

Diabetes and Risk of Fracture

The Blue Mountains Eye Study

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OBJECTIVE — To examine associations between measures of diabetes and risk of fracture in a population-based sample of older Australians.

RESEARCH DESIGN AND METHODS — This was a prospective study of 3,654 subjects aged 49 years and older who were residents in the Blue Mountains, west of Sydney, Australia. At baseline, subjects were asked questions about history and treatment of diabetes, and fasting blood samples were taken. Photographs were taken of the retina and lens to grade retinopathy and cataract. Details of fractures (excluding rib and vertebral fractures) were collected by a combination of self-report and medical record searches; all fractures were radiologically confirmed.

RESULTS — After 2 years of follow-up, we found that several diabetes-related factors were significantly associated (in multivariate models) with increased risk of all fractures combined, including presence of diabetic retinopathy (adjusted RR 5.4, 95% CI 2.7–10.8), diabetes duration ≥ 10 years (3.3, 1.3–8.2), cortical cataract involving $\geq 25\%$ of the lens area (2.5, 1.3–4.7), and insulin treatment (5.9, 2.6–13.5). The proximal humerus was the only individual fracture site associated with diabetes. Diabetic retinopathy (10.3, 2.2–48.0), diabetes duration (for ≥ 10 years duration; 11.4, 2.4–54.2), and insulin treatment (18.8, 4.0–88.7) were all associated with proximal humerus fracture.

CONCLUSIONS — These data suggest a significantly increased risk of fracture associated with diabetic retinopathy, advanced cortical cataract, longer diabetes duration, and insulin treatment. However, there are some shortcomings in this study that may limit these findings.

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Many studies have examined the relationship between presence of diabetes and bone density. In general, non-insulin-dependent diabetes has been associated with increased bone density, (1–4) whereas insulin-dependent diabetes has been associated with decreased bone density (5–8). However, fewer studies have examined the risk of fracture in people with diabetes. Of these, some have found no associations, (9,10) whereas other larger prospective studies have found strong associations between diabetes and risk of fracture (11–14).

For instance, the Study of Osteoporotic Fractures, a large prospective study of older women, found that diabetes was associated with increased risk of foot (11) and proximal humerus fracture (12), but not with hip fracture (15). However, two prospective Norwegian studies found associations between diabetes and risk of hip fracture (13,14).

Given the conflicting results in previous studies, we therefore aimed in this report to explore the associations between diabetes and risk of fracture in a prospective population-based study of older Australians.

RESEARCH DESIGN AND METHODS

The Blue Mountains Eye Study is a population-based survey of vision and common eye diseases in the Blue Mountains, west of Sydney, Australia. Details of the survey methods and procedures have been described previously (16–18). All noninstitutionalized residents aged 49 years or older in two post-code areas were identified in a census. From a total of 4,433 eligible residents, 3,654 (82.4%) attended the baseline eye examination and interview in 1992 and 1993.

Baseline assessment

Visual acuity was recorded with current glasses and after subjective refraction using a logMAR (MAR, minimum angle of resolution) chart (19). Contrast sensitivity was measured after refraction for subjects in the first postcode area using the Vectorvision CSV-1000 chart (Vectorvision, Dayton, OH) (20).

Each participant had stereoscopic 30° photographs taken using a Zeiss FF3 Fundus camera and Kodachrome 25 slide film (Kodak). Photographs were assessed for age-related maculopathy (18) and diabetic retinopathy (21). The three principle cataract types were assessed using the Wisconsin Cataract Grading System (16,22). Slit-lamp photographs of the lens were taken using a Topcon SL-7E slit-lamp camera (Topcon Optical, Tokyo), and retroillumination lens photographs were taken using a Neitz CT-R camera (Neitz Instruments, Tokyo). Nuclear cataract was assessed by comparing photographs from the Topcon camera with a set of four Wisconsin standards (22). Presence and severity of cortical and posterior subcapsular cataract opacities were graded from Neitz photographs using a circular grid (16,22).

At the clinic visit, a questionnaire including demographic characteristics, medications, visual function, medical history, and self-rating of general health was administered. BMI was calculated from measured weight and height. A fasting blood sample was taken within 3 months of the baseline examination, and serum

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

was analyzed for glucose. Diabetes was diagnosed from a self-reported positive physician-diagnosis.

