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admetan

A new, comprehensive meta-
analysis command

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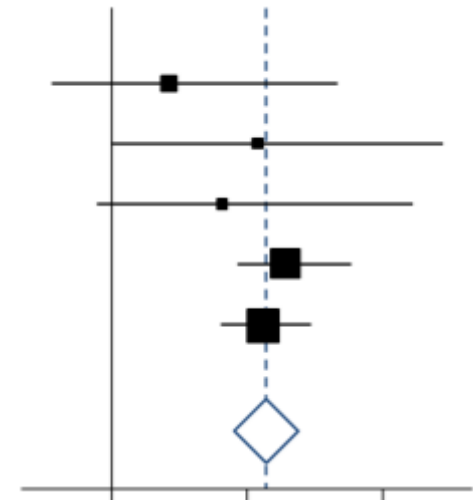
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Introduction to meta-analysis (MA)

- A statistical analysis which combines the results of several independent studies considered by the analyst to be 'combinable' (Huque 1988)
- Aggregate data (AD) MA uses published results; typically one observation (effect + variance) per *study*
- Individual participant data (IPD) MA uses original, raw data; single observation per *patient*.
- Basic inverse-variance approach with AD:

$$\theta_{pooled} = \frac{\sum_i w_i \theta_i}{\sum_i w_i}$$

where $w_i = 1/Var(\theta_i)$ = inverse of variance in study i .



(Image source: Wikipedia)

A brief history of meta-analysis in Stata

1997: **meta** (Sharp & Sterne)

1998: **metan** (Bradburn, Deeks & Altman)

Two packages released around the same time; slightly different functionality and capabilities; pre-**twoway** graphics

2008: **metan** (Harris, Bradburn, Deeks, Harbord, Altman & Sterne) – a comprehensive update, with **twoway** graphics etc.

2010: last SSC update to **metan**

2010: **metaan** (Kontopantelis & Reeves) released.

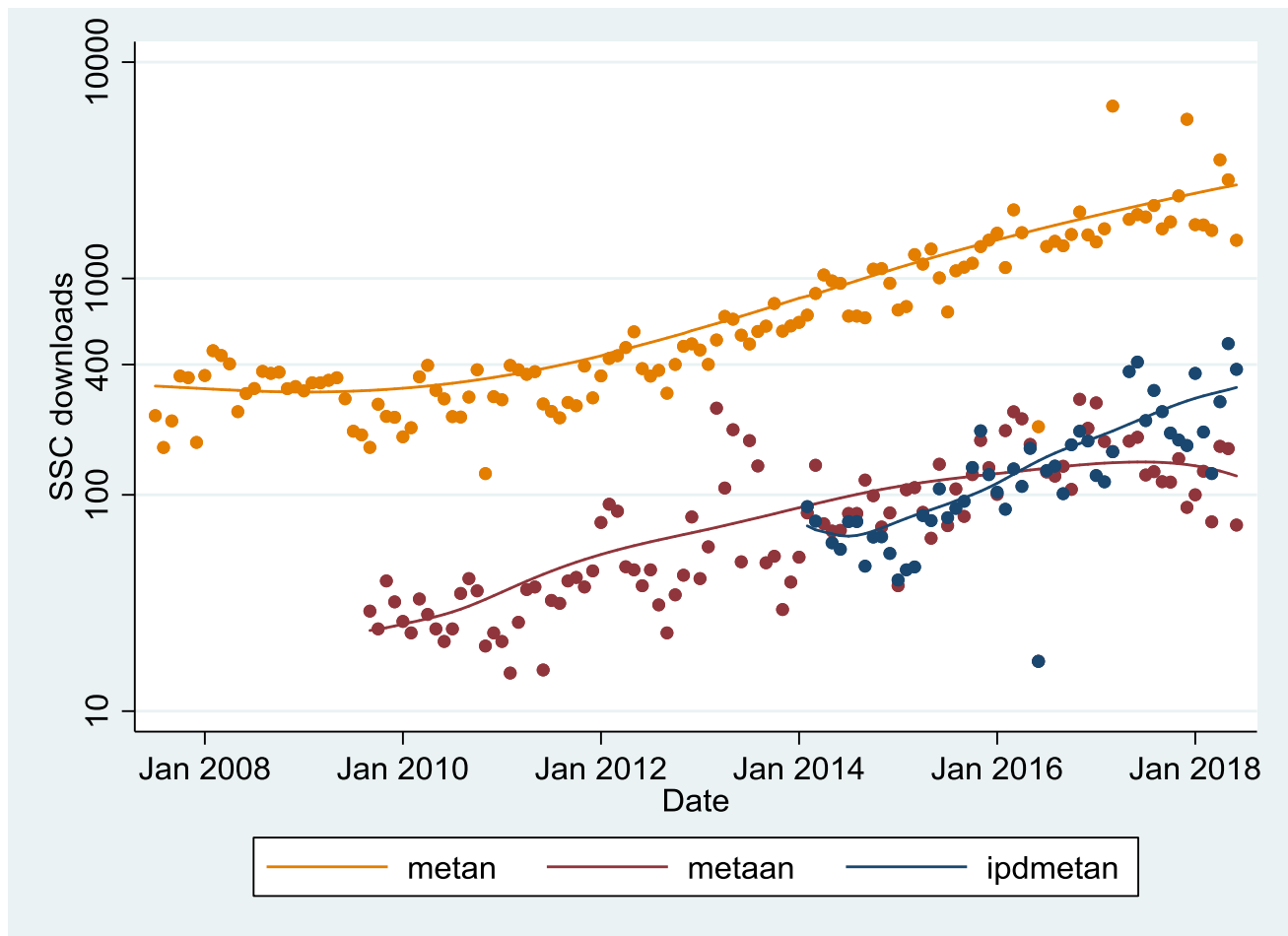
Focus on random-effects models, but fewer general features than **metan**

