DAMOCLES: Issues in data monitoring for RCTs & a Charter for DMCs

Matthew Sydes
MRC Clinical Trials Unit, London, UK

for the DAMOCLES study group
FAQs

1. What are DMCs?
2. What was the DAMOCLES project?
3. Why a Charter?
4. Why this Charter?
5. How and when should I use it?
6. What does the Charter look like?
7. How does it help with contentious issues?
8. Where do I get a copy of the Charter?
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Data Monitoring Committees

- A group responsible for reviewing accruing information from clinical trials
- Many names used for this committee
  - 46 names in 662 trials
- Recommend “DMC”
  - Standardisation helpful
  - Short
  - Doesn"t emphasise only some roles (eg safety)
  - ICH GCP
FAQs

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Background

- Formal monitoring of trials becoming more common
- Monitoring function delivered mainly through DMCs
- Wide variation DMC structure / organisation
- Little guidance on how they should operate
The DAMOCLES study

- Commissioned by the HTA Programme
- Aims:
  - to investigate the processes of monitoring accumulating trial data
  - to identify ways of increasing the likelihood that DMCs make good decisions
- Underlying principle:
  - Examine DMC processes and identify how “right” decisions are made
DAMOCLES study group

BSU, Cambridge
  David Spiegelhalter

CSM, Oxford
  Doug Altman

CTU, London
  Abdel Babiker
  Janet Darbyshire
  Mahesh Parmar
  Matthew Sydes

HRSU, Aberdeen
  Marion Campbell
  Adrian Grant
  Sharon McLeer
  Anne Walker
  Sheila Wallace

LSHTM, London
  Felicity Clemens
  Diana Elbourne
  Stuart Pocock
DAMOCLES methodology

1. Systematic review of literature on DMCs
2. Systematic review of small group processes relevant to DMCs
3-6 Surveys:
   - DMC use in published RCT reports
   - DMC use in recent RCTs
   - DMC use in ongoing RCTs
   - DMC policies of relevant organisations
7. Case studies DMCs
8. Interviews with experienced DMC members
## DAMOCLES study group

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23 questions about DMCs

- Role of DMC (5)
- Structure and organisation (5)
- Information available to DMC (3)
- Decision-making and reporting (10)
Example questions

4 Does the DMC have a role before the trial recruitment phase?
11 What material should be available to a DMC?
15 What decisions/recommendations should be open to the DMC?
16 How should the decision or recommendation be reached within the DMC?
Systematic review of literature on DMCs
Review - methods

- Keyword online search 4007
  Of MEDLINE, PREMEDLINE, EMBASE, CINAHL and HealthSTAR

- Removal of duplicates by hand 3525
  Double review by group - grading into categories of interest (303)

- Articles relevant to DMCs 116
  Review by all group members as suitable for first collection

- Graded as worthy of retrieval 84

- Supplementary sources 16
  Library searches, books, references from other articles

- Total 100
Review – data collection

- All articles were obtained

- Coded in ATLAS.ti using 23 questions

- Variable amounts written for each question
  - 2124 quotes (range 8 – 305)

- Some easier to summarise than others
Review – selected results

• Q14: Is the DMC advisory or executive?
  ▪ General agreement DMC is advisory
  ▪ Advisory to Trial Steering Committee
  ▪ DMC not organising the trial, so should limit to recommendations
  ▪ DMC recommendations generally prevail
Review – selected results

- Q10: What training & preparation needed?

  Consensus of qualities needed:
  
  - Knowledge of disease area
  - Experience of clinical trials
Q3: **Primary** role of the DMC?

- review interim analyses of outcome data
- monitor trial for safety
- monitor trial for early convincing benefit
- protect the trial subjects
- ensure patients risks are reasonable
- participant safety and trial integrity
- protect patients in the trial *and* other patients with the disease in question
Review - selected results

- Q3: Role of the DMC
  - Role may be reflected in names *(later)*
  - Role may differ according to the trial
  - DMCs do not specify analysis but may advise
  - DMCs do not assess treatment effects on individual patients
  - DMCs ensure credibility and integrity by allowing PI to remain free of knowledge
• Q2: DMC responsible to who?
  ▪ Patients in the trial
  ▪ Future patients to be enrolled in the trial
  ▪ Future patients in target population treated after the trial
  ▪ Society in general
  ▪ Principal investigators
  ▪ Steering committee
  ▪ Sponsor
Systematic review of small group processes relevant to DMCs
Background

