Supplementary Appendix

Sensitivity analysis

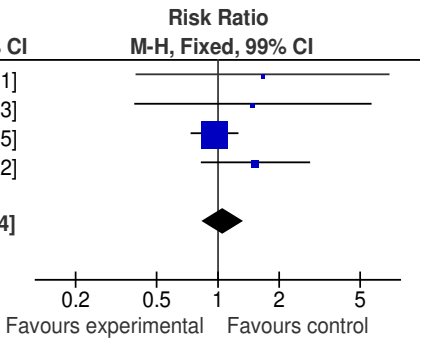
Primary outcome

1. All-cause mortality

Study or Subgroup	Intensive Events	Total	Standard Events	Total	Weight	Risk Ratio M-H, Fixed, 99% CI
Dargie	8	110	5	114	2.2%	1.66 [0.40, 6.91]
HOME	9	196	6	194	2.7%	1.48 [0.39, 5.63]
PROactive	177	2605	186	2633	82.6%	0.96 [0.74, 1.25]
UGDP a	64	408	21	205	12.5%	1.53 [0.83, 2.82]
Total (99% CI)		**3319**		**3146**	**100.0%**	**1.06 [0.84, 1.34]**
Total events	258		218			

Heterogeneity: Chi² = 4.42, df = 3 (P = 0.22); I² = 32%

Test for overall effect: Z = 0.67 (P = 0.50)

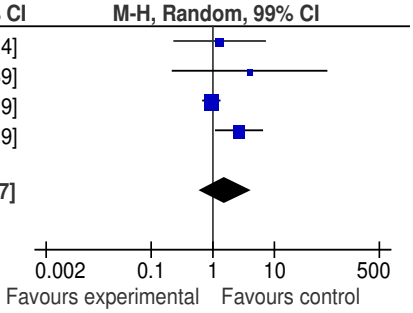


2. Cardiovascular deaths

Study or Subgroup	Intensive Events	Total	Standard Events	Total	Weight	Risk Ratio M-H, Random, 99% CI
Dargie	5	110	4	114	18.5%	1.30 [0.24, 7.04]
HOME	4	196	1	194	9.0%	3.96 [0.22, 69.69]
PROactive	127	2605	136	2633	40.7%	0.94 [0.69, 1.29]
UGDP a	53	408	10	205	31.8%	2.66 [1.13, 6.29]
Total (99% CI)		**3319**		**3146**	**100.0%**	**1.58 [0.60, 4.17]**
Total events	189		151			

Heterogeneity: Tau² = 0.33; Chi² = 10.09, df = 3 (P = 0.02); I² = 70%

Test for overall effect: Z = 1.22 (P = 0.22)

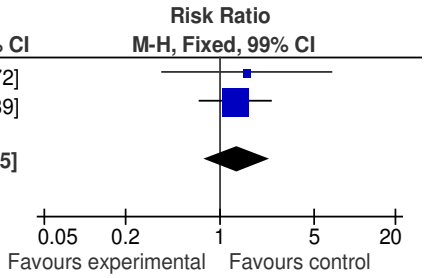


Macro-vascular events

1. All myocardial infarctions

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	8	196	5	194	14.6%	1.58 [0.37, 6.72]
UGDP a	57	408	22	205	85.4%	1.30 [0.71, 2.39]
Total (99% CI)		**604**		**399**	**100.0%**	**1.34 [0.77, 2.35]**
Total events	65		27			

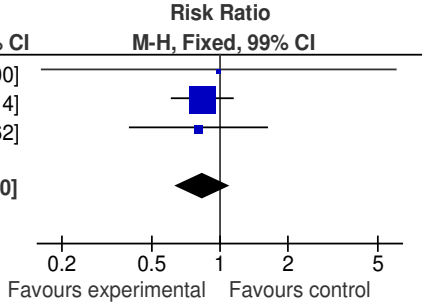
Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 1.36 (P = 0.17)



2. Non-fatal myocardial infarctions

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	4	196	4	194	2.3%	0.99 [0.16, 6.00]
PROactive	119	2605	144	2633	82.4%	0.84 [0.61, 1.14]
UGDP a	32	408	20	205	15.3%	0.80 [0.40, 1.62]
Total (99% CI)		**3209**		**3032**	**100.0%**	**0.83 [0.63, 1.10]**
Total events	155		168			

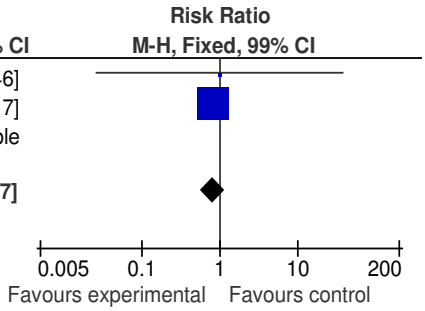
Heterogeneity: Chi² = 0.08, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 1.66 (P = 0.10)