2013: **ipdmetan** (Fisher) presented at Stata London meeting; Stata Journal article followed in 2015; **admetan** is an ancillary ado-file

2018: **admetan** presented in its own right.

SSC monthly downloads

- Using `ssccount` (Choodari-Oskoei & Morris, SJ 2016)



A recurring theme?

- “Stata should have a meta-analysis command [...] but does not” (Stata manual, c.1998?)
- “Supporting it [**meta**] is difficult ... quite a lot of [employer] time has gone into this ... [in the future] I will likely not have the opportunity, save in my own time, to continue this” (Sterne, 2004)
- “I’d be delighted if someone else took responsibility for **metareg** ... I have no interest in this any more” (Sharp, c.2004)
- Luckily, Ross Harris took over **metan** in ~2008 and pushed it into the 2010s ... but he too has long since changed jobs and priorities
(N.B. I have his blessing for the **admetan** project)
- Is **admetan** any different??
 - While originally based heavily on **metan**’s code, **admetan/ipdmetan** has evolved to be (hopefully) more general, and more easily editable/updateable by others in the future

What can `admetan` do?

- Everything that `metan` can do...
 - caveat: some (very few) things could be done *directly* with `metan` but only *indirectly* with `admetan`
- ... but in many cases better ...
 - forest plots with improved defaults (e.g. aspect, x -axis labelling); increased flexibility
 - better handling of returned values and added variables
- ... plus a whole lot more!
 - much larger range of random-effects models
 - cumulative and influence meta-analysis
 - integration with `forestplot` and `ipdmetan`
 - input can be a matrix instead of variables
 - more continuity-correction options
 - etc.

Syntax

- Based on, and very similar to, syntax of **metan**:

admetan *varlist* [*if*] [*in*]

[, *main_options* `forestplot` (*forestplot_options*)]

... where *varlist* can be:

ES seES

effect size and std. error

ES lci uci

effect size and 95% conf. limits

event_treat noevent_treat

cell counts from 2x2 table

event_ctrl noevent_ctrl

n_treat mean_treat sd_treat

N, mean and SD, by treatment group

n_ctrl mean_ctrl sd_ctrl

oe v

O-E and V from log-rank/Peto analysis
(with **logrank** option)