- Decision-making process is considered to be one of the most important group tasks

- Current literature is not conclusive on how best to optimise performance

- Most based within cognitive, social & organisational psychology, sociology & management sciences
Aim & Methods

• To identify factors that make errors more or less likely in small decision-making groups
• Review focused primarily on reviews of empirical studies of small task-orientated decision making groups in:
  ▪ (i) laboratory settings
  ▪ (ii) naturally occurring groups (esp juries, political task-orientated decision-making groups)
• 9 electronic databases searched
• 3187 review abstracts identified & assessed
• 57 reviews included
Group size

- Group size may affect the quality of the decision-making process
- Smaller groups tend to make poorer quality decisions because the range of views expressed is limited
- In larger groups, members may be reluctant to express their views and bias may occur towards riskier decision making
Group roles

• A degree of diversity within the group membership tends to result in better quality decisions

• The Chair can have an important influence on decision-making process and outcome

• If large status differences among group members, decision tends to be the one preferred by more powerful members
Communication in groups

• Groups tend to be more efficient if there is active communication between members, preferably face-to-face
• Effects of telephone conferences on decision quality or outcome are not conclusive
• Effects of electronic communication in context of electronic decision support systems unclear
  ▪ Work predates video conferencing, Webex, Adobe Connect, etc
Information given to groups

- The way in which information is framed can have a significant impact on decision outcomes

- Jury studies show that strength of evidence (quantity & quality) is a major determinant of decision outcome
Group decision-making

- Quality improved if range of opinions are expressed and all members have an opportunity to participate
- Jury studies: decision rule influences decision quality
  - i.e. unanimous decisions better quality
- Voting useful if it follows a full discussion of all views
- Formal methods of reaching decisions generally as good or better than informal methods
- Studies of decision support systems using electronic forms of communication inconclusive
Interviews and case studies
Interviews and case studies

- Qualitative methods used to explore working practices of DMCs
- Data derived from:
  - In-depth interviews with experienced DMC members across a range of trials
  - In-depth case studies of trials where decision-making had been "difficult"
Methods

- Purposive sample of DMC members and case studies
- 14 general interviews
  - Experiences of DMC decision-making across range of trials
- 4 in-depth case studies
  - "Difficult" DMC decision-making situations across different clinical areas
  - n=23 interviews
- Interviews in-person or by phone
  - Audio-recorded and transcribed verbatim
Size and composition of DMCs

- Consensus that between 3-6 members works well
- DMCs should be large enough to provide appropriate diversity of perspectives and experience
- Statistical and clinical expertise essential
- Strong views about selecting the "right people"
- Concerns about effect of a "maverick" member, especially on a small DMC
Size and composition of DMCs

- Mixed feelings about "consumer input" on DMCs - needs to be explored further
  - Consumer involvement in TMGs greater now
- Involvement of ethicists in some DMCs not seen as successful
- Chairperson crucial in influencing discussions and decision outcome
- Previous experience as chair (preferably of DMC) essential
Practical arrangements

• Not always enough time at the beginning of a trial for DMC to discuss issues such as terms of reference, reviewing the protocol etc

• Advantages of pre-trial meeting:
  ▪ facilitate an easier atmosphere for members to get to know each other (must be face-to-face if possible)
  ▪ enable discussion of hypothetical scenarios

• Preference for face-to-face meetings

• Teleconferences accepted but concerns about its impact on communication
Decision-making

- Agreement that decision-making process is neglected
- No experiences of DMCs with pre-agreed procedures, apart from stopping guidelines
- Favoured approach is for decisions to be reached by discussion leading to development of opinion and unanimous agreement
- Mixed feelings about voting or other formal decision-making methods being used
Training issues

- Concerns that increasing demand for DMCs has led to appointment of members with insufficient experience or expertise
- Lack of DMC background information and reading material for new members
- Unclear as to "what they are there to do"
- "Observer role" for new DMC members considered potentially helpful
Survey of published RCT reports
Survey - methods

• Eligible trials
  ▪ Randomised controlled trial
  ▪ Human subjects
  ▪ Intention to evaluate therapeutic or preventive health care interventions
  ▪ Main published report of trial results

