domised controlled trials in health services research—they quote seven adequate trials out of 1000—suggests that randomised controlled trials are not the right way to show that a service, a package of interventions, is an improvement in terms of either where it is provided or what is provided.

Should palliative care be excused from randomised controlled trials? The design of McWhinney and colleagues' trial did not make life easy. The authors had been providing their palliative care at home for 18 months before the trial began and, not surprisingly, believed that it was better than no service. Patients were randomised either to immediate support or to support delayed for one month. For those randomised to the delayed group care was meant to be provided by the family doctor, who had referred the patient in the first place. The authors measured pain, nausea, patients' quality of life, and care givers' health at the beginning of the trial and at one month. Patients expected to live more than two months were approached, yet 36 of the 146 who were randomised died within the month of the study. Others, who were not entered because they were not expected to live for two months, did so; such problems will be familiar to those who do randomised controlled trials in palliative care.

Clearly the failure of this study alone would not justify excusing palliative care from randomised controlled trials. The authors go on to raise the problems of the ethics of randomisation in palliative care in general. As they say, using patients on the waiting list as controls may be ethical in chronic stable conditions, but in this study, and in palliative care in general, randomisation to treatment versus delayed treatment is hard to justify. This does not mean that all randomisations in palliative care are unethical. Comparison of two interventions, neither of which is known to be superior, would be the classic equipoise requirement for ethical randomisation. Two constructive

options are that multicentre randomised controlled trials of particular interventions can circumvent the problem of small numbers in a single centre and that some interventions lend themselves to study by randomised controlled trials in single patients (n of 1 trials).⁴⁻⁶ In this particular case randomisation to either the full intervention or to some component might have worked better.

The provision of a service is much more subjective than the provision of an intervention. It depends more on local conditions and, indeed, on local enthusiasms. What works in one set of circumstances may not be right for another. Health care consumes a large segment of our national wealth and touches the lives of everyone. The time has come when we should put an end to the casual use of "effectiveness" as an easy way out and begin to take a harder line. If you say that it is effective then prove it. As Archie Cochrane wrote more than 20 years ago, "There will be a marked reduction in the use of ineffective remedies and of effective remedies used inefficiently."⁷

HENRY MCQUAY
Clinical reader in pain relief
ANDREW MOORE
Consultant biochemist

Pain Relief Unit,
The Churchill,
Oxford OX3 7LJ

- 1 Advisory Group on Health Technology Assessment. *Assessing the effects of health technologies*. London: Department of Health, 1992.
- 2 Eddy DM. Three battles to watch in the 1990s. *JAMA* 1993;270:520-6.
- 3 McWhinney IR, Bass MJ, Donner A. Evaluation of a palliative care service: problems and pitfalls. *BMJ* 1994;309:1340-2.
- 4 Guyatt G, Sackett D, Taylor WD, Chong J, Roberts R, Pugsley S. Determining optimal therapy—randomised trials in individual patients. *N Engl J Med* 1986;314:889-92.
- 5 McQuay HJ. N of 1 trials. In: Max MB, Portenoy RK, Laska EM, eds. *The design of analgesic clinical trials*. New York: Raven Press, 1991:179-92. (Advances in pain research and therapy Vol 18.)
- 6 March L, Irwig L, Schwarz J, Simpson J, Chock C, Brooks P. n of 1 trials comparing a non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis. *BMJ* 1994;309:1041-6.
- 7 Cochrane AL. *Effectiveness and efficiency. Random reflections on health services*. London: Nuffield Provincial Hospitals Trust, 1972:84.

Changes in semen and the testis

All the trends suggest a decline in the health of the male reproductive system

Infertility currently affects at least one man in 20, but we are unable to assess whether it is becoming more prevalent because we have extremely poor past records. Male reproduction has been given little attention scientifically and in medical practice. However, our recent meta-analysis in the *BMJ* of 61 papers on semen quality, which clearly pointed to a decrease over the past 50 years,¹ has been repeatedly quoted in the *BMJ*,²⁻⁴ *Science*,⁵ and the popular media.

