Possible Drug Safety Methods Group

Notes of a meeting at the RSM, London, on 11 Dec 2000 1400-1730

[taken by Andrew Herxheimer]

1. **Participants (all came as individuals, not representing an organisation)**:

Andrew Boshier, DSRU Southampton [GP]
Stephen Evans, Medicines Control Agency [statistician]
Andrew Herxheimer, UKCC [clinical pharmacologist] – Co-chair
Anne Kehely, Lilly UK [clinical pathologist]
Nicholas Moore, Bordeaux [clinical pharmacologist] (delayed in air traffic)
Saad Shakir, DSRU Southampton [pharmacoepidemiologist] – Co-chair & convener
Apologies from Alain Li Wan Po, Birmingham [pharmacoepidemiologist]

2. **A separate MG or a subgroup?**

Mike Clarke, the coordinator of Methods Groups, had suggested the possibility that the DSMG might be established as a subgroup within the Non-randomised Studies Methods Group (NRSMG), instead of applying for registration as a separate methods group. All present thought this made good sense, because the NRSMG is working on methods of linking data from randomised data, which the DSMG would wish to use.

Other methodological issues were also the same. Where drug safety involved different issues, these should anyway be considered by a subgroup without encumbering the NRSMG. There appeared to be no disadvantages. If later it seemed desirable to work as a separate MG, then that could be constituted.
It was AGREED to approach the NRSMG with this proposal.

3. **Coordination**

Saad Shakir offered the facilities of the DSRU in Southampton for coordinating the group, and suggested that Andrew Boshier there could act as the contact person.
This offer was gratefully accepted.

4. **Draft recommendations for considering adverse effects of interventions in Cochrane reviews**

The draft recommendations, proposed in 1998, have been to some extent used in Cochrane reviews. They are now available on two websites: www.dsru.org and www.aston.ac.uk/pharmacy/cebp
It was AGREED to circulate them to a wide group of interested and experienced people, to amend them in the light of their comments and then to propose their inclusion in the Cochrane Handbook.

5. **Reviews and trial reports should include both 'Serious adverse events' and 'intolerance'**

Pharmacovigilance work in regulatory agencies and pharmaceutical companies focuses mainly on relatively uncommon serious adverse events; common reversible side effects ('intolerance', the reciprocal of tolerability) are not consistently reported or investigated, though many are important for patients and their doctors.
It was AGREED that trial reports and reviews should consider both categories.

6. **Adverse events reported to pharmaceutical companies**

It was noted that generally such adverse events remain in the files of companies and are not accessible to reviewers. This is probably an important source of bias. Since the UK pharmaceutical industry has agreed in principle to disclose the results of unpublished clinical trials, it would be reasonable for companies to disclose data on adverse events too.

It was AGREED to approach the Association of the British Pharmaceutical Industry (ABPI), asking companies to make these data available in the same way as data on efficacy and effectiveness.

7**. Information flow from companies to regulators**
At present the emphasis is on prompt reporting of adverse events, but the events are often poorly analysed and catalogued. They might be catalogued in a more meaningful way, providing improved access for those interested. Stephen Evans offered to develop a proposal for discussion.

8. **Laboratory test results and assessment of drug safety**
Abnormal results can be considered on a population basis or for individual patients. The implications are quite different. Guidance is needed on the interpretation of deviations from 'normal' laboratory values in both randomised and other types of studies; it would be useful in the Handbook.

9. **Updating the CONSORT statement**
The CONSORT statement on improving the quality of reporting randomised trials (JAMA 1996;276:637-9) does not deal with the reporting of adverse events or intolerance of treatments, and needs updating in this respect.
AH agreed to write about this to David Moher in Ottawa, the coordinator of the CONSORT group.

10. **Methodological papers that participants in the group need to write**
a. A sample survey of Cochrane reviews examining how they deal with adverse events/ effects. The results of such a survey by Li Wan Po and colleagues were presented at the Cape Town colloquium. The same authors will report it in full, together with comments on recent efforts to improve this aspect of reviews.

b. A paper introducing the draft recommendations discussed in para 3 above.

c. Statistical methods for analysing adverse event reports. Stephen Evans noted that papers by Gary Koch and Mitchell Levine had discussed meta-analysis; he will take the lead on this paper.

It was AGREED that these papers should preferably be written for one or more journals that are in MEDLINE

11. **Expanding participation in the group**
Personal contact with people working in pharmacovigilance was considered the best way of gathering strength and momentum. A first list of contacts was made and is appended.

10. **Meetings in 2001 with opportunities for airing the group's work**

Cochrane meetings

a. UK Cochrane contributors' meeting, Oxford, 26-27 March	action AH
b. Cochrane Colloquium, Lyon, 9-14 Oct	action AH

Pharmacovigilance/ pharmacoepidemiology meetings

c. ?European p'vigilance meeting, Umeå, Sweden, 14-15 June	action AH ?
d. ?? Int Soc of Pharmacoepidemiology [ISPE] Toronto, Aug	action SS/NM
e. Int Soc of Pharmacovigilance [ISOP], Tunis 18-24 Oct	action SS/NM

APPENDIX – Preliminary list of people to be invited to join the MG [in addition to those who have already expressed an interest]

JK Aronson	UK	D Henry	AUS	A Miners	NL
D Busetto	I	S Hill	AUS	R Nelson	
D Coulter	NZ	P Honig	USA	A Szarfman	USA
R Edwards	S	J-R Laporte	ES	G Tognoni	I
D Graham	AUS	J McEwen	AUS	J Urquhart	USA/NL
J Hasford	D	R Meyboom	NL		

AH 22.12.00