

The relationship between hypertension, chronic renal disease and cardiovascular risk in diabetes: cohort study.

AP McGovern^{1,2}, B Rusholme¹, S de Lusignan¹, J van Vlymen¹, S Jones¹, QICKD Trial Investigators¹

¹Clinical Informatics, Department of Healthcare Management and Policy, University of Surrey, Guildford, UK

²Royal Surrey County Hospital, Guildford, UK



Introduction

There is a complex interrelationship between chronic kidney disease (CKD), hypertension and cardiovascular risk in people with diabetes. We explore this relationship using a large community based cohort study.

The two components of CKD; reduced estimated glomerular filtration rate (eGFR) and proteinuria have been shown to be independently associated with cardiovascular events and mortality in the general population and in high risk populations (1-3). Information on the interaction between these components of renal disease in diabetes is limited

Study aims:

1. Characterise the relationship between hypertension, proteinuria and reduced eGFR in people with diabetes.
2. Compare this relationship with that of the non-diabetic population.
3. Identify the combined effects on cardiovascular risk of hypertension, proteinuria, and reduced eGFR in people with diabetes.

Methods

A cohort of adults with type 1 and type 2 diabetes (N=35,502), was identified from the Quality Improvement in Chronic Kidney Disease (QICKD) trial database (3). This database comprises the GP records from all patients registered at 127 GP practices across England between 2006 and 2011.

This data was divided into two periods. The first 2.5 years was used to define the baseline characteristics of the population. The subsequent 2.5 years was used as the follow up period. A composite cardiovascular outcome of mortality, myocardial infarction, stroke, transient ischaemic attack and cardiac revascularisation procedures was used.

Statistical analysis comprised three components:

- Simple descriptive analysis
- Survival analysis (Kaplan-Meier analysis)
- Multilevel logistic regression.

Results

The study population comprised 599,257 people of which 35,502 had diabetes. We found 84% of people with diabetes and hypertension also have chronic kidney disease (compared with 56% in people without diabetes). Conversely, 96% of people with diabetes and chronic kidney disease have hypertension (compared with 88% in people without diabetes). Figure 2 demonstrates the proportion of people with multiple disease components in people with and without diabetes.

A total of 3,144 people (8.9%) in the diabetes cohort had an adverse outcome during the follow up period: 1,495 (4.2%) died and, 1,531 people (4.3%) had a non-fatal cardio-vascular events. Each renal disease component (reduced eGFR, and proteinuria) was found to contribute separately to cardiovascular risk when adjusting for known cardiovascular risk factors (table 1). A survival analysis is shown in Figure 3 for people with diabetes and hypertension.

