia found a protective role of severe acne (presence of facial scarring in adulthood) on prostate cancer, whereas other markers of androgen action in puberty, such as an early growth spurt and an early age at first ejaculation, showed a higher risk (36). The role of androgens on the prostate gland has not been elucidated, and whether they induce prostate cancer or facilitate the growth of existing lesions is not clear (26). During puberty, prostate-specific antigen levels increase, and prostate epithelial differentiation occurs (37), indicating that changes in adolescence may modify later risk of prostate cancer. A review of prospective studies showed no compelling evidence that testosterone levels are causally related to prostate cancer (1). A meta-analysis reported a higher risk of prostate cancer with higher levels of sexual activity, a marker of higher testosterone levels (38), whereas Leitzmann et al. (37) found that a high ejaculation frequency was associated with lower, not higher, risk of total and localized prostate cancer. Vertex baldness has also been associated with higher prostate cancer risk (39).

Other hormonal changes in acne

Growth hormone and insulin-like growth factors undergo dramatic changes during puberty. Growth hormone rises during pubertal development because of increases in gonadal sex steroids in boys and girls, but its secretion decreases after puberty (40). Similarly, insulin-like growth factor levels rise during puberty and decrease 1–2 years thereafter. This pattern corresponds closely with that of acne development and remission, but the role of these hormones in acne production remains largely unknown (19). Growth hormone seems to facilitate the effect of androgens on pubic hair growth; that is, the testosterone level required to induce pubic hair in growth hormone-deficient boys is much higher than that needed by boys with normal growth hormone levels (19). Some of the androgen effect on hair growth may be mediated through insulin-like growth factors, since these factors have been found to induce important alterations in the hair growth cycle (19). Given that achieved adult height is associated with an increased risk of prostate cancer (41) but a lower risk of cardiovascular disease (42–45) and type II diabetes (46), growth hormone levels during puberty could account for both the protective effect of a history of acne on coronary heart disease and the higher risk of prostate cancer. However, in our study, height measured at the university or self-reported in adulthood was similar in students who reported a history of acne and those who did not, providing no support for this hypothesis. Moreover, growth during early life is mainly due to increases in leg length, while postpubertal growth occurs through increases in both leg and trunk length (47). The association of greater height with increased cancer risk and lower cardiovascular disease and type II diabetes risk seems to be due to increased leg length, suggesting that the height-related exposures are more likely to occur before puberty (41, 46, 48, 49).

Confounding

Although we adjusted for available risk factors, confounding may still remain an issue in observational studies (50). Adjustment for more detailed categorizations of
potential confounders did not change the magnitude of the associations. A higher proportion of students with a history of acne did not smoke while at the university compared with those that reported no history of acne. In adulthood, men with a history of acne reported more often to have never smoked, but we could not account for potential adulthood confounders in the mortality analysis.

The pattern of cause-specific mortality risk observed in our study allows us to evaluate whether confounding is a plausible explanation for these results, as follows. Lower socioeconomic circumstances during childhood are associated with higher coronary heart disease and stroke risk (51), results also found in this cohort (52). Therefore, poorer childhood circumstances among those with a history of acne cannot explain a lower coronary heart disease risk. If a lower prevalence of smoking among students with a history of acne was responsible for the observed lower coronary heart disease mortality, then, given the stronger association of smoking with lung cancer, we should have also observed lower lung cancer mortality, which was not the case. In addition, the association between history of acne and coronary heart disease mortality was similar among students who were nonsmokers at the university to that of the whole cohort.

Another potential confounder to consider is diet. Those reporting a higher prevalence of history of acne were of a lower childhood socioeconomic position (although still higher than that of the population that did not attend the university) and could therefore have been exposed to a less healthy diet. This, however, cannot explain the lower coronary heart disease risk in men who had acne in earlier life. On the other hand, fat restriction might have been prescribed to those students who had acne (mainly carbohydrate and also fat restriction were prescribed as treatment for acne at that time) (53, 54). This could potentially explain the lower coronary heart disease risk later in life. However, the association of total fat intake or specific dietary fats with prostate cancer risk is not established (55) and higher, not lower, fat intake would be associated with higher risk of prostate cancer mortality.

Progressively after the 1950s, tetracyclines were used for the treatment of acne (56, 57). Infectious contributions, including from *Chlamydia pneumoniae*, to coronary heart disease risk have been proposed, although these remain controversial (58, 59). However, if *C. pneumoniae* infection is causally related to coronary heart disease, men who had their acne treated with antibiotics could consequently be at lower coronary heart disease risk. On the other hand, tetracycline or its derivatives have been shown to inhibit cell growth in prostate cancer (60), and therefore we would not expect a higher risk of prostate cancer mortality in the acne group.

Finally, mortality due to external causes (accidents, suicide, and violence) was not related to history of acne, whereas if acne relates to coronary heart disease mortality because of behavioral confounders, a relatively low mortality from external causes—unlikely to be related to androgen levels or activity—would also be expected.

Overall, this evidence suggests that confounding does not explain the pattern of mortality observed in our study. The members of the Glasgow Alumni Cohort were more affluent than those of the general population: in 1951–1961, 53.8 percent of the Glasgow Alumni Cohort were from social classes I and II compared with 6.6 percent of similarly aged individuals in the general Scottish population (10). However, it seems unlikely that the influence of androgen activity on coronary heart disease risk should differ among men of low and high social class. In addition, associations reported from this cohort between early life exposures and later disease will be less likely to have resulted from confounding by adult socioeconomic circumstances, given the relative homogeneity of adulthood social circumstances in this group.

Studies examining the role of exposure to endogenous hormone levels or hormone activity in adult life in coronary heart disease or prostate cancer etiology have not been conclusive. We have shown that an early life measure related to puberty development was associated with these outcomes. Other studies assessing early life exposure to hormone activity may provide a better understanding of the role of hormones. In addition, studies based on principles of Mendelian randomization, using genetic polymorphisms related to hormone levels or hormone activity, are more likely to provide unconfounded estimates of disease risks associated with endogenous hormonal exposures (61). Such studies can assist in establishing the role of early life influences in coronary heart disease and prostate cancer and in providing insight into the mechanisms that may explain these associations, which, in turn, can lead to the development of preventative interventions.

Conclusion

Higher androgen levels or higher androgen activity could plausibly explain the observed lower coronary heart disease and higher prostate cancer mortality among men with a history of acne. Confounding was unlikely to explain these results. The effects of androgenic hormone activity in early life warrant more research with alternative study designs.

ACKNOWLEDGMENTS

The authors would like to acknowledge the financial support of the Stroke Association; Chest, Heart and Stroke Scotland; the National Health Service Research and Development Cardiovascular Disease Programme; and the World Cancer Research Fund. G. D. S. holds a Robert Wood Johnson Foundation Investigators Award in Health Policy Research. Funds from this award partly supported B. G. In addition, P. M. is supported by a career scientist award funded by the Research and Development Office for Health and Personal Social Services in Northern Ireland. The Centre for Public Health Research (Massey University, Wellington, New Zealand) is supported by a Programme Grant from the Health Research Council of New Zealand.

The authors’ work was independent of the funding sources.
REFERENCES