• General vs specialist journals
• 1990 vs 2000
# Survey - journals included

<table>
<thead>
<tr>
<th>General medical journals</th>
<th>Specialist - Cancer</th>
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<tbody>
<tr>
<td>NEJM</td>
<td>Journal National Cancer Institute</td>
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<tr>
<td>JAMA</td>
<td>Journal Clinical Oncology</td>
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<tr>
<td>Lancet</td>
<td>Cancer</td>
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<tr>
<td>Annals Internal Medicine</td>
<td>Leukemia</td>
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<td>Archives Internal Medicine</td>
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<tr>
<td>Circulation</td>
<td>Archives General Psychiatry</td>
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<td>Journal American College Cardiology</td>
<td>American Journal Psychiatry</td>
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<td>Stroke</td>
<td>Neuropsychopharmacology</td>
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<td>European Heart Journal</td>
<td>Journal Clinical Psychiatry</td>
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<td></td>
<td>British Journal Psychiatry</td>
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<tr>
<th>Specialist - Infectious diseases</th>
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<tr>
<td>AIDS</td>
<td>Journal Infectious Diseases</td>
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<tr>
<td>Infection &amp; Immunity</td>
<td>Journal Antimicrobial chemotherapy</td>
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### Survey - comparisons

<table>
<thead>
<tr>
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<th>1990</th>
<th>2000</th>
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<tr>
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<tr>
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<th>2000</th>
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<tbody>
<tr>
<td>General</td>
<td>204</td>
<td>282</td>
</tr>
<tr>
<td>Specialist</td>
<td>x</td>
<td>x</td>
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<tbody>
<tr>
<td>General</td>
<td>x</td>
<td>282</td>
</tr>
<tr>
<td>Specialist</td>
<td>x</td>
<td>380</td>
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## Survey - reported DMC use

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<tr>
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<th>1990</th>
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<tr>
<td><strong>General</strong></td>
<td>21</td>
<td>70</td>
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<td></td>
<td>205 (10%)</td>
<td>282 (25%)</td>
</tr>
<tr>
<td><strong>Specialist</strong></td>
<td>x</td>
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<td>380</td>
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<tr>
<td></td>
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<td>(13%)</td>
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Reported DMC use...

... more likely if
- Multi-centre trial
- Larger planned sample size
- Drug company involvement
- Factorial design
- Vital status endpoint

... less likely if
- Cross-over design

Based on data for 2000
## Stopping rules reported

<table>
<thead>
<tr>
<th>Methodology for interim rule</th>
<th>1990 General</th>
<th>2000 General</th>
<th>2000 Special</th>
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<tbody>
<tr>
<td>Frequentist (Group Sequential)</td>
<td>5 31%</td>
<td>12 34%</td>
<td>7 35%</td>
</tr>
<tr>
<td>Frequentist (Group Sequential) and Decision Theory</td>
<td>0 3%</td>
<td>1 3%</td>
<td>0 0%</td>
</tr>
<tr>
<td>Frequentist (Continuous)</td>
<td>5 31%</td>
<td>8 23%</td>
<td>6 30%</td>
</tr>
<tr>
<td>Likelihood (Haybittle-Peto)</td>
<td>4 25%</td>
<td>9 26%</td>
<td>3 15%</td>
</tr>
<tr>
<td>Bayesian</td>
<td>0 0%</td>
<td>0 0%</td>
<td>1 5%</td>
</tr>
<tr>
<td>Other</td>
<td>1 6%</td>
<td>1 3%</td>
<td>1 5%</td>
</tr>
<tr>
<td>None</td>
<td>1 6%</td>
<td>4 11%</td>
<td>2 10%</td>
</tr>
<tr>
<td>Missing</td>
<td>12 43%</td>
<td>49 50%</td>
<td>45 69%</td>
</tr>
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</table>

Based on trials reporting DMC use or planned interim analyses
Survey - DMC nomenclature

- 44 different names for DMC role
- Most commonly used words in name:
  1. Monitoring 125 89%
  2. Safety 107 76%
  3. Data 104 74%
  4. Committee 75 53%
  5. Board 65 46%

No other word >4%
Percentage based on trials reporting DMC
A standard name?