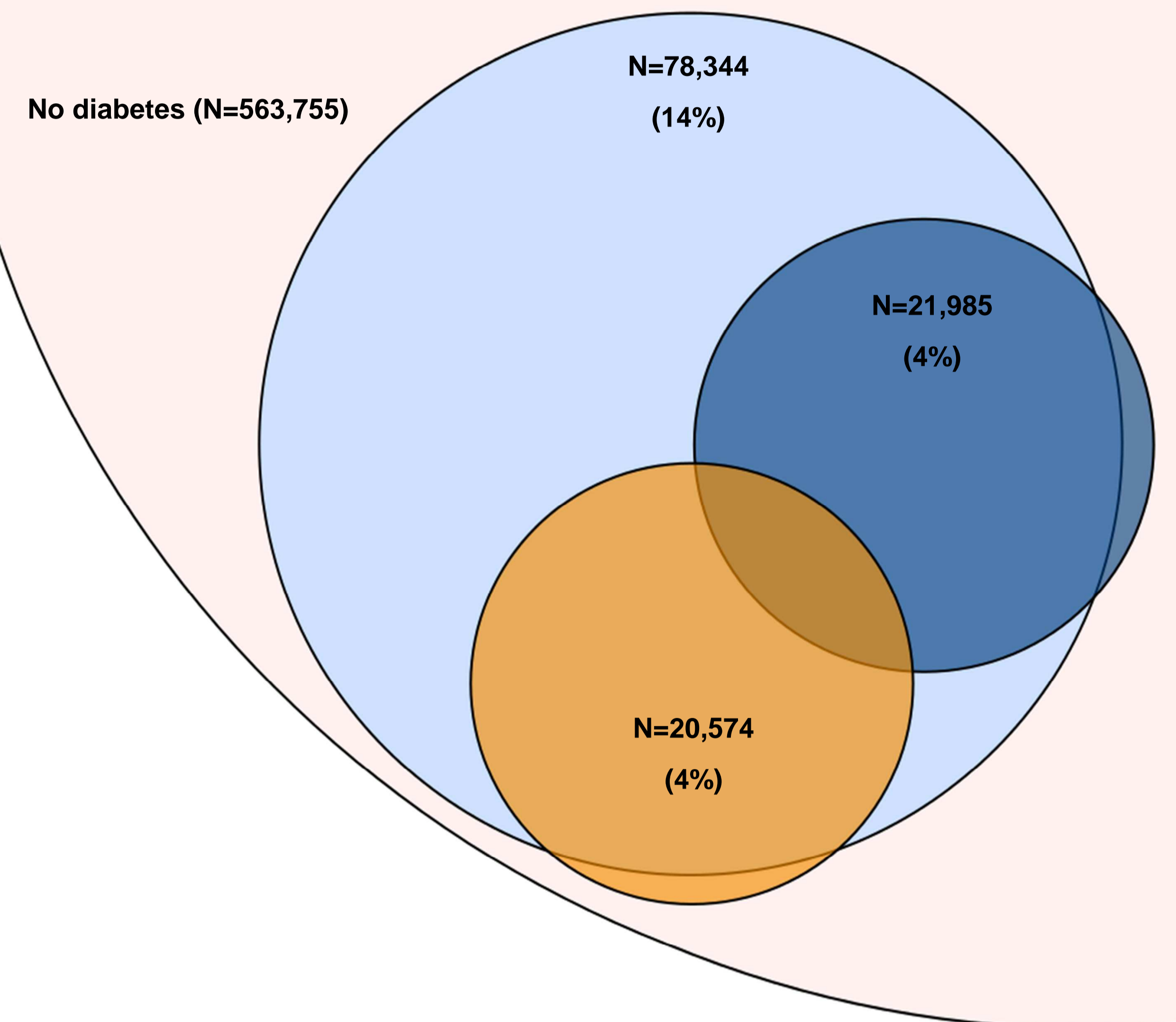
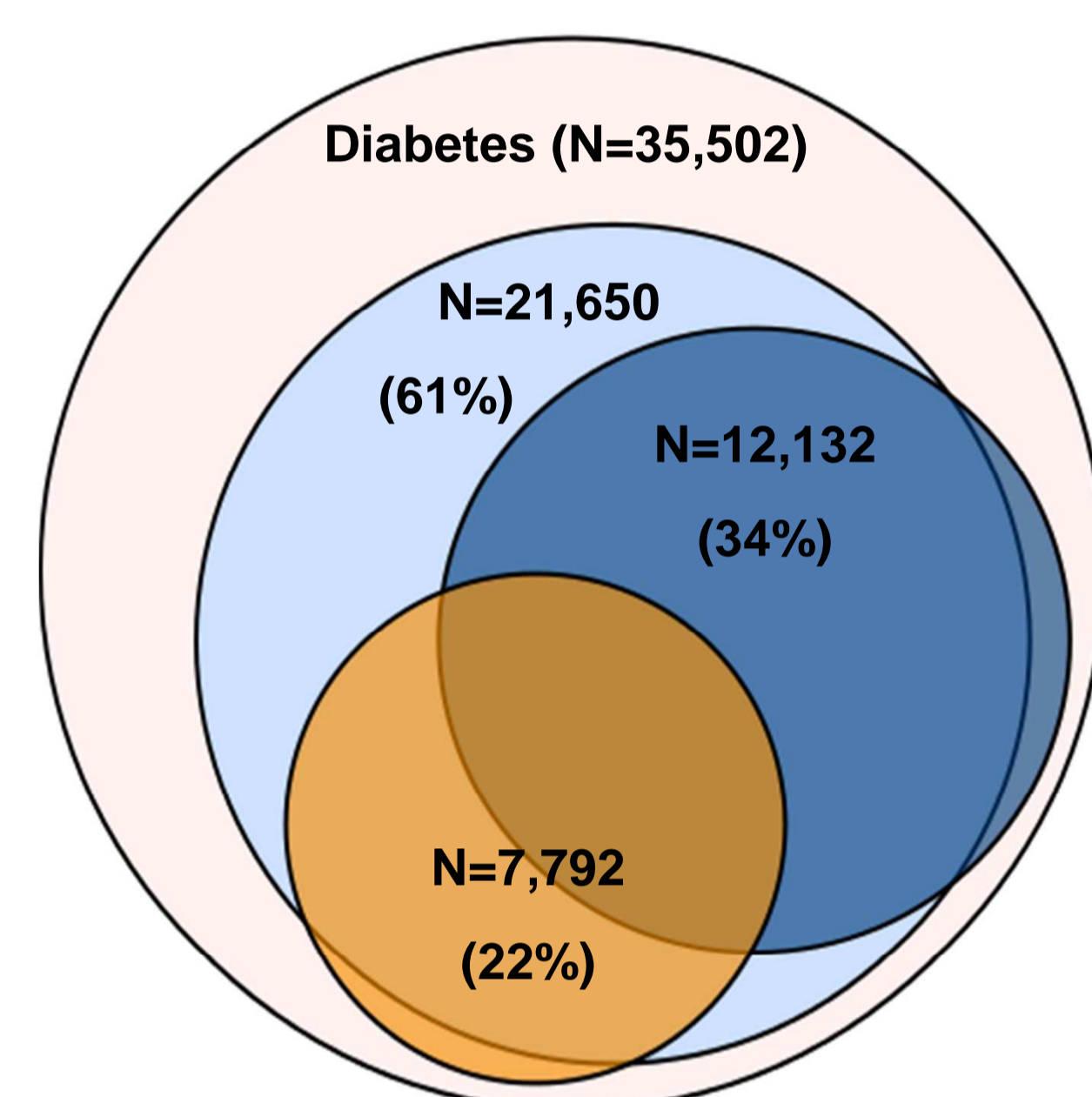