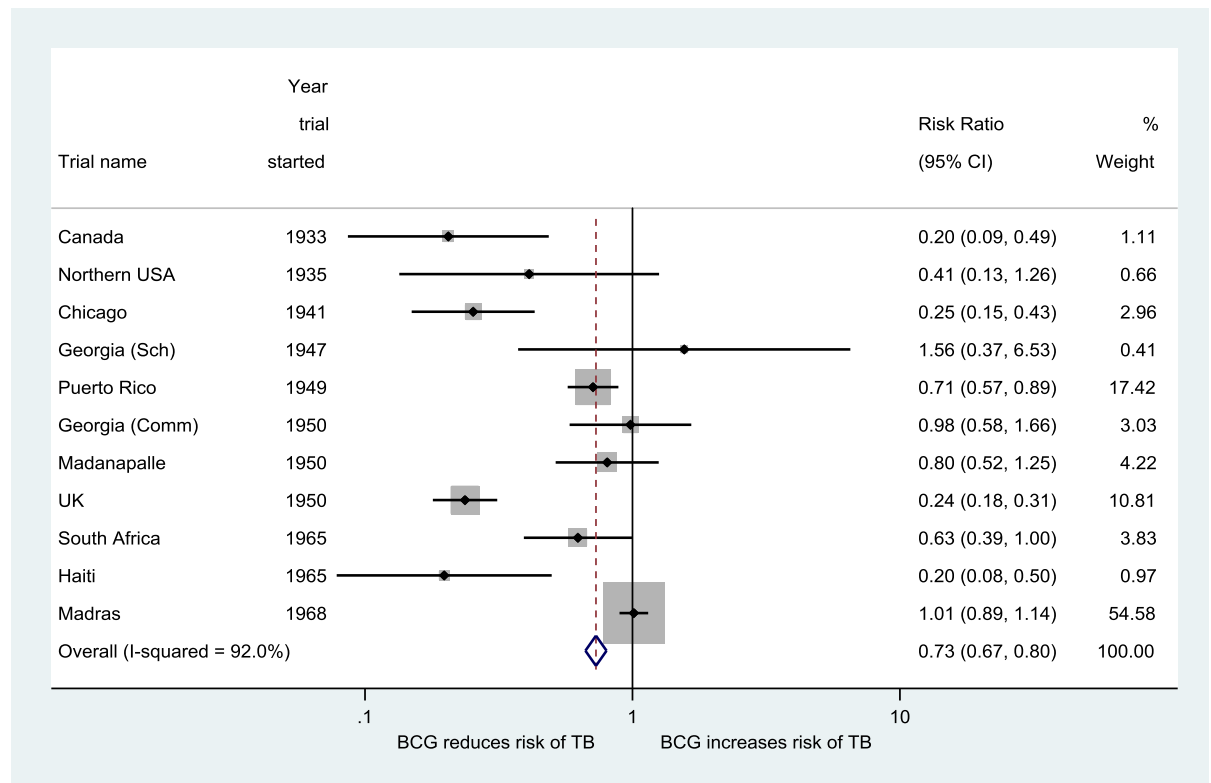
A basic example

Taken from Harris et al, SJ 2008

```
. use bcgtrial, clear
```

```
. metan tcases tnoncases ccases cnoncases, rr fixedi lcols(trialnam startyr)  
xlabel(0.1, 10) favours(BCG reduces risk of TB # BCG increases risk of TB)
```

```
. admetan tcases tnoncases ccases cnoncases, study(trialnam) iv  
forestplot(lcols(startyr) xlabel(0.1 10) favours(BCG reduces risk of TB # BCG  
increases risk of TB))
```



Random-effects models

- Assume the true treatment effect is randomly, normally distributed between studies, with heterogeneity variance τ^2
- (By contrast, the fixed-effect model assumes a single true treatment effect, with all study variability due to residual error)
- Standard inverse-variance model:

$$\theta_{pooled} = \frac{\sum_i w_i^* \theta_i}{\sum_i w_i^*}$$

where $w_i^* = 1/\{Var(\theta_i) + \tau^2\}$ with τ^2 estimated from the data.

