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Sir David Cooksey
Cooksey Review Secretariat
HM Treasury, 4th Floor
1 Horse Guards Road
London SW1A 2HQ

27th July 2006

Dear Sir David,

Re: Review of UK Health Research

I welcome this opportunity to submit comments on current and future Government health reforms, specifically as they relate to the new NHS strategy *Best Research for Best Health* and the UK's world class medical science base. It is good, proper and wise to be seeking counsel from across a broad spectrum of interests.

My particular contribution pertains to the discipline and application of medical statistics within health research, from the perspective of someone who has seen some notable improvements in the last two decades or so but who is aware that much more could, and I strongly suggest ought, to be done to help enhance the overall quality of medical research.

By way of background, a good starting point is to review the classic editorial published in the *British Medical Journal* by Doug Altman (*BMJ* 1994; **308**:283-84) entitled: "The scandal of poor medical research". His remarks, it should be said, are by no means targeted at UK research only. He laments the pitiful state of much so-called research, arguing that too much is done for the wrong reasons, namely for the sake of getting a publication to add to a researcher's *curriculum vitae* for personal promotion purposes, rather than for the benefit of medical science *per se*, or indeed for future patients in particular.

I shall structure my remaining comments and observations broadly around (1) positive trends and (2) negative trends, with obvious implication that where financial commitments are involved, these are to be fostered and reversed, respectively, by any changes implemented in research funding streams. Lastly, I shall close with some further thoughts about (3) possible future trends, including some suggested contributions towards meeting the aims and objectives of the Review.

(1) Positive trends in medical research: Encouraging signs

Recognition of the importance of the role and input of medical statistics for ensuring high-quality methodology is properly applied to the research process has grown in recent years. Thus, although the actual importance has never changed, the perception has, largely due to a combination of numerous reasons including those outlined below.

1.1 Development of Evidence-Based Medicine (EBM)

EBM originated in Canada and emerged worldwide in the 1990's as a concept, and even a journal, although the philosophy was not uniformly warmly-received in the medical community. This was perhaps because of some enthusiasts giving the false impression that one only needed critical appraisal skills and sound Internet search strategies to become a world expert on any health-related topic under the sun! However, suitably toned down, EBM has evolved into a helpful paradigm in which a healthy balance is sought between (i) data-based, and data-driven, decision-making and (ii) clinical experience. At the heart of EBM lies an appreciation of statistical reasoning: understanding of sound research design and analysis, and general principles of interpretation of quantitative information produced by medical studies.

1.2 General Medical Council recommendations

The 1990's also saw the publication of GMC recommendations on the undergraduate medical curricula in the UK, causing an increase in the awareness of basic statistical principles as applied to medical research.

1.3 Biomedical journals: statistical review and other initiatives

In the UK, general medical journals (notably *Lancet* and *BMJ*) paved the way ahead for some specialist journals by adopting formal statistical refereeing as part of their peer review processes for handling research articles submitted for publication. The *BMJ* required, for example, confidence intervals for primary outcomes to be reported not only in the body of the text but in the more widely disseminated abstract. For clinical trial papers, some journals now insist on adherence to the CONSORT statement with its flow diagrams and checklists to help boost accuracy and depth of reporting, with similar initiatives for the reporting of observational studies, diagnostic studies, and meta-analyses. All of these have helped foster an improved research culture, for clearly the requirement by journals to receive high-quality reports can only have exerted upward pressure on the quality of the research as conducted in the first place.

1.4 Research Ethics Committees (RECs)

Yet another UK trend from the last decade was the expansion of Research Ethics committees from Local RECs to Multi-centre RECs (thence to over-arching Central Office of RECs), with increasing recognition given to the role of statisticians/research

methodologists within them. Originally LRECs were too numerous to include an individual specifically trained in medical statistics (there being too few available to serve on over 200 committees). However, it was sensibly decided to ensure a statistician sat on each of the MREC's so that large-scale research at least was vetted in advance not only for "individual ethics" but also for "collective" or "research ethics". In my discipline there is something of a mantra that "Bad statistics is bad ethics!" so the mandate for professional statistical involvement was a good step in the right direction. Previously, some research was being approved by LRECs that may not have passed the scrutiny of a statistician.

