

Could metformin be an effective drug for limiting abdominal aortic aneurysm growth and requirement for surgery?

No related conflict of interest



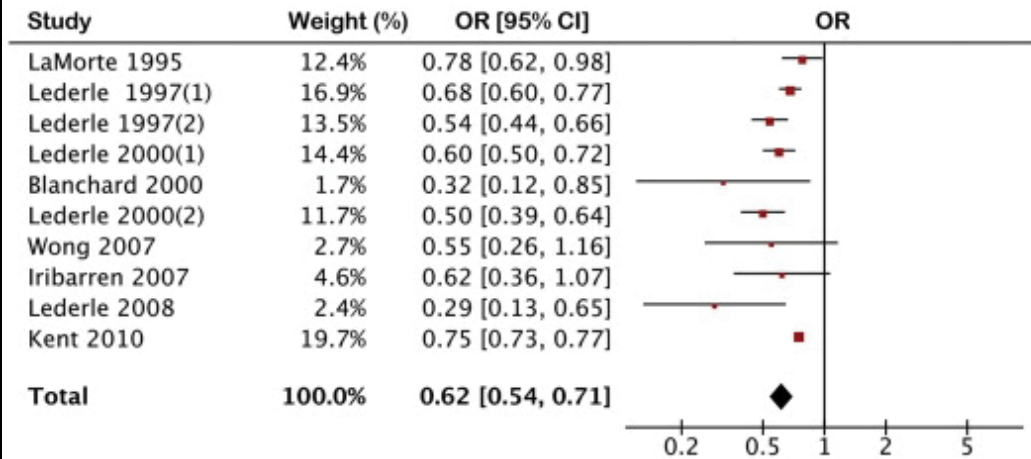
QRCPPVD

Queensland Research Centre for
Peripheral Vascular Disease

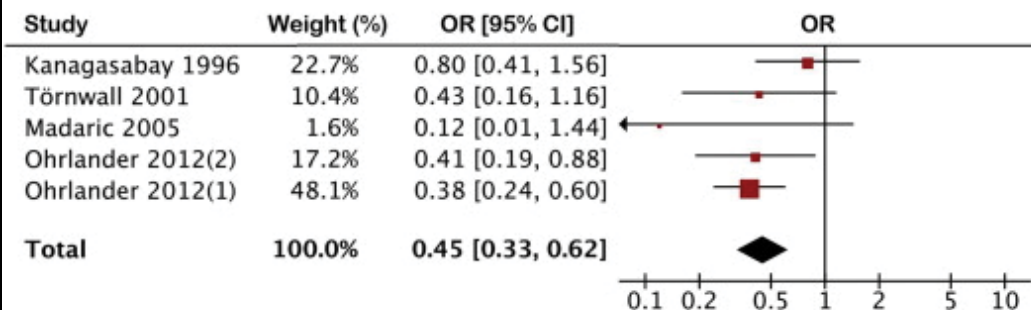
Diabetes and AAA prevalence

Geography/Adjusted

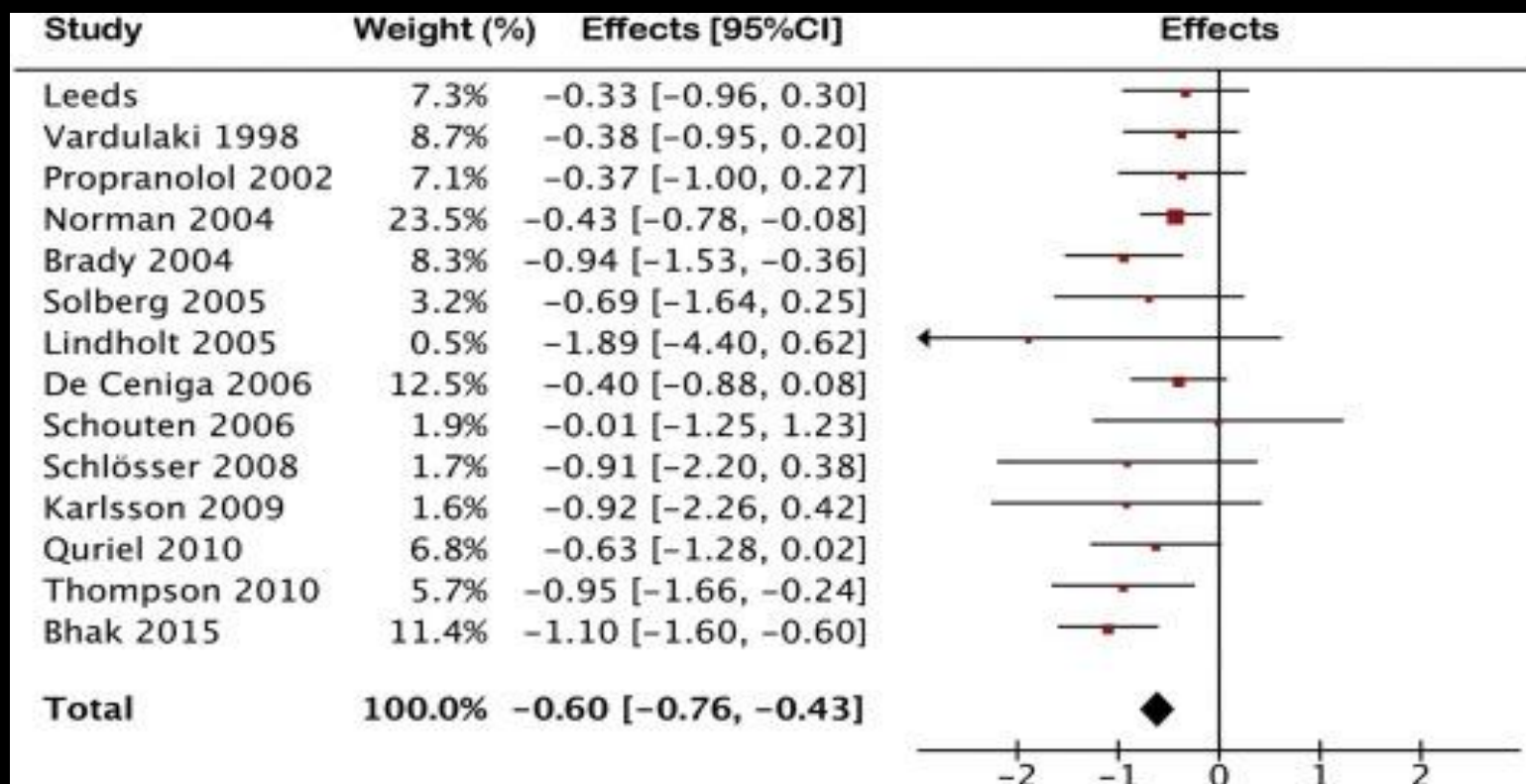
(A) North America



(B) Europe

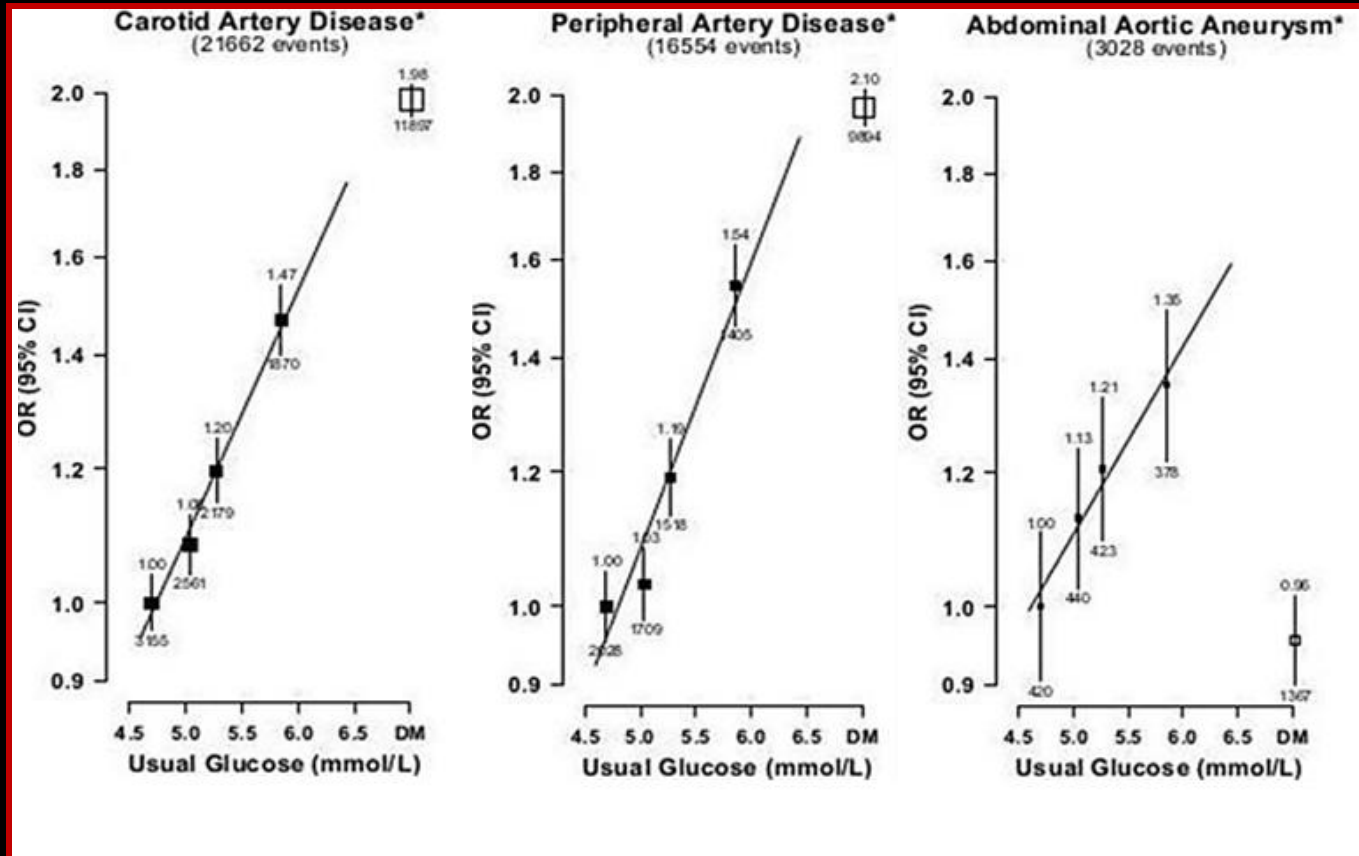


Diabetes and AAA growth



IJC. 2016;221:484-95.