Collection of follow-up data

Fracture data were collected in three ways: self-report, radiology reports, and hospital discharge summaries (for hip fracture only). Five-year follow-up clinic visits were conducted between May 1997 and December 1999. At the clinic, subjects completed a second detailed questionnaire that inquired about fractures sustained since age 49 years, as well as details of the fracture(s). We verified all self-reported nonrib or nonvertebral fractures by obtaining the radiology report. In addition, a review was conducted in July 1997 of all radiology reports at the local hospital for all subjects in the study. Discharge summaries were also obtained for all subjects with hip fractures who had been admitted to the hospital between July 1997 and September 1999. Each radiology report was reviewed by a specialist radiologist (A.P.) who assessed the presence and type of fracture. We were able to obtain films for 25 of the 62 subjects with a radiology report of hip fracture, and the study radiologist (A.P.) confirmed the hip fracture in all 25 cases.

Person-time for hip fracture analyses was calculated from the date of the baseline examination to the date of the first hip fracture, the date of death, or 30 September 1999, whichever came first. For non-hip fracture analyses, person-time was calculated from the date of the baseline examination to the date of the first fracture of that type, the date of death, or 1 July 1997 (as the date when hospital radiology records were searched for fractures for all subjects), whichever came first. For the analysis of the all-fractures category, person-time was calculated from the date of the baseline examination to the date of the first fracture of any type (excluding rib and vertebral fractures), the date of death, or 1 July 1997, whichever came first.

Statistical methods

Fracture data were analyzed by survival analysis using Cox proportional hazards models in SAS version 6.12 (Cary, NC). We assessed confounding by known risk factors for fractures (age, sex, BMI, health status, history of stroke or Parkinson's disease, history of falls, use of psychotropic medication, thiazide diuretics or

hormone replacement therapy, smoking, physical activity, walking difficulties, and use of a cane or stick) if they were associated with the vision variables and diabetes variables in our data and if they were statistically significantly associated with fracture after adjusting for age and sex. Variables fulfilling these criteria were retained in multivariable models if their exclusion changed the relevant vision-hip fracture RR by $\geq 10\%$. Time-dependent covariates for each vision variable were introduced into models to test the proportional hazards assumption. Interaction terms were introduced into the final models to assess interaction between the main effects and both age and sex.

Results are presented as RR and 95% CI. P values < 0.05 were used to indicate statistical significance.

RESULTS — At baseline the mean age of the 3,654 study subjects was 66.2 years (range 49–97 years), and 56.7% were women. There were 216 (6%) subjects who reported that they had been diagnosed with diabetes by a physician. Of these, 96 (44%), 38 (18%), and 69 (32%) reported having diabetes for, respectively, 0–4, 5–9, and ≥ 10 years. There were 157 (73%) subjects treated by diet or tablets and 47 (22%) treated by insulin.

Mean length of follow-up was 5 years for hip fractures and 4.7 years for other types of fracture. At the end of follow-up, there were 59, 53, 26, and 36 subjects who had sustained, respectively, a fracture of the hip, distal forearm, proximal humerus, and ankle. In all, 251 subjects sustained a fracture of any type, excluding rib and vertebral fractures. After 2 years of follow-up, 17, 23, 11, and 11 subjects had sustained, respectively, a fracture of the hip, distal forearm, proximal humerus, and ankle. A total of 99 had a fracture of any type.

Table 1 presents age- and sex-adjusted associations between risk factors and fractures after 2 years of follow-up. Having diabetes duration ≥ 10 years, insulin treatment, blood glucose > 7 mmol/L, $\geq 25\%$ of the lens involved by cortical cataract in the worst eye, or the presence of diabetic retinopathy in either eye was associated with increased risk of all fractures combined. Having diabetic retinopathy, insulin treatment, or diabetes duration > 5 years was associated with an increased risk of proximal humerus fracture, but apart from these association,

there were no other statistically significant associations between either diabetic retinopathy or cortical cataract and the individual sites of fracture.

After follow-up was complete (age- and sex-adjusted), presence of diabetic retinopathy was statistically significantly associated with risk of all fractures combined, as was treatment with insulin (Table 2). After follow-up, having diabetes duration ≥ 10 years or insulin treatment was also associated with increased risk of proximal humerus fracture.