1.5 Academic centres of medical statistics

Hosted in a number of UK Universities with medical schools, and sponsored through partnership with NHS R&D or DH funding sources, centres of medical statistics have been recently established. These are critical mass sized clusters of consulting (and communicating!) statisticians who work together to provide a local service for clinical researchers needing advice on study design, research methodology, data analysis and interpretation, etc. Occasionally, but by no means universally, statistical advice turns into full-fledged research collaboration and joint papers for publication ensue from multi-disciplinary research teams spanning medical and statistical expertise. Another function of these clusters is to put on short training courses addressing basic or common statistical needs of medical researchers.

Doug Altman led the first of these groups in Oxford, with the Centre for Statistics in Medicine being founded there in 1995, just one year after his BMJ editorial appeared. My own group, with the geographically-appropriate acronym Centre for Applied Medical Statistics (CAMS) started in 1996. Further details on the activities and functions of CAMS are available on www.phpc.cam.ac.uk/cams. A number of other, similar groups have also been created UK-wide. There are important issues concerning the ongoing financial support of these centres that need to be addressed in the present Review to ensure that these groups remain on a sound footing. Doug and I now both have ten or more years' experience of how--and how not to--fund these groups successfully and would be glad to discuss further what has worked well and what has caused problems. I was gratified to see the avowed intention within *Best Research for Best Health* to foster links between NHS and University academic research units such as those described.

(2) Negative trends in medical research: Worrying signs

If the above catalogue of positives told the whole story then UK Health Research would itself be diagnosed as being in good health. Alas, this is not the case with the following points indicating there remains much scope for further improvement.

2.1 Motivation for doing research

It is not clear that progress has been made regarding the deep-seated problem addressed in "The scandal of poor medical research". Junior doctors' career paths dictate the need for publishing research and so there remains a proportion of research

conducted for poor reasons. This is not to say all such research is necessarily futile but with the pressure to gain coveted publications the over-riding concern there is temptation to take short cuts with the research itself or to report preferentially only findings that attract the nomenclature “statistically significant”. This belies a misunderstanding of statistical reasoning, as if research were merely a chase to get a p-value below the magical threshold of 0.05. There are clear dangers when poor research is disseminated. I do not claim to know the solution to this problem but selective citation of literature, publication bias, under-reporting of “negative” results, preferential reporting of unexpected non-primary outcomes are just a few of the symptoms that remain as proverbial tips of icebergs.

2.2 Timeliness of statistical input

CAMS has adopted as its motto a tongue-in-cheek quotation from pioneer statistician RA Fisher. He said, as long ago as 1938: “*To consult the statistician after the experiment is finished is often merely to ask him to conduct a post-mortem examination. He can perhaps say what the experiment died of.*” Too many researchers who ought to do so never approach a statistician at all, or do so only when forced to by comments from statistical reviewers on their journal submissions. Others arrive only after collecting masses of data and expect the statistician to unravel problems caused by the lack of clear objectives and the poor methods used. Widespread education is needed, either during or after clinical training, so that all researchers know their own limitations and are aware of the benefits of seeking timely statistical input into their projects. This should become deeply embedded within research culture so that statistical thinking is applied from the earliest phases of a research project’s lifetime, from grass roots small-scale research upwards, not just from top-level, multi-million pound, multi-centre studies downwards.

2.3 Funding for statistical support

It has been my experience from directing CAMS that in broad terms everyone wants ready access to statistical advice but no-one wishes to pay for it. Only rarely does an individual approach CAMS early enough in the research process to consider inserting a budget line item into a grant application to carry out the research. This behaviour though needs to be encouraged and to run in tandem with the provision of central funding to enable statistical expertise to be available in the first place for the benefit of researchers undertaking smaller scale research. If statistical advice is not provided free at the point of delivery, so to speak, many would muddle along without such input. Some may think they do not need it, some of whom may be correct, but many others would go on to discover, perhaps at the statistical refereeing stage if they have submitted to a leading journal, that they were wrong.