Screening study suggests risk of AAA in people without DM greater for those with higher blood sugar



Could treatment of diabetes be the factor limiting AAA prevalence and growth?



Aim: Examine association of metformin with AAA growth and AAA events

1. Cohort 1 (n=1357): Followed by repeat US for a mean of 3.6 years;
2. Cohort 2 (n=287): Followed by repeat CT for a mean of 2.9 years;
3. Cohort 3 (n=53): Two CTs 12 months apart

Metformin and AAA growth

Diabetes diagnosis	No	Yes	Yes	P value for comparing		
Metformin treatment	No	Yes	No	All 3 groups	Groups 2 and 1	Groups 3 and 1
Group	1	2	3			
Cohort 1 (US imaging)	N=1140	N=118	N=99			
Mean (\pm SD) annual growth (mm)	1.62 \pm 2.45	1.03 \pm 2.68	1.60 \pm 2.94	0.026	0.012	0.217
Mean (\pm SD) percentage growth	4.52 \pm 8.21	2.94 \pm 7.45	4.13 \pm 7.66	0.017	0.010	0.140
Cohort 2 (CT imaging)	N=218	N=39	N=30			
Mean (\pm SD) annual growth (mm)	2.55 \pm 3.04	1.40 \pm 2.99	2.18 \pm 2.96	0.013	0.004	0.514
Mean (\pm SD) percentage growth	6.26 \pm 7.26	3.29 \pm 6.73	5.30 \pm 7.11	0.010	0.003	0.423