Table 3 presents associations between both risk factors and all fractures combined and fractures of the proximal humerus after 2-year follow-up, derived from multivariate models. Although many potential confounders were assessed, only age, sex, and BMI were found to actually confound the associations between risk factors and risk of fracture. Many diabetes-related factors were statistically significantly associated with fracture risk (after adjusting for age, sex, and BMI): diabetic retinopathy, long duration of diabetes, treatment with insulin, high blood glucose, and presence of cortical cataract.

Fewer variables were associated with fractures at 5-year follow-up. After adjusting for age, sex, and BMI, presence of diabetic retinopathy was significantly associated with risk of all fracture (adjusted RR 3.2, 95% CI 1.9–5.5, $P < 0.0001$), as was diabetes duration of 5–9 years (3.0, 1.2–7.4, $P = 0.02$) and insulin treatment (3.8, 2.0–7.1, $P < 0.0001$). After adjusting for age, sex, and BMI, duration of diabetes was significantly associated with risk of proximal humerus fracture during 5 years of follow-up (≥ 10 years duration adjusted RR 4.6, 95% CI 1.1–19.6, $P = 0.04$), as was insulin treatment (7.4, 1.7–31.5, $P = 0.007$).

After 2 or 5 years of follow-up, posterior subcapsular cataract was not associated with risk of any type of fracture (data not shown).

To assess whether the association between the risk of fracture and both diabetic retinopathy and cortical cataract was due to the effects of poor vision, we adjusted for various vision variables to see whether they explained the association. Diabetic retinopathy remained statistically significantly associated with risk of all fracture (with 2 years of follow-up) after separately adjusting for visual acuity, contrast sensitivity (six cycles per degree),

Table 1—Age- and sex-adjusted associations between diabetes variables and risk of fractures after 2 years of follow-up

Risk factor	n (%)	All fractures		Hip		Distal forearm		Ankle		Proximal humerus	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Diabetes (self-reported)											
History of diabetes	216 (6)	0.7	0.4–1.2	0.9	0.3–2.9	0.9	0.4–2.3	0.4	0.08–2.2	2.0	0.5–8.3
Diabetes by duration											
No diabetes	3,459 (94.4)	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
0–4 years duration	96 (2.6)	1.4	0.4–4.4	*	—	2.2	0.3–16.1	*	—	*	—
5–9 years duration	38 (1.0)	2.2	0.5–8.8	*	—	*	—	*	—	11.4	1.4–91.9
≥10 years duration	69 (1.9)	2.9	1.2–7.0	2.8	0.4–21.5	2.8	0.4–20.9	*	—	11.0	2.3–51.8
Trend P		0.01	—	0.4	—	0.4	—	*	—	0.0009	—
Diabetes by treatment type											
No diabetes	3,450 (94.4)	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
Diet or tablets	157 (4.3)	1.1	0.4–3.0	*	—	1.4	0.2–10.2	*	—	2.7	0.3–21.7
Insulin	47 (1.3)	5.1	2.2–11.6	3.8	0.5–29.0	3.5	0.5–26.5	*	—	18.4	3.9–86.8
Diabetic retinopathy											
No retinopathy	3,501 (97.7)	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
Any retinopathy	82 (2.3)	4.6	2.3–9.1	3.4	0.4–26.1	2.0	0.3–15.2	4.1	0.5–32.3	9.4	2.0–43.5
Blood sugar (mmol/l)											
<5	1,619 (20.3)	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
≥5<6	1,238 (38.4)	0.7	0.4–1.2	0.3	0.07–1.6	0.9	0.4–2.3	2.0	0.5–8.3	0.4	0.08–2.2
≥6<7	191 (5.9)	0.7	0.3–2.0	0.9	0.1–7.7	*	—	2.4	0.2–23.7	1.2	0.1–10.2
≥7	173 (5.4)	2.1	1.1–4.2	*	—	1.0	0.1–7.5	2.8	0.3–27.1	2.9	0.6–15.0
Trend P		0.1	—	*	—	*	—	0.3	—	0.2	—
Cortical cataract worst eye %											
0–4	2,618 (76.2)	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
5–24	599 (17.4)	1.2	0.7–2.0	3.5	1.0–12.7	0.5	0.1–2.0	0.4	0.05–3.2	1.7	0.4–7.9
≥25	218 (6.3)	2.3	1.2–4.3	2.4	0.4–13.9	1.7	0.5–6.3	1.1	0.1–9.6	3.5	0.6–20.2
Trend P		0.009	—	0.3	—	0.6	—	0.9	—	0.2	—

*Insufficient data.

or visual field (along with age, sex, and BMI). However, the association between advanced cortical cataract and risk of all fracture did not remain statistically significant after adjusting for contrast sensitivity at six cycles per degree (adjusted RR 1.6, 95% CI 0.6–3.8), although adjusting for visual acuity or visual field did not have this attenuating effect.

