Stratified Medicine:
Misunderstandings and Misconceptions

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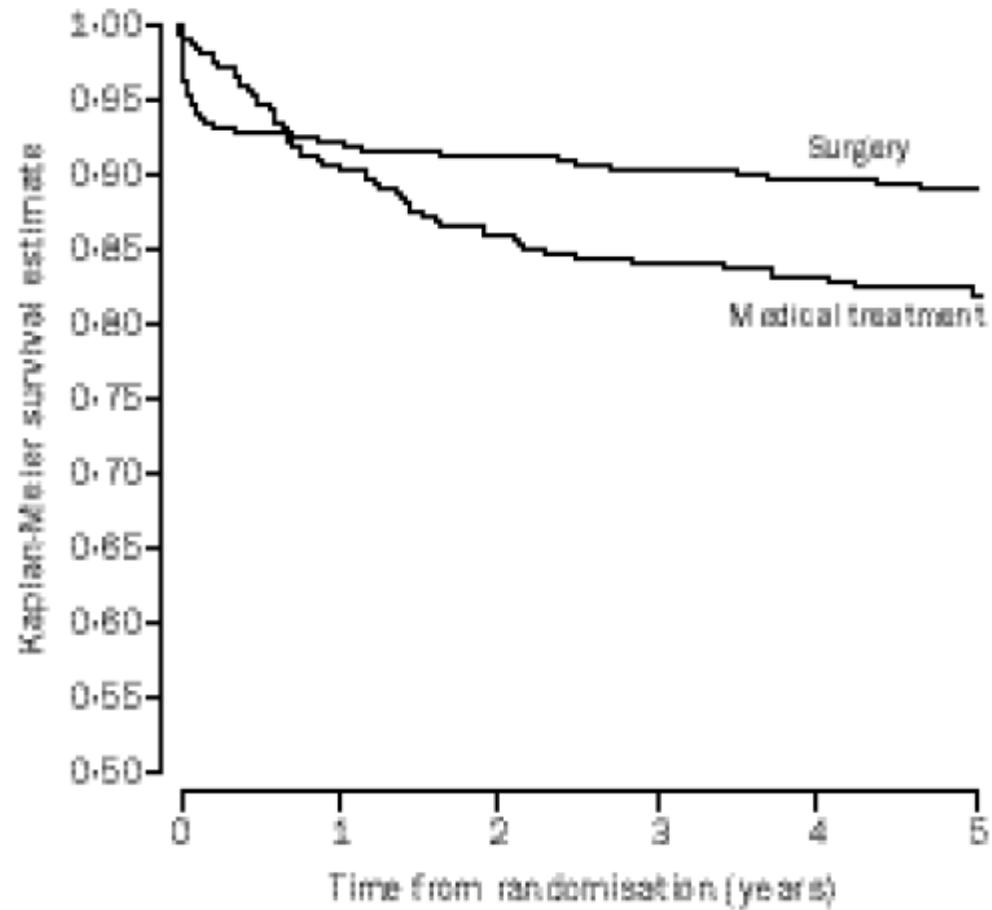
Edinburgh Hub

Misconceptions?

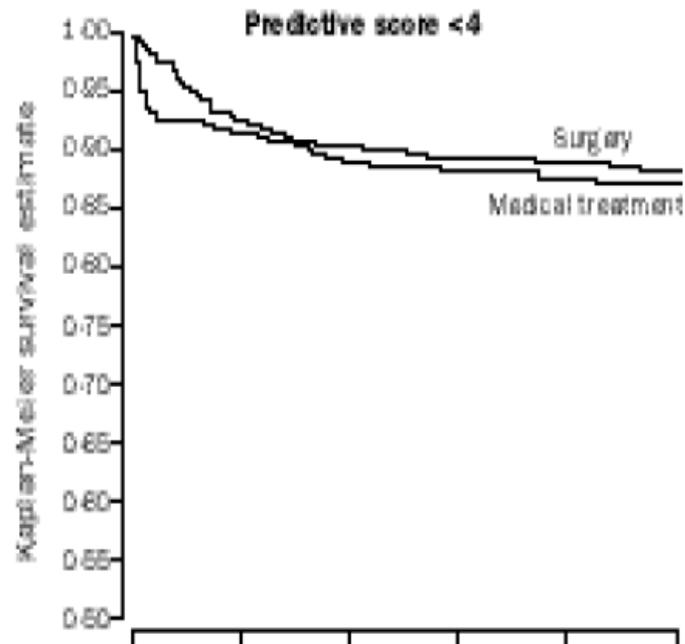- **Stratified medicine is a new idea**

Misconceptions?