3. All strokes

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	1	196	1	194	0.9%	0.99 [0.03, 37.46]
PROactive	86	2605	107	2633	99.1%	0.81 [0.56, 1.17]
UGDP a	0	408	0	205		Not estimable
Total (99% CI)		**3209**		**3032**	**100.0%**	**0.81 [0.57, 1.17]**
Total events	87		108			

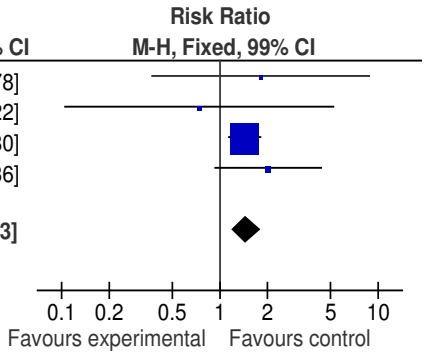
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.45 (P = 0.15)



4. Congestive Heart Failure

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
Dargie	7	110	4	114	1.8%	1.81 [0.37, 8.78]
HOME	3	196	4	194	1.8%	0.74 [0.11, 5.22]
PROactive	281	2605	198	2633	88.7%	1.43 [1.14, 1.80]
UGDP a	51	398	13	205	7.7%	2.02 [0.94, 4.36]
Total (99% CI)		**3309**		**3146**	**100.0%**	**1.47 [1.19, 1.83]**
Total events	342		219			

Heterogeneity: Chi² = 2.15, df = 3 (P = 0.54); I² = 0%
Test for overall effect: Z = 4.64 (P < 0.00001)

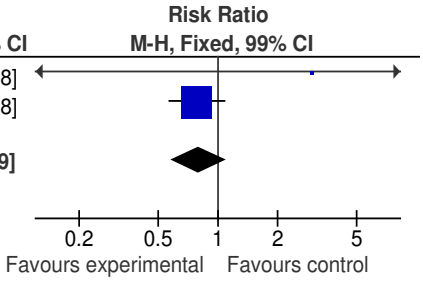


Micro-vascular events

1. New or worsening retinopathy

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	1	196	0	194	0.6%	2.97 [0.04, 197.68]
UGDP a	98	291	67	156	99.4%	0.78 [0.57, 1.08]
Total (99% CI)		**487**		**350**	**100.0%**	**0.80 [0.58, 1.09]**
Total events	99		67			

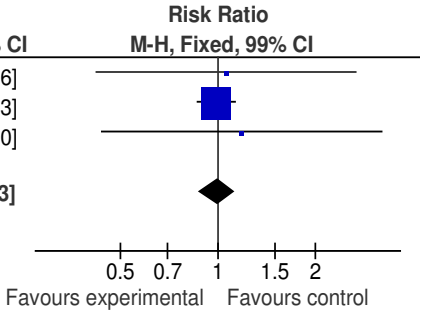
Heterogeneity: Chi² = 0.67, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 1.84 (P = 0.07)



2. New or worsening microalbuminuria

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	15	196	14	194	2.4%	1.06 [0.42, 2.66]
PROactive	555	2218	563	2225	95.5%	0.99 [0.87, 1.13]
UGDP a	22	384	9	186	2.1%	1.18 [0.44, 3.20]
Total (99% CI)		**2798**		**2605**	**100.0%**	**0.99 [0.87, 1.13]**
Total events	592		586			

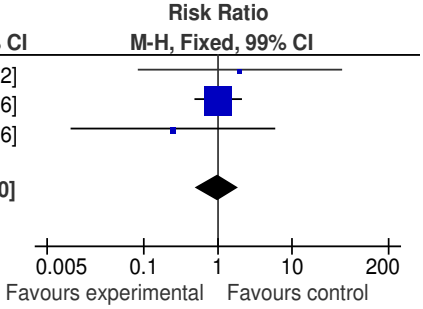
Heterogeneity: Chi² = 0.25, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.11 (P = 0.92)



3. Fatal or non fatal amputation

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	2	196	1	194	3.4%	1.98 [0.09, 45.92]
PROactive	26	2605	26	2633	87.5%	1.01 [0.50, 2.06]
UGDP a	1	392	2	194	9.1%	0.25 [0.01, 5.76]
Total (99% CI)		**3193**		**3021**	**100.0%**	**0.97 [0.50, 1.90]**
Total events	29		29			

Heterogeneity: Chi² = 1.61, df = 2 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)



4. Peripheral Vascular Events

Study or Subgroup	Intensive Events	Intensive Total	Standard Events	Standard Total	Weight	Risk Ratio M-H, Fixed, 99% CI
HOME	7	196	8	194	8.5%	0.87 [0.23, 3.20]
PROactive	80	2605	65	2633	68.7%	1.24 [0.81, 1.90]
UGDP a	59	367	16	182	22.7%	1.83 [0.92, 3.64]
Total (99% CI)		**3168**		**3009**	**100.0%**	**1.34 [0.95, 1.90]**
Total events	146		89			

Heterogeneity: Chi² = 2.30, df = 2 (P = 0.32); I² = 13%
Test for overall effect: Z = 2.20 (P = 0.03)