Most common names:

- Data & Safety Monitoring Board/Committee 32%
- Data Monitoring Board/Committee 15%
- Data Monitoring Committee
Surveys of policy and practice
Surveys of policies & practice

- Survey of investigators’ practice in recently completed RCTs
- Survey of investigators’ practice in ongoing RCTs in UK
- Survey of policies of major organisations involved with RCTs
Aim
• To describe data monitoring practice in a sample of trials published in 2000

Methods
• 45 trials selected from database of trials published in 2000
• Contacted principal investigators
  ▪ Failing that, contacted sponsors and colleagues
45 trials identified

31 investigators contacted

28 agreed to survey
- 24 had no DMC
- 4 had a DMC

3 didn’t agree

3 didn’t reply, info from trial report

11 didn’t reply, no info available

3 had a DMC
Recent practice: results

- Disappointing response rate (69%) reflected difficulty in contracting PIs for trials conducted several years previously.
- Reasons given for not having DMC included:
  - Trial not blinded, investigators monitoring
  - Low risk of adverse outcomes
  - Small number of patients
  - Short duration
  - Said would have had a DMC if starting now
Survey of current practice: training

- None of the 20 respondents provided training for the DMC members
- One investigator suggested a formal training programme
Current practice: aim & methods

Aim
• to describe data monitoring practice in a stratified sample of ongoing trials

Methods
• 40 UK-based trials sampled from MRC, HTA, MREC and LREC registers
• Investigators interviewed by telephone
Survey of current practice: remarks

- Difficult to describe industry practice because only 4 trials gave information on data monitoring in industry trials

- Small pool of experts able to sit on a DMC
  - training may be necessary
Current practice: results

40 ongoing trials

- 12 MRC-funded trials
  - 11 with DMC

- 12 HTA-funded trials
  - 5 with DMC

- 10 MREC trials
  - 4 with DMC

- 6 LREC trials
  - 0 with DMC

20 had DMC information available
Current practice: selected results

- 75% followed MRC guidelines
- 60% membership nominated by PIs or TSC
- All included a statistician or epidemiologist
- Trial statistician present at all or part of meetings
- General agreement that members should be "independent" but not defined and only one had policy for formal declaration of conflicts
Policies: aim & methods

Aim
• to describe the data monitoring policies of some of the major organisations involved in RCTs

Methods
• 25 organisations involved with RCTs identified
• information sought from websites
• supplemented by personal contact
Policies: organisations involved

25 Organisations

- UK (11):
  - 4 governmental
  - 3 charity
  - 2 R&D
  - 1 industry
  - 1 regulatory

- USA (6):
  - 5 R&D
  - 1 regulatory

- Europe (3):
  - 1 R&D
  - 1 international
  - 1 regulatory

- Other (5):
  - 3 R&D
  - 1 industry
  - 1 international
Policies: selected results

- 18/25 had formal policies for their DMCs
  - Many implemented only recently
  - Some less formal but *de facto*
  - Remainder were planning to review
- Half thought DMC as default for all trials
- 11 had policy of declaration of potential conflicts of interests
- 10 had policy about payment (expenses)
# DAMOCLES publications


Guidance

- Consider all trials for DMC

- Not all need IDMC
  - Internal DMC may suffice
  - May not need any DMC

- Always report reasoning for choice

- Mention independence where relevant
  - IDMC
Which trials need IDMCs?

- Efficacy of a new intervention
- Efficacy in a new indication
- High-risk treatments
- Treatments with possible safety issues
- Long-term follow-up period
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Why any charters?

- Clarity from variety
- Increase in use of SOPs
- Process documentation
Why a DMC charter?

- Systematic and transparent approach
  - Structure
  - Operation
  - Policy
  - Process
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Why this Charter?

- Not original idea
- Little explicit guidance elsewhere
- Areas for consideration come from project
- Broad and comprehensive structure
  - Highlights areas not routinely considered
- Guidance based on multi-faceted project
- Flexibility
- Readily available
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Implementation