Likewise, to assess whether the association between the risk of fracture and both treatment type and duration of diabetes (Table 3) might be attributable to diabetes-related visual impairment, we adjusted for diabetic retinopathy. Adjusting for diabetic retinopathy markedly reduced RRs for all fractures: the RR for diabetes for >10 was reduced from 3.3 to 1.0, and the RR for treatment with insulin was reduced from 5.9 to 1.9. Adjusting for diabetic retinopathy had less of an impact on RRs for shoulder fractures: the RR for diabetes duration >10 years was reduced from 11.4 to 7.5, and the RR for insulin treatment was reduced from 18.8 to 10.8.

CONCLUSIONS — There is a substantial body of literature on the associations between diabetes and bone metabolism. Non-insulin-dependent diabetes has been associated with increased bone density (1–4), whereas insulin-dependent diabetes has been associated with decreased bone density (5–8). A recent study comparing people with type 1 and type 2 diabetes with healthy control subjects confirmed lower bone mineral density in those with type 1 diabetes (23), a finding that could not be explained by insulin treatment. Fracture rates were also higher in those with type 1 diabetes than in those with type 2 diabetes in this study. The authors suggested that the lower bone mineral density could be attributed to the direct effect of insulin-dependent diabetes or its treatment on bone metabolism (23). Other studies have hypothesized that in patients with diabetes, low bone formation retards bone accumulation during youth, poor glycemic control and its metabolic effects lead to increased bone resorption and loss in young adults,

and low bone turnover retards age-related loss (24). However, it is possible that high BMI associated with non-insulin-dependent diabetes may cancel out any adverse effect of the diabetic process on bone.

Other studies have examined the associations between diabetes and fracture, with some (11–14), but not all (9,10), finding positive associations. The Study of Osteoporotic Fractures found that insulin-dependent diabetes was associated with increased risk of foot fractures (adjusted RR 2.9, 95% CI 1.2–7.2) (11) and proximal humerus fractures (3.8, 1.2–12.4) (12). However, diabetes was not associated with an increased risk of hip fracture (1.3, 0.8–2.1) (15). In contrast, a prospective Norwegian study found a strong association between diabetes and risk of hip fracture in both women (9.2, 3.4–24.9) and men (9.4, 2.9–30.5) (14). Another prospective Norwegian study found that risk of hip fracture in women aged 50–74 years was associated with type 2 diabetes duration >5 years, type 1 diabetes, and use of insulin (13).

Table 2—Age- and sex-adjusted associations between diabetes variables and risk of fractures after 5 years of follow-up