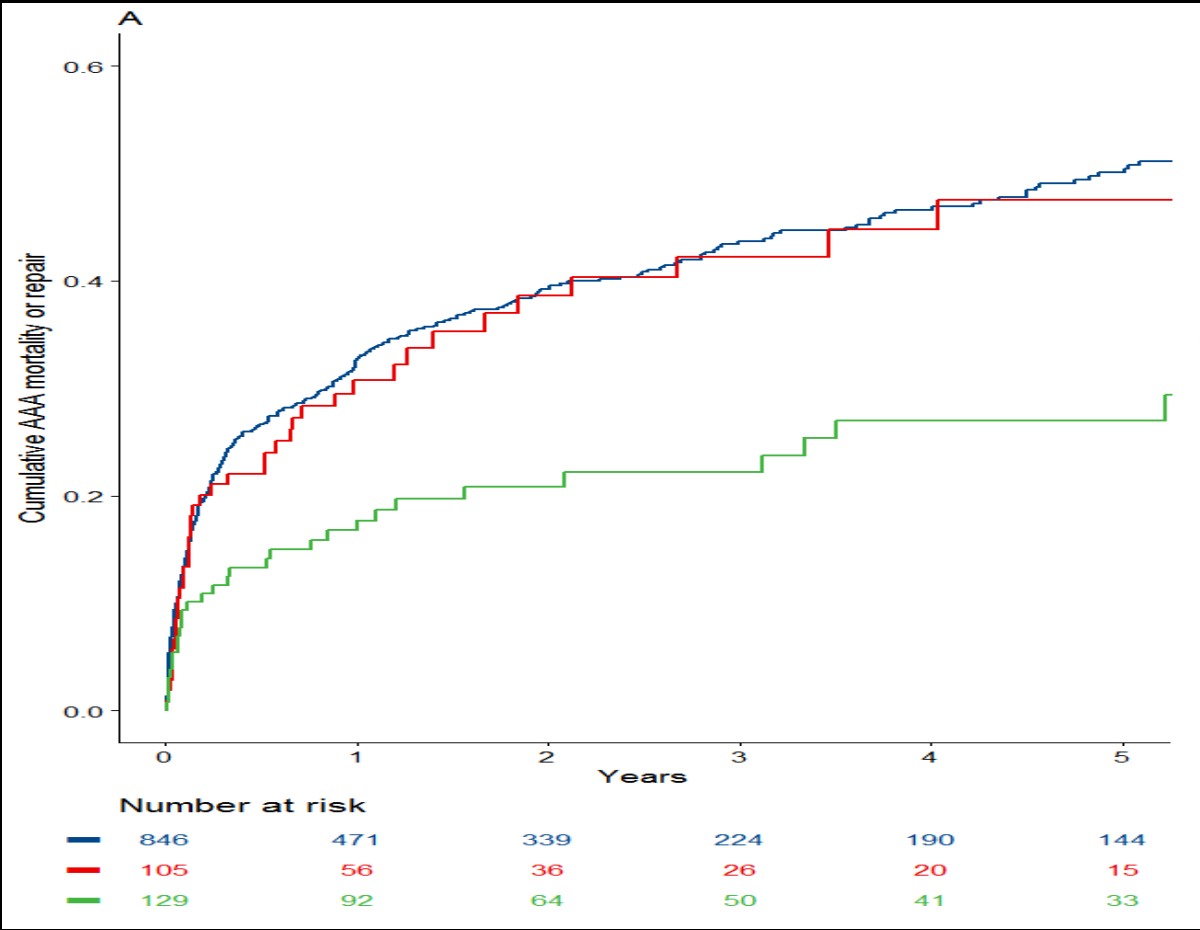
Independent association of metformin with reduced AAA growth medians

	Odds ratio	95% CI	P value
Cohort 1	0.59	0.39-0.87	0.008
Cohort 2	0.38	0.18-0.80	0.011
Cohort 3	0.13	0.03-0.61	0.010