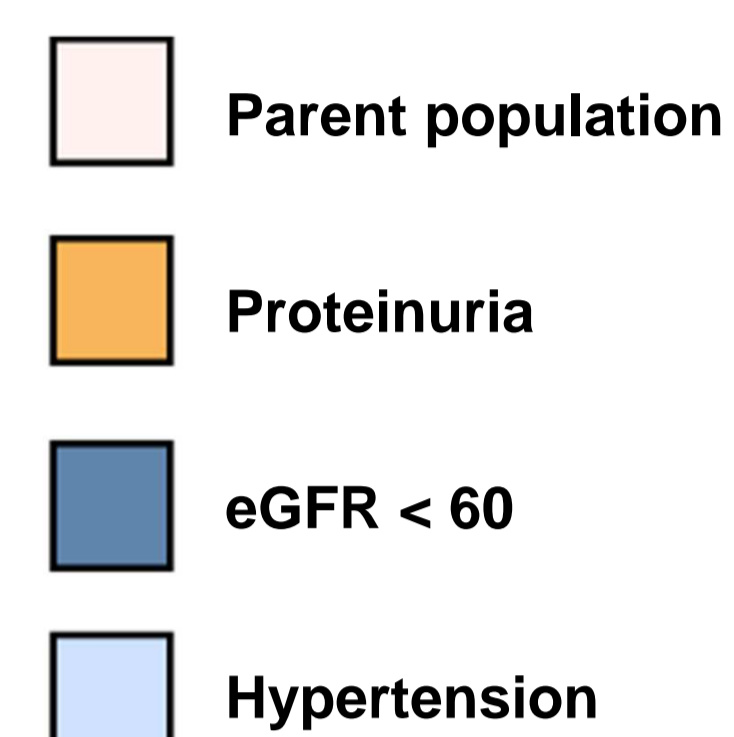