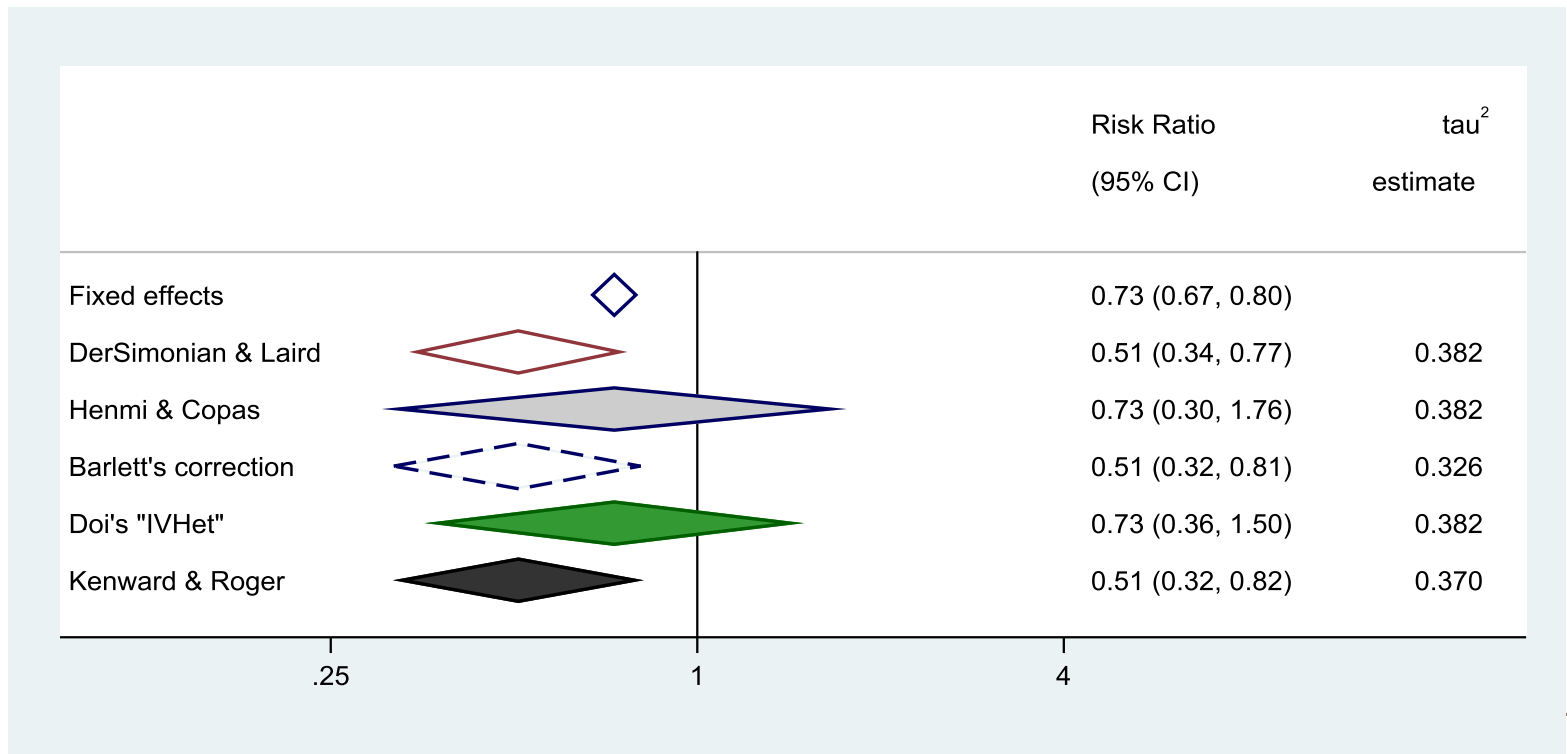
Random-effects models

- **metan** only has DerSimonian-Laird estimator of τ^2
- **ipdmetan** and **metaan** are examples of recent commands with a range of random-effects options
- **admetan** extends the range still further:
 - All models available in **ipdmetan** are carried over (Fisher SJ 2015)
 - More recent additions include
 - Henmi and Copas's gamma approximation method (Henmi and Copas 2010)
 - Bartlett's correction with Profile Likelihood (Huizenga et al 2011)
 - Doi's "Quality Effects" model (Doi et al 2015)
 - An ADMA version of Kenward & Roger's mixed-model variance correction for REML (Morris et al 2018)