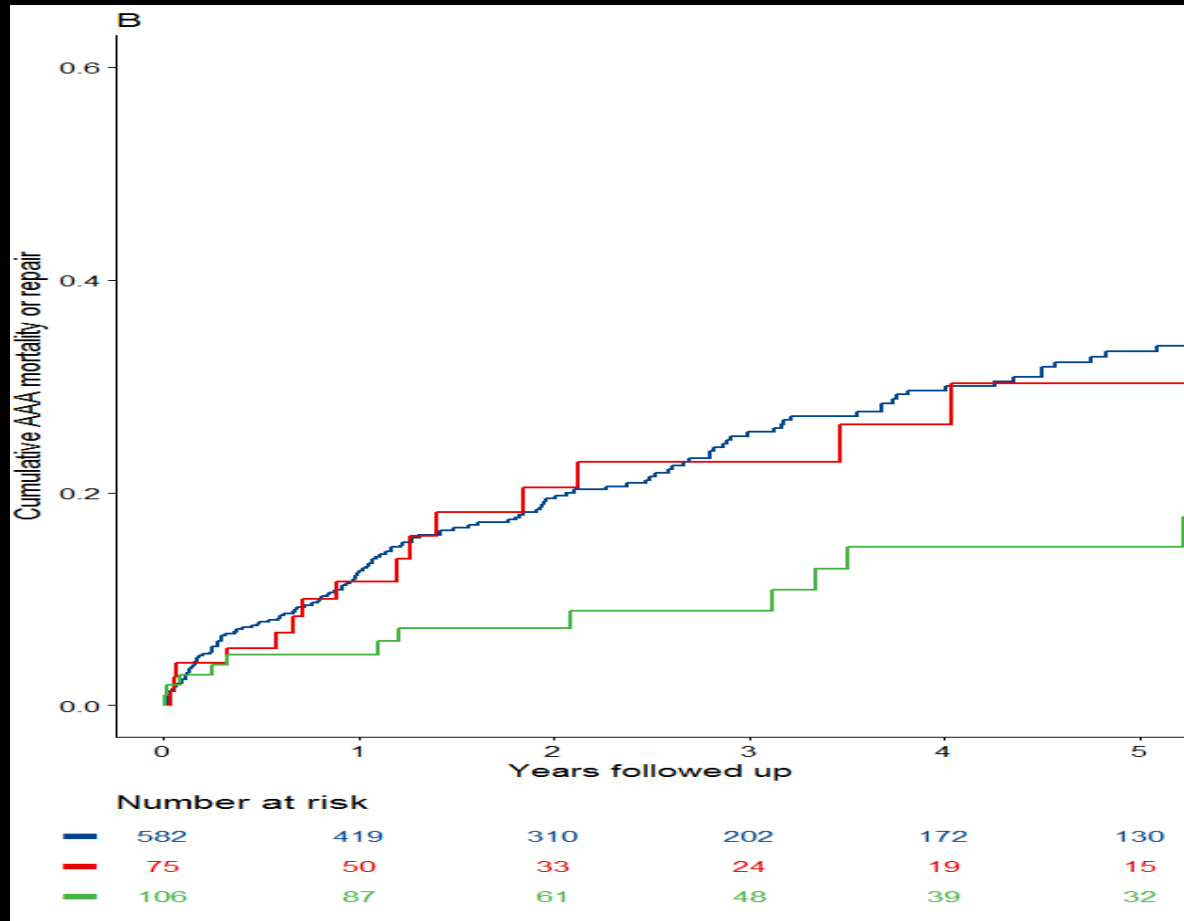
Adjusted for smoking, IHD, initial AAA diameter and sex

BJs 2017;104(11):1486-1493.

