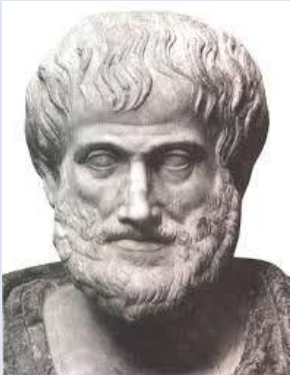


A GCIIG Mega-Database

Ros Glasspool on behalf of the Mega-
Database committee

Tokyo Nov 2015

A GCIG Mega-Database of Trials



“The whole is greater than its parts”

Aim: To perform individual patient level meta-analyses in order to address questions that cannot be answered by individual trials.

Potential

- Validation of surrogate markers (eg PFS/OS)
- Increase the power to detect an effect of a specific therapy
- Investigation of the effect within sub-groups
 - rare histologies, elderly patients, BRCAm
- Investigation of prognostic and predictive markers

GASTRIC: **G**lobal **A**dvanced/**A**djuvant **S**tomach **T**umour **R**esearch **I**nternational **C**ollaboration

Individual patient-level meta-analysis of all RCTs of adjuvant chemotherapy:

Aims

- Quantify the benefit of chemotherapy over surgery: OS and DFS
- Validity of DFS as a surrogate of OS
 - 31 trials 6390 patients identified in literature search
 - 17 trials (3838 patients) included with a median follow-up exceeding 7 years.
 - OS (HR 0.82; 95% CI 0.76-0.90; $P < .001$)
 - DFS (HR, 0.82; 95% CI 0.75-0.90; $P < .001$)
 - 5YS increased from 49.6% to 55.3% with chemotherapy

ACCENT - Colorectal

ACCENT database: 33, 000 patients from 25 adjuvant chemotherapy trials (1977-2008)

– Adjuvant 5FU/Leucovorin

- Stage II and III (3 trials)
- Stage II (+2 trials)
- Elderly (+2 trials)
- Nodal status, stage and grade independently prognostic
- Treatment effect across groups but benefit in stage III>II

– Surrogacy of DFS for OS

- 13 trials (including oxaliplatin/irinotecan)
- 3 Y DFS α OS
- Factors associated with post recurrence survival
- Improved post progression survival weakens DFS/OS relationship
- Can be strengthened by longer OS follow up
- More modern regimens decreased relationship between DFS and OS



Role of the GCIG

Success depends upon:

- Commitment from everyone
- Careful selection of the initial key questions
- Dedicated team

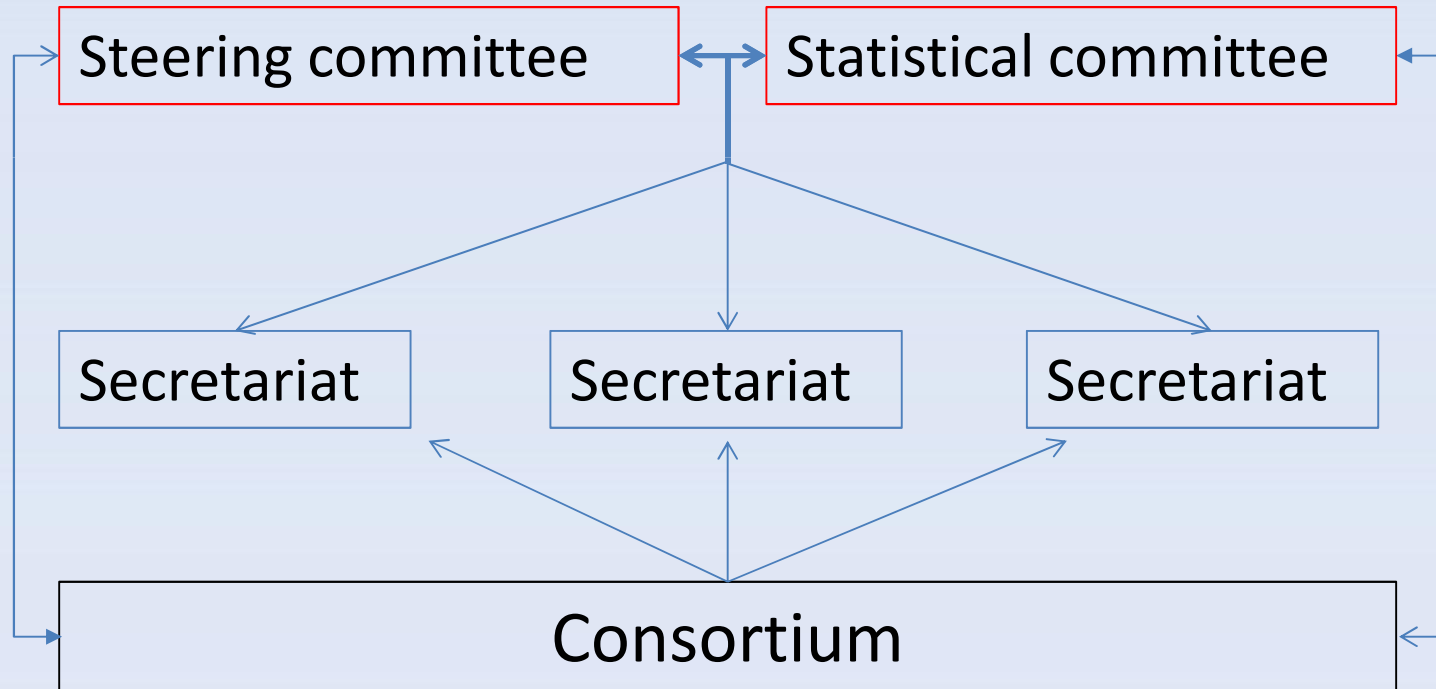


Process and Principles

Resource open to all members

Terms of reference

Structure



Process and Principles

Secretariats

- Collect and secure data
- Check data with common procedures (see Stewart *et al*)
- Organize the data
- Analyze data

A comparison of the results of checked versus unchecked individual patient data meta-analyses (Stewart et al Health technology 2011)

The Role of the Translational Committee

- Contribute questions
- Expertise on:
 - What data exists
 - Types of data sets
 - Different platforms
 - Combining clinical and translational data sets

Next Steps

- Proposals
 - Assess the validity of PFS as a surrogate for OS in ovarian cancer trials.
 - Assess prognosis and outcomes following treatment in first line and at relapse in different histological sub-types of cervical cancer.