Risk factor	All fractures		Hip		Distal forearm		Ankle		Proximal humerus	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Diabetes (self-reported)										
History of diabetes	0.9	0.7–1.2	0.6	0.2–2.2	0.7	0.2–2.3	1.1	0.6–1.9	0.5	0.08–3.6
Diabetes by duration										
Nondiabetic	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
0–4 years duration	0.5	0.2–1.7	*	—	0.9	0.1–6.5	*	—	*	—
5–9 years duration	2.3	0.9–5.5	1.9	0.3–13.8	*	—	3.1	0.4–22.7	4.4	0.6–32.9
≥10 years duration	1.6	0.7–3.3	0.7	0.1–5.4	1.1	0.1–7.8	*	—	4.5	1.1–19.0
Trend <i>P</i>	0.2	—	0.8	—	0.9	—	0.6	—	0.03	—
Diabetes by treatment type										
No diabetes	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
Diet or tablets	0.5	0.2–1.3	*	—	0.5	0.08–4.0	0.8	0.1–5.7	1.0	0.1–7.7
Insulin	3.5	1.9–6.6	2.1	0.5–8.4	1.4	0.2–10.4	*	—	7.1	1.7–30.2
Diabetic retinopathy										
None	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
Any retinopathy	2.8	1.6–4.7	1.8	0.4–7.5	0.8	0.1–6.0	2.7	0.7–11.4	3.7	0.9–15.6
Blood sugar (mmol/l)										
<5	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
≥5<6	0.7	0.5–0.9	0.4	0.2–0.9	0.9	0.5–1.7	1.0	0.5–2.2	0.7	0.3–1.7
≥6<7	0.9	0.5–1.6	0.8	0.2–2.5	1.4	0.5–4.1	1.3	0.3–5.5	0.6	0.07–4.4
≥7	1.3	0.7–2.2	0.8	0.2–2.5	0.4	0.06–3.2	0.8	0.1–5.8	1.3	0.3–6.0
Trend <i>P</i>	0.9	—	0.4	—	0.6	—	0.9	—	0.9	—
Cortical cataract worst eye %										
0–4	1.0	reference	1.0	reference	1.0	reference	1.0	reference	1.0	reference
5–24	1.1	0.8–1.6	1.8	0.9–3.4	1.1	0.5–2.2	0.4	0.1–1.3	0.8	0.3–2.4
≥25	1.2	0.8–1.9	1.0	0.4–2.7	0.7	0.2–2.2	1.0	0.3–3.5	1.3	0.4–4.6
Trend <i>P</i>	0.4	—	0.8	—	0.6	—	0.7	—	0.8	—

*Insufficient data.

Our study found strong associations among presence of diabetic retinopathy, blood glucose levels, diabetes duration, and treatment type and the risk of both all fractures and fractures of the proximal humerus, with the presence of severe cortical cataract also associated with all fractures. The significant associations among blood glucose levels, diabetes duration, and treatment type and the risk of both all fractures and fractures of the proximal humerus were explained, at least partly, by the presence of diabetic retinopathy. However, the association between presence of diabetic retinopathy and risk of fracture remained significant after adjusting for visual impairment. There are two possible explanations: it is possible that the association between diabetic retinopathy and fracture was due to the effects of poor vision, and that our measures of visual impairment did not measure the degree of visual impairment appropriately. We believe the more likely explanation is that the presence of diabetic retinopathy may be acting as a proxy for severe dia-

betic microvascular disease. It is possible that the metabolic effects of diabetes on bone (such as acidosis and hypercalciuria) (25) could explain the increased fracture rate found in our study. A further possibility is that more severe diabetes is associated with an increased likelihood of peripheral neuropathy (including loss of proprioception, with impaired balance and increased risk of falling). Unfortunately, we had poor or no measures of neuromuscular impairment or neuropathy, although another study has shown that foot neuropathy is not associated with fractures (11).

Both longer duration of diabetes and insulin, rather than diet or oral treatment, were significantly associated with increased risk of both fracture of the proximal humerus and all fractures combined. This further suggests that the associations found may be attributable to the severity of the disease. Although it is not possible to determine accurately what proportion of subjects had type 1 diabetes, the ages of onset suggest that most of those treated

with insulin had type II diabetes. Irrespective of type, insulin treatment represents more severe disease. However, it must be noted that measures of duration of diabetes are subject to recall bias, and many individuals with diabetes remain undiagnosed for many years.

We found very strong associations between diabetic retinopathy, diabetes duration, and insulin treatment and the risk of proximal humerus fracture, supporting the results from the Study of Osteoporotic Fractures (12). However, that study proposed that proximal humerus fractures were more common in women who were frail and less healthy (12), and so our stronger findings may be due to our inability to control for frailty in this population.

In our study, associations between diabetes-related risk factors and risk of fractures were stronger after 2 years than after 5 years of follow-up. Stronger associations for the shorter period may be expected if the association is attributable to the effects of poor vision because the level

Table 3—Associations between vision variables and risk of all fractures combined and fractures of the proximal humerus, adjusted for age, sex, and BMI after 2 years of follow-up