Random-effects models

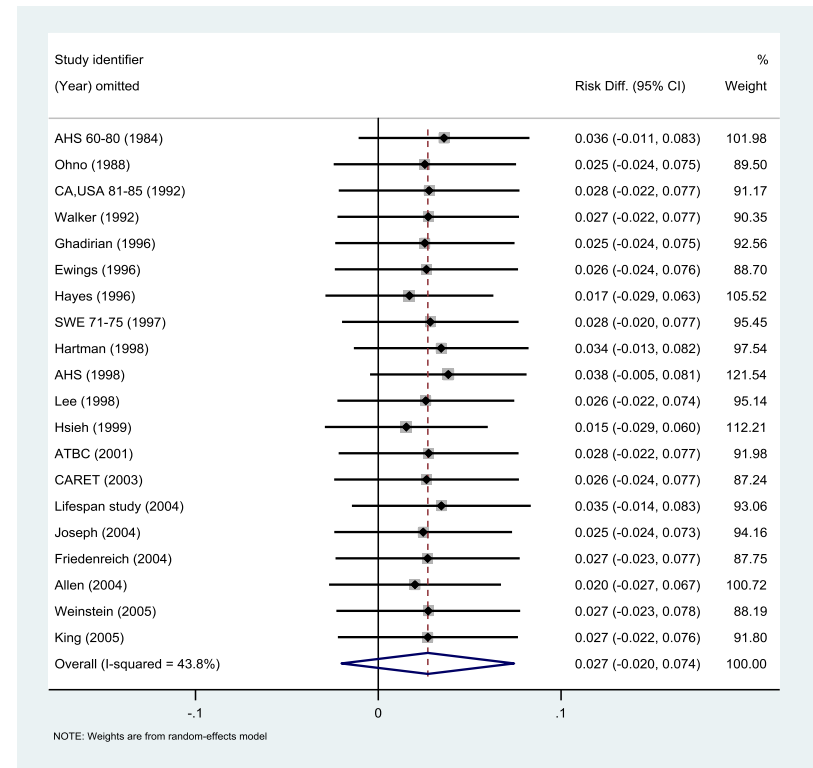
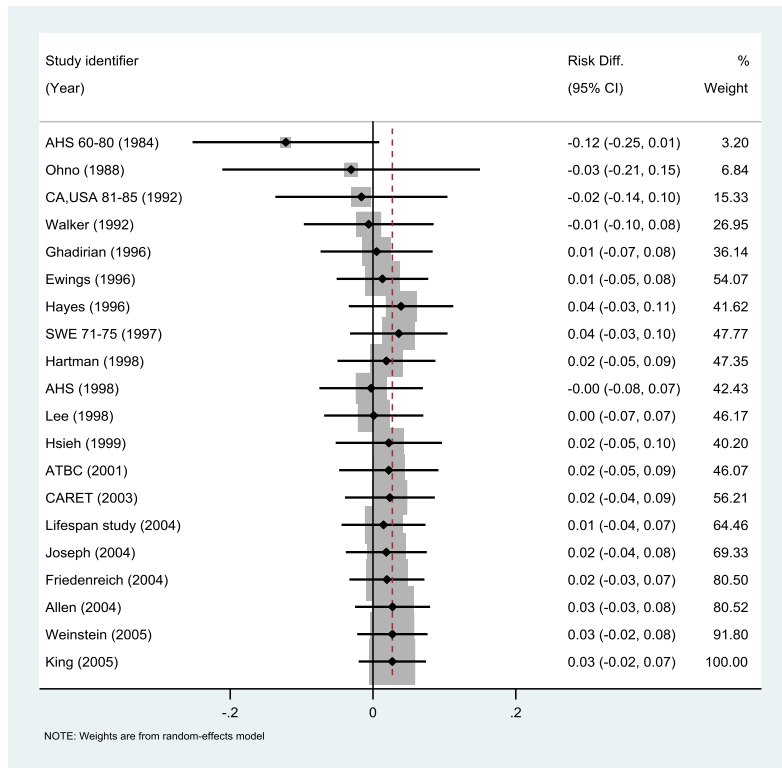
...with some colourful `forestplot` options

- (same example dataset as before, from Harris et al SJ 2008)
- I previously discussed how to specifying colour/pattern options for plot elements in the context of `ipdmeta` (Fisher SJ 2015)
 - New: diamonds now constructed using `twoway rarea`, allowing *fill colour*



Cumulative and Influence MA

- **cumulative** and **influence** options to **admetan** give similar functionality to existing commands **metacum** and **metainf**
 - But benefit from integration with rest of **admetan** and **forestplot**!



Saved datasets (“results sets”)