Figure 2. Area proportional Venn diagrams demonstrating the relative prevalence of disease components in people with and without diabetes. In diabetes the very high burden of hypertension and CKD is evident. It is also apparent that there is more overlap between disease components in diabetes compared to the population without diabetes: there is clustering of these disease components.

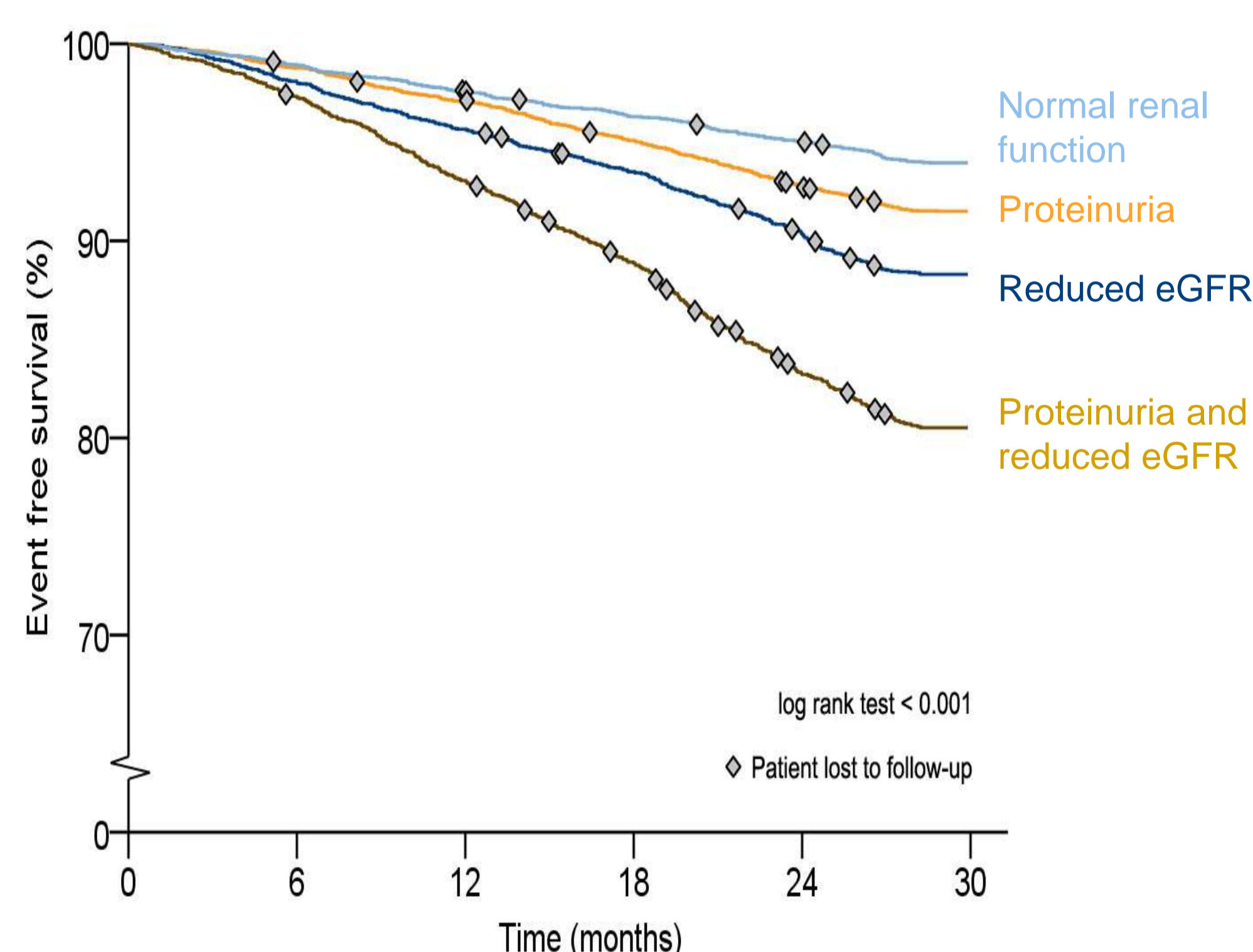


Figure 3. Kaplan Meier cardiovascular event free survival analysis of people with diabetes and hypertension.

	n	Odds ratio (95% confidence interval)	P value
No Hypertension			
No CKD	15,229	1.00 [reference]	-
CKD stages 1-2	440	1.62 (1.004 - 2.63)	0.048
CKD stages 3-5	51	1.82 (0.78 - 4.25)	0.164
CKD stages 3-5 with proteinuria	78	2.02 (1.06 - 3.84)	0.033
Hypertension			
No CKD	5,862	0.96 (0.83 - 1.11)	0.609
CKD stages 1-2	7,581	1.21 (1.06 - 1.40)	0.006
CKD stages 3-5	3,987	1.16 (1.001 - 1.34)	0.049
CKD stages 3-5 with proteinuria	3,676	1.62 (1.39 - 1.88)	<0.001

Table 1. Odds ratios for cardiovascular events and mortality of 35,502 people with diabetes, over 30 months of follow up, by CKD and hypertension category. Odds ratios are adjusted for known cardiovascular risk factors (age, gender, smoking status, dyslipidaemia, and previous cardiovascular events).

Summary

We analysed the relationship between three disease components (reduced eGFR, proteinuria and hypertension) in diabetes when compared to the general population:

- Renal disease is disproportionately more common than hypertension in diabetes.
- People with one disease component are disproportionately more likely to have another in diabetes when compared to the non-diabetic population. There is clustering of disease components in diabetes.

We analysed the effect on cardiovascular risk of these disease components in diabetes:

- Both proteinuria and reduced eGFR contribute separately to cardiovascular risk.

References

1. Mahmoodi BK, Matsushita K, Woodward M, et al.: Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet*, 2012
2. van der Velde M, Matsushita K, Coresh J, et al.: Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. *Kidney Int* 79: 1341-1352, 2011
3. Nitsch D, Grams M, Sang Y, et al.: Associations of estimated glomerular filtration rate and albuminuria with mortality and renal failure by sex: a meta-analysis. *BMJ* 346: f324, 2013
4. de Lusignan S, Gallagher H, Chan T, et al.: The QICKD study protocol: a cluster randomised trial to compare quality improvement interventions to lower systolic BP in chronic kidney disease (CKD) in primary care. *Implementation science* : IS 4: 39, 2009