- Ideally before or at first DMC meeting
  - Can be set up once trial is under way
- Early agreement on potential difficult issues
- Should be drawn up with input from
  - Trial investigators (TMG)
  - DMC members
  - Sponsor, funder, executive body (TSC)
- All should agree on the Charter contents
- Iterative process – expect agreement on most areas
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<th><strong>COMMENTS FROM DAMOCLES AND ILLUSTRATIVE EXAMPLES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Introduction</strong></td>
<td></td>
</tr>
<tr>
<td>Name (and sponsor’s ID) of trial plus ISRCTN and/or EUDRACT number</td>
<td>Insert name (and sponsor’s ID) of trial and registration number (eg ISRCTN and/or EUDRACT number)</td>
</tr>
<tr>
<td>Objectives of trial, including interventions being investigated</td>
<td>Insert objectives of trial, including interventions being investigated from protocol. Suggest including a flow chart of the trial design (insert as Figure 1).</td>
</tr>
<tr>
<td>Outline of scope of charter</td>
<td>Summary of the purpose and content of this document.</td>
</tr>
<tr>
<td><strong>Illustrative example:</strong></td>
<td>The purpose of this document is to describe the roles and responsibilities of the independent DMC for the ### #### trial, including the timing of meetings, methods of providing information to and from the DMC, frequency and format of meetings, statistical issues and relationships with other committees.</td>
</tr>
<tr>
<td><strong>2. Roles and responsibilities</strong></td>
<td></td>
</tr>
<tr>
<td>A broad statement of the aims of the committee</td>
<td><em>Illustrative example:</em></td>
</tr>
<tr>
<td></td>
<td>“To protect and serve [trial] patients (especially re: safety) and to assist and advise Principal Investigators so as to protect the validity and credibility of the trial.”</td>
</tr>
<tr>
<td></td>
<td>“To safeguard the interests of trial participants, assess the safety and efficacy of the interventions during the trial, and monitor the overall conduct of the clinical trial.”</td>
</tr>
<tr>
<td>Terms of reference</td>
<td><em>Illustrative example:</em></td>
</tr>
<tr>
<td></td>
<td>The DMC should receive and review the progress and accruing data of this trial and provide advice on the conduct of the trial to the Trial Steering Committee. The DMC should inform the Chair of the steering committee if, in their view:</td>
</tr>
<tr>
<td></td>
<td>(i) the results are likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community, that one trial arm is clearly indicated or contraindicated, and there was a reasonable expectation that this new evidence would materially influence patient management; or</td>
</tr>
<tr>
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<td>(ii) it becomes evident that no clear outcome would be obtained.”</td>
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# DMC charter

## CHARTER FOR TRIAL MANAGEMENT GROUP

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<tr>
<th>CONTENT</th>
<th>DETAILS OF TMG</th>
</tr>
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<tbody>
<tr>
<td><strong>1. Introduction</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Name (Sponsor’s ID) of trial</strong></td>
<td>RADIUS (MRI BR10/NC12 BR13): Radiotherapy and Androgens Deposition in Combination After Local Surgery (EUCRITN-400143911) EUDRACT 2006-003039-54</td>
</tr>
<tr>
<td><strong>Objectives of trial, including interventions being investigated</strong></td>
<td>Although the number of radical postmastectomy being performed is increasing, there is considerable uncertainty over the optimal management strategy for patients that have had a postmastectomy. The two main management questions relate to the timing of radiotherapy and the use of hormone therapy with post-operative radiotherapy. RADIUS will address each of these questions. A study summary diagram is included in Figure 1 and 2.</td>
</tr>
<tr>
<td><strong>Outline of scope of charter</strong></td>
<td>The purpose of this document is to describe the membership, terms of reference, roles, responsibilities, authority, decision-making and relationships of the Trial Management Group (TMG) for this trial, including the timing of meetings, frequency and format of meetings and relationships with other trial committees.</td>
</tr>
</tbody>
</table>

## 2. Roles and responsibilities

A broad statement of the aims of the TMG

- To manage the trial, including the clinical and practical aspects.

Specific roles of TMG members

The specific roles of the TMG will be to:

- Attend TMG meetings and advise on availability for future TMG meetings
- Input into and comment on the protocol and case report forms
- Allow contact details to be included in the protocol
- Promote the trial
- Develop strategies to encourage recruitment and address any issues with recruitment at each trial centre
- Be involved in the day-to-day running of the trial by supporting the Chief Investigator and MRC CTU
- Provide clinical or other expert guidance to MRC CTU and participating sites on trial-based matters such as clinical and practical questions and interpretation of information recorded on CRFs
- Maintain confidentiality of any trial information that is not in the public domain
- Respond to trial correspondence and any questions in a timely fashion
- Encourage completion of case report forms (CRFs) and monitor reported CRF completion rates
- Input into the monitoring and classification of serious adverse events (SAEs)
- Input into the meetings of the Trial Steering Committee (TSC), if appropriate
- Input into the meetings of the Independent Data Monitoring Committee (IDMC), where appropriate (open sessions only)
- Provide responses to any issues or concerns raised by TSC
- Consider the implications of any recommendations made by the IDMC and accepted by the TSC
Roles & responsibilities

- **Specific roles of DMC**
  - Interim review of the trial's progress including updated figures on recruitment, data quality, and main outcomes and safety data.