Risk factor	All fractures			Proximal humerus		
	RR	95% CI	P	RR	95% CI	P
Diabetic retinopathy						
None	1.0	reference	—	1.0	reference	—
Any retinopathy	5.4	2.7–10.8	0.0001	10.3	2.2–48.0	0.003
Diabetes by duration						
No diabetes	1.0	reference	—	1.0	reference	—
0–4 years duration	1.8	0.6–5.7	0.3	*	—	—
5–9 years duration	3.1	0.8–12.7	0.1	15.7	1.9–132.6	0.01
≥10 years duration	3.3	1.3–8.2	0.01	11.4	2.4–54.2	0.002
Trend P	0.004	—	—	0.0007	—	—
Diabetes by treatment						
No diabetes	1.0	reference	—	1.0	reference	—
Diet or tablets	1.4	0.5–3.9	0.5	3.1	0.4–25.5	0.3
Insulin	5.9	2.6–13.5	0.0001	18.8	4.0–88.7	0.0002
Blood sugar (mmol/l)						
<5	1.0	reference	—	1.0	reference	—
≥5<6	0.8	0.5–1.3	0.4	0.5	0.09–2.5	0.4
≥6<7	0.9	0.3–2.6	0.9	1.4	0.2–13.0	0.7
≥7	2.8	1.4–5.8	0.004	3.6	0.7–19.8	0.1
Trend P	0.01	—	—	0.1	—	—
Cortical cataract worst eye %						
0–4	1.0	reference	—	1.0	reference	—
5–24	1.2	0.7–2.1	0.4	1.7	0.4–7.9	0.5
≥25	2.5	1.3–4.7	0.004	3.5	0.6–19.8	0.2
Trend P	0.005	—	—	0.2	—	—

*Insufficient data.

of visual impairment present at the time of a fracture would be much better reflected by a recent eye examination than one performed many years in the past. If the associations with fracture were attributable to severity of microvascular disease, it might be expected that longer duration of follow-up would be more predictive of fracture. However, it is possible that frailer individuals, and those with more severe diabetes, were more likely to die before the end of the 5-year follow-up, which could have attenuated this effect. We found that the age- and sex-adjusted RR of dying in diabetic patients on insulin treatment was 2.7 (95% CI 1.7–4.4) after the 5-year follow-up.

Several studies have shown diabetes is a risk factor for both cortical and posterior subcapsular cataract (26,27). Cortical cataract is a frequent type of age-related cataract, and in this study advanced cortical cataract affected 6% of the subjects, whereas advanced posterior subcapsular cataract affected <2%. The lack of association between posterior subcapsular cataract and fractures could have

been attributable to the smaller numbers of subjects. Many previous studies have reported associations between cortical cataract and reduced contrast sensitivity (28–30). The significant association between advanced cortical cataract and risk of fracture in this study was attenuated by adjusting for contrast sensitivity, suggesting that a component of this association is poor vision rather than the effects of severe long-standing diabetes.

The Blue Mountains Eye Study was primarily undertaken to determine risk factors for eye disease. As such, the data collected on risk factors for fracture and diabetes are imperfect. There were no measures of bone mineral density, neuromuscular impairment, history of fractures at baseline, family history of fractures, or cognitive impairment. We also did not measure HbA_{1c}, which would have been a better indication of diabetes than a one-time measure of fasting blood glucose. It is likely that blood glucose level was not as strongly associated with fracture compared with the other diabetes variables (duration of disease, insulin treatment, and retinopa-

thy) because it is a poor measure of diabetes control and disease severity.

Another limitation of this study is that up to 11% of nonhip fractures could have been missed. Although we are certain that most hip fractures would have been identified, of nonhip fractures reported by subjects who attended the five year follow-up examination 30% were treated away from the Blue Mountains District Hospital. It is thus likely that 11% of the nonhip fractures were missed overall (30% of 36% of subjects not seen in the follow-up study).

Clearly, with the multiple comparisons made in this study, the significance testing must be viewed with a degree of caution because adjustment has not been made for multiple comparisons. However, all the statistically significant associations we found after the 2-year follow-up had *P* values ≤0.01, suggesting that the associations were not attributable to chance.

In conclusion, presence of diabetic retinopathy, advanced cortical cataract, diabetes duration, and treatment with insulin were significantly associated with increased risk of fractures in our study. These diabetes-related variables are all indicators of more severe diabetic disease. The mechanism by which more severe diabetes causes fractures is unclear: there could be a direct metabolic effect on bone and/or diabetes-related peripheral neuropathy increasing the risk of falls. Physicians and geriatricians should strive for optimal glycemic control and be aware of the need to refer older patients with advancing cataract.

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