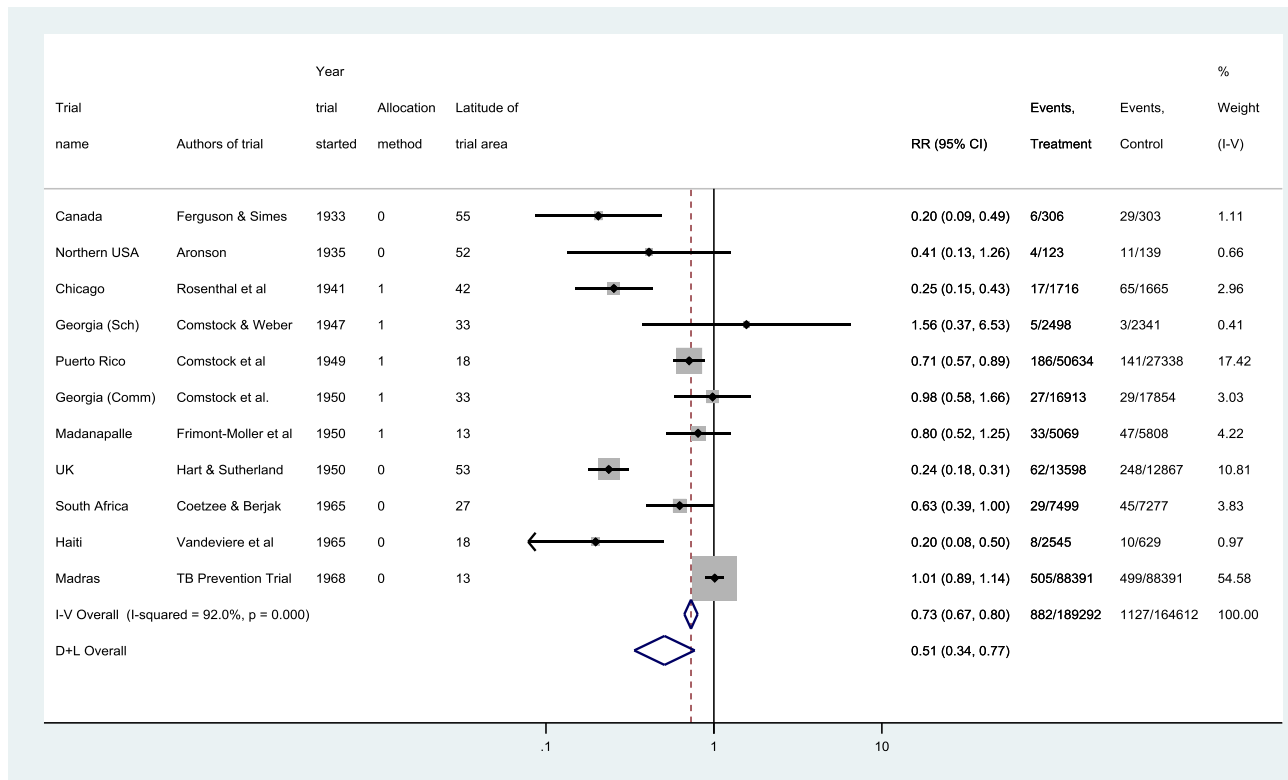
- Save data in a format from which **forestplot** can build a plot automatically, with no statistical modelling and minimal option-specification
 - Allows huge flexibility for forest plots
 - I’ve previously mentioned this in connection with **ipdmetan**
- Example use case: recreate **metan**’s “**second()**” option (not currently available with **admetan**) for e.g. displaying fixed- and random-effects results on same forest plot
- Psuedo-code:
 1. Run first (e.g. fixed-effects) analysis; save results set
 2. Run second (e.g. random-effects) analysis; save results set
 3. Load first results set; append second results set
 4. Apply any additional tweaks
 5. Run **forestplot**.

Result using metan

(taken from Harris et al, SJ 2008)

```
. use bcgtrial, clear
```

```
. metan tcases tnoncases ccases cnoncases, rr fixedi second(random)  
lcols(trialnam authors startyr alloc latitude) counts astext(70)  
textsize(200) boxsca(80) xlabel(0.1,10) notable xsize(10) ysize(6)
```