- **Select specific aspects from following list:**
  - assess data quality
  - monitor recruitment & loss to follow-up
  - monitor compliance
  - monitor trial conduct
  - monitor main efficacy outcome measures
  - monitor evidence for treatment harm
Roles & responsibilities

• Specific roles of DMC (cont)
  ▪ recommendations on recruitment
  ▪ suggest additional analyses
  ▪ advise on protocol modifications
  ▪ monitor planned sample size assumptions
  ▪ monitor appropriateness of patient information
  ▪ compliance with previous DMC recommendations
  ▪ ethical implications of recommendations
  ▪ assess impact & relevance of external evidence
FAQs

1. What are DMCs?
2. What was the DAMOCLES project?
3. Why a Charter?
4. Why this Charter?
5. How and when should I use it?
6. What does this Charter look like?
7. How does it help with contentious issues?
8. Where do I get a copy of the Charter?
Contentious issues

- Composition
  - Membership
  - Independence of members
  - Decision-making
- Relationships
- Role of trial statistician
- Meeting format
Composition

- Small number (3-6)
- 1+ clinician, 1+ statistician, consumers?
  - Balance full range of opinions with lack of suitable people
  - Practicalities and timings for when the trial needs review
  - Non-attendees (quoracy)
  - Lessen the impact of any one dud member!
- Independence (competing interest forms)
- Is an odd number necessary?
Decision-making

- How “decisions” are reached
  - Methods for guiding deliberations
  - Consensus preferable to voting
  - Role of Chair

- Role of formal statistical methods
  - Stopping rules vs stopping guidelines

- List of recommendations available to DMC
  - Recommendations not decisions
Relationships and reporting

DMC: Data Monitoring Committee

TSC: Trial Steering Committee

TMG: Trial Management Group

Trials Unit

Sponsor/ Funder

Participating centres

Trial expert panels

DMC feedback to TSC & TSC response to DMC via Trials Unit

Report from Trials Unit

Question & Feedback

Report from Trials Unit

Question & Feedback
Responsibilities & formatting

- Trial statistician
  - Produces report?
  - Attends meeting?

- Meeting organisation
  - Closed and open sessions?
  - Who should be present?
  - In person or teleconference?
FAQs

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A proposed charter for clinical trial data monitoring committees: helping them to do their job well

DAMOCLES Study Group

Formal monitoring of data from randomised controlled trials (RCTs) is becoming more common. Wide variation exists in the structure and organisation of data monitoring committees (DMCs), with little guidance on how they should operate. We used various strategies to consider the behavioural, procedural, and organisational aspects of data monitoring in RCTs: systematic reviews of DMCs and small group processes in decision making; surveys of reports of RCTs, recently completed and ongoing RCTs, and the policies of major organisations connected with RCTs; detailed case studies of four DMCs that faced difficult decisions; and interviews with experienced DMC members. The findings aided the development of a template for a charter for DMCs. We summarise the findings and outline the key considerations at every stage of the data monitoring process. Widespread use of a charter for the structure and organisation of DMCs would promote a systematic and transparent approach, and enable them to operate more effectively and efficiently.

Lancet 2005; 365: 711-22

*Members listed at end of report

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Examples in practice

- Asphyxial Encephalopathy – TOBY
- Bell"s palsy - BELLS
- Cognitive and retinal function - OPAL
- Colorectal cancer diagnosis - SIGGAR1
- Diabetes - DAPIT
- Hepatocellular carcinoma – TACE
- Neonatal cooling – NEST
- Osteosarcoma – EURAMOS 1
- Lung cancer - multi-trial IDMC
- Prostate cancer – STAMPEDE
- Renal cancer - RE04
- Respiratory failure - CESAR
Summary on Charter

• Provides consistent and transparent frame
• Includes aspects of data monitoring are not often addressed in existing DMC ToRs
• Can be customised.
  ▪ Framework still useful even if not using DAMOCLES guidance!
• Use structure for all MRC CTU committees
  ▪ TMG
  ▪ TSC
Email to:  
CTUEnquiries@ctu.mrc.ac.uk

Paper:  
The DAMOCLES study group. A proposed charter for clinical trial Data Monitoring Committees: helping them to do their job well. Lancet 2005, 365: 711-722
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