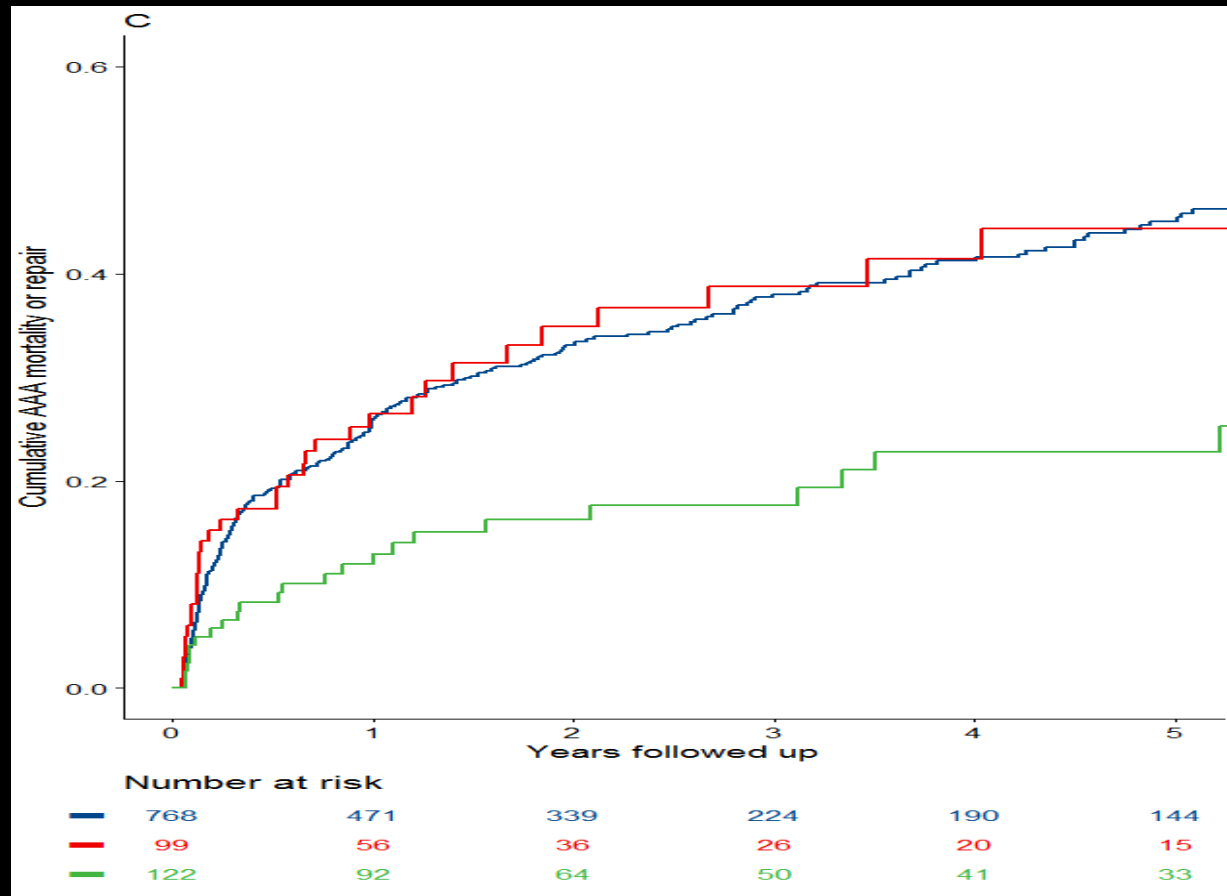
Metformin and AAA repair or mortality (full cohort, n=1080)



Metformin and AAA repair or mortality ($\leq 50\text{mm}$, $n=763$)



Metformin and AAA repair or mortality ($\geq 6m$ f/u, n=989)



Hazard ratios for AAA events

	Diabetes on metformin	Diabetes other treatments
Total cohort (n=1080)	0.63 (0.44-0.93)	1.15 (0.83-1.59)
AAA diameter \leq 50 mm (n=763)	0.48 (0.27-0.87)	1.16 (0.70-1.93)
\geq 6 months follow-up before event or loss (n=989)	0.57 (0.37-0.87)	1.28 (0.90-1.82)

Reported cf. patients with no diabetes; Adjusted for age, sex, smoking, initial AAA diameter, hypertension, ischemic heart disease, statin, frusemide, angiotensin converting enzyme inhibitor, and angiotensin receptor blocker; EJVES In press.

Limitations

- Association studies subject to residual confounding
- Therefore impossible to be certain if effect secondary to metformin or diabetes

In support of true effect of metformin:

- Consistent association in multiple cohorts plus an independent cohort (JVS. 2016;64:46-54);
- Other dm treatments not associated

Conclusions

- Metformin consistently associated with reduced AAA growth and AAA repair or AAA-related mortality (unlike other DM treatments)
- Impossible to rule out effect of DM as opposed to metformin
- RCT warranted

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