2.4 Recruitment of medical statisticians

There has long been a shortage of trained medical statisticians. Recruitment of sufficient numbers of adequately skilled people is a difficulty faced in both the public sector and private sector, and as far as I am aware, worldwide. The skills required to be successful include the obvious mathematical, computing and numerate skills to

cope with data analyses but almost as important are the communication skills to be able to discuss and explain in jargon-free terms what researchers need to do and what their findings really mean. Arguably, some of these skills may only be learned on the job rather than, say, in a Master's level course. Fundamentally, to enhance the quality of UK health research there needs to be a noticeable expansion in numbers of suitably skilled medical statisticians.

It is well worth asking who goes into medical statistics as a career? How can would-be medical statisticians be encouraged? There is a sad element of truth in the old joke that "medical statisticians spend their careers furthering the careers of *other* people."

2.5 Retention of medical statisticians

Recruiting medical statisticians is only one half of the problem of their dearth. Retention is also a serious issue, and one very likely to persist with the large disparities between clinical vs. non-clinical academic salary structures in Universities. Indeed, academic medical statistics has the biggest problem with issues of retention, with bright capable statistical staff often lured away by salaries only available outside the academic sector, notably in the pharmaceutical industry. In CAMS, for example, and despite negotiating with the University substantial (>10%) pay increases on starting salaries, I have been unable to retain for more than 3 years many of the statistical staff that were so hard to recruit in the first place. Thus, another question to investigate is what changes to career structures might encourage medical statisticians to continue to put their skills to use for publicly-funded research?

(3) Future trends?

Any major overhaul of the funding streams for medical research presents an opportunity to take stock, review and make changes for the better. Here are just a few suggestions, although these do not attempt to encompass all the issues raised above.

3.1 Statistical training of clinical researchers

Clinical researchers do not need to become statisticians, just as, mercifully, statisticians do not need to know the ins and outs of e.g. brain surgery to contribute to neurological research. However, to maximise effective communication across disciplines it does help if both parties know more about the other's area of expertise. As such, encouraging medical researchers to learn more about statistical and research methods may help alleviate problems and enhance overall quality of research. This can be accomplished by further changes to medical school curricula (possibly beyond remit of current Review) or by supporting widespread provision of intensive, short training courses in relevant aspects of methodology.

3.2 Advanced training opportunities

A minority of researchers who may well go on to apply successfully for research funding would benefit from more extensive, specialist training courses at Master's

level covering Medical Statistics/Research Methods/Clinical Trials. While a few UK universities already offer a course in medical statistics, there is scope for introducing new courses targeting specifically interested doctors and other clinical researchers, not just those entering from mathematical backgrounds seeking a career-satisfying (albeit not presently a financially well-rewarding) area of application. Embedding the NHS workforce with especially well-trained research methodologists should have wider benefits as their expertise would filter through to colleagues at a local level. I suspect some Universities may be unable or unwilling to institute new courses along these lines without external financial support.

3.3 Funding basis for centres of medical statistics

As alluded to earlier, there is a case for more stable, central rather than local, long-term, financial underpinning of centres of statistical excellence to enable them to increase in number and become stronger, and hence more influential on medical research and furthermore, more attractive places to work, with suitable career structures in place both to recruit and retain medical statisticians qualified to offer sound and timely methodological advice. This latter aspect could occur as a by-product of creating a workforce of better methodologically-trained clinical researchers.

In closing, I am grateful for this opportunity to feed into the Review process. If you wish to discuss further any issues I have raised from my medical statistics perspective I would be very glad to do so. I look forward with interest to learning the outcome of the Review in due course.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'CR Palmer', with a horizontal line underneath.

Christopher R Palmer MA(Oxon) MA(Cantab) MS PhD