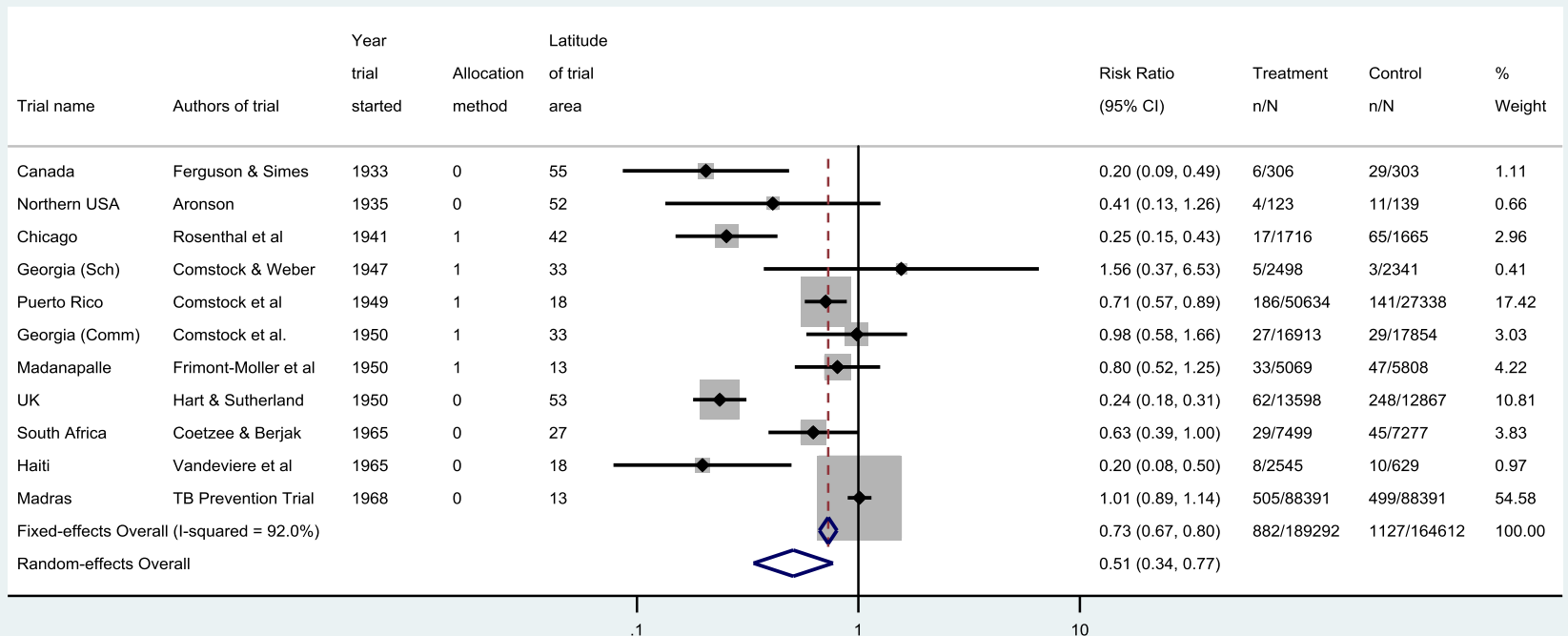


Code using admetan

```
// Run random-effects model, using "summaryonly" option
. admetan tcases tnoncases ccases cnoncases, re nograph summaryonly
saving(random.dta)

// Run fixed-effects model, and create "results set"
. admetan tcases tnoncases ccases cnoncases, rr iv study(trialnam)
forestplot(lcols(authors startyr alloc latitude) counts switch(counts) xlabel(.1
1 10) astext(70) leftj) nograph saving(fixed.dta, replace)
. preserve
. use fixed.dta, clear
. local lblfmt : format _LABELS
. replace _LABELS = "Fixed-effects " + _LABELS in `=_N'
. append using random.dta
. replace _LABELS = "Random-effects Overall" in `=_N'
. replace _WT = . in `=_N'
. format `lblfmt' _LABELS
. forestplot, useopts
. restore
```

Result using admetan



Note the improved defaults with `admetan` relative to `metan` for aspect ratio, text size and box scaling

The future?

- Together, **admetan** and **forestplot** now provide a huge amount of functionality and flexibility
 - **ipdmetan** (and **ipdover**) provide additional capabilities for IPD
 - Results/coefficients from complex regression models can be passed to **admetan** or **forestplot** for presentational purposes (e.g. one-stage IPD MA!)
- Code is (hopefully) efficient, up-to-date and clear enough (e.g. comments; subroutines) for others to modify, add to, or take over entirely in the future
 - GitHub? ResearchGate?
- Issues for your consideration:
 - Repositories (SSC, SJ; **findit**) refer to **ipdmetan**; but **admetan** now arguably “core”
 - Partly for this reason, **admetan** lags way behind **metan** in terms of SSC downloads
 - How to resolve this? Should **admetan** have its own SSC page? How should **forestplot**, **ipdmetan** etc. be “bundled”?
 - Contact **metan** authors and propose that **admetan** “takes over”? (with suitable acknowledgments going forward)

Acknowledgments

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- Contact: d.fisher@ucl.ac.uk

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