- **Stratified medicine is a new idea**

See, for example, Rothwell PM and Warlow CP, on behalf of the European Carotid Surgery Trialists' Collaborative Group. "Prediction of benefit from carotid endarterectomy in individual patients: a risk-modelling study". *Lancet* **1999;<u>353</u>:2105-10.**
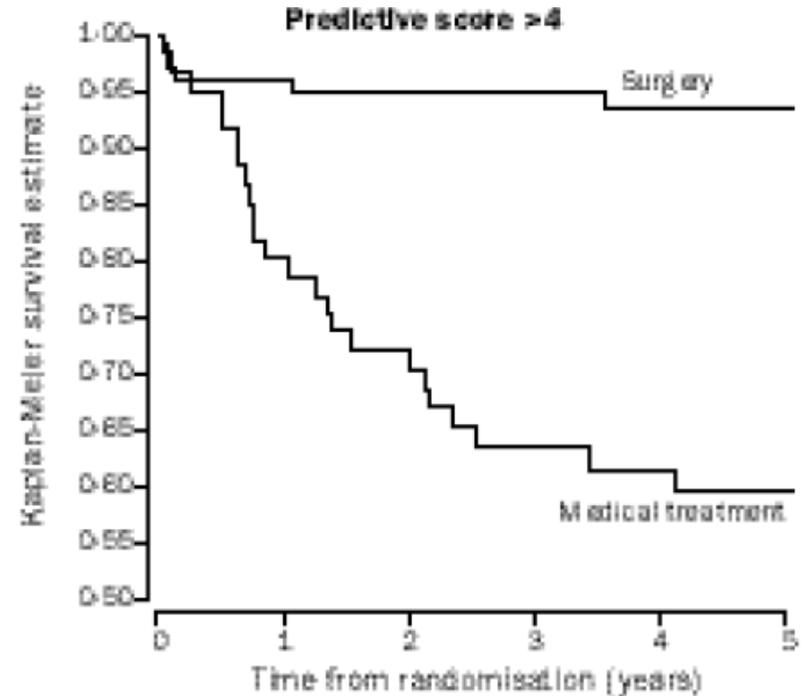
Overall trial results
(survival free of major stroke)

Stratified trial results

Predictive score <4

Kaplan-Meier survival estimate

Surgery

Medical treatment

Number of patients					
Surgery	495	430	411	375	310	244
Medical treatment	333	294	265	239	203	138

Predictive score >4

Kaplan-Meier survival estimate

Surgery

Medical treatment

Time from randomisation (years)

Number of patients					
Surgery	101	95	89	77	69	50
Medical treatment	61	46	40	36	33	24

Misconceptions?

- Stratified medicine is a new idea
- Stratified medicine is all about identifying a high risk, high response subgroup (so that trials can have small sample sizes, reducing the development time, etc)

Example (indication modified to protect the guilty)

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- **Current management: annual colonoscopy**

- **Proposal: develop biomarker to identify high risk subgroup; within high risk subgroup (~20%?), run RCT of annual colonoscopy versus definitive surgery; switch low risk subgroup to colonoscopy every three years**

Misconceptions?

- Stratified medicine is a new idea
- Stratified medicine is all about identifying a high risk, high response subgroup (so that trials can have small sample sizes, reducing the development time, etc)
- As long as a stratified medicine trial is 'well' designed, there is no need for a sense check

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- Hypothesis: a complex marker relating to nerve conductance will identify a high response subgroup (25% of all patients, with 90% responding to SSRIs), with only 50% of the 'marker negative' patients responding to SSRIs.

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- Hypothesis: a complex marker relating to nerve conductance will identify a high response subgroup (25% of all patients, with 90% responding to SSRIs), with only 50% of the 'marker negative' patients responding to SSRIs.

- Proposal: run a stratified RCT, powered to be able to detect this treatment/marker interaction.

Summary Recommendations/Conclusions

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Summary Recommendations/Conclusions

- **Stratified/personalised medicine is as old as medicine itself.**

- **Funders are increasingly recognising the need to bridge the gap between trials which show that interventions work 'on average' and evidence-based decisions at the level of individual patients.**

- **Stratified medicine trials need expert statistical input.**

- **Even more so than for conventional trials, stratified medicine trials need close collaboration between clinicians and methodologists.**