We have already responded to the various technical criticisms, several of which concerned the known limitations of meta-analysis.⁶⁻⁸ Though the data for 1970-90 were compatible with a decrease as well as with no change or an increase in semen quality, the cautious general conclusion is that a real decline in semen quality did occur over the full period 1940-90. Three recent reports have found that semen quality has declined among candidate semen donors during the past 20 years.⁹⁻¹¹ Two of these studies not only included data on sperm count but also showed that important measures of quality—morphology of sperm heads and motility—had also deteriorated.^{9,10}

These changes are all the more worrying since the quality of "normal" human semen is already very poor when compared with that of other mammalian species—

more than half of our sperm usually have one or more morphological abnormalities compared with less than 5% in some other species—and several studies have shown a relation between abnormal sperm heads and infertility.¹² Whether the prevalence of abnormalities in human sperm has always been so high is not known; some recent reports indicate that a change might have occurred.^{9,10} The relatively high number of abnormal sperm may explain in part our low fecundity compared with that of most mammals.

The evidence of a decline in the quality of semen is not the only indicator that the human testis is at risk. For a generation or more, cancer of the testis has been becoming more common.¹³ This is a disorder of young men and is associated with a high rate of other abnormalities of the testis, including undescended testis and poor semen quality. One quarter of men with unilateral cancer of the testis have severe impairment of the contralateral testis, including the "Sertoli cell only" pattern and spermatogenic arrest. Furthermore, the incidence of both hypospadias and undescended testes has been reported to be rising in the general population. The evidence of declining semen quality should be seen in the light of these trends in other reproductive disorders in men.¹²

We believe, then, that there are grounds for concern about the function of the testes. Cancer of the testis is clearly associated with undescended testis and dysgenetic testis, but we do not know its cause. Nor do we know that of undescended testis, and the causes of poor semen quality are in most cases obscure.

What possible explanations have been put forward? Many years ago oestrogens were suggested as playing a part in cancer of the testis,¹⁴ and epidemiological data show that administration of stilboestrol during pregnancy may lead to an increase in cancer of the testis and other abnormalities, including undescended testis and a low sperm count. Clearly only a few men were exposed to stilboestrol in utero, and neither it nor other drugs can be blamed for the general trends, but many manmade toxins in the environment may act as oestrogens,^{15 16} and these pose a theoretical risk to the male fetus if ingested by the mother before or during pregnancy.

This "oestrogen hypothesis,"¹⁷ which has received wide coverage in the media, is just that—a hypothesis—but progress in science must be based on refutable ideas. Much more basic and clinical research work is needed. When research in male reproduction is compared with that in many other branches of medicine our understanding of disorders of the testis is seen to be extremely limited.¹² Much more work is needed on the environmental toxins that are potentially oestrogenic.¹⁸ How are they absorbed and metabolised? Are they bioaccumulative? Several chemicals, including isomers of dicophane (DDT), polychlorinated biphenyl compounds, and certain surfactants, have been shown to be oestrogenic, and the list of such chemicals is still growing. We still do not know what concentrations and mixtures of these chemicals might be hazardous to male reproductive function.

In the meantime we should, perhaps, try to obtain better

prospective data on the function and health of the testes of men in the general population.

NIELS E SKAKKEBAEK
Professor

Department of Growth and Reproduction,
Rigshospitalet,
DK-2100 Copenhagen,
Denmark

NIELS KEIDING
Professor

Department of Biostatistics, University of Copenhagen,
Panum Institute,
DK-2200 Copenhagen,
Denmark

- 1 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.
- 2 Bromwich P, Cohen J, Stewart I, Walker A. Decline in sperm counts: an artefact of changed reference range of "normal"? *BMJ* 1994;309:19-22.
- 3 Suominen J, Vierula M. Semen quality of Finnish men. *BMJ* 1993;306:1579.
- 4 Farrow S. Falling sperm quality: fact or fiction? *BMJ* 1994;309:1-2.
- 5 Stone R. Environmental estrogens stir debate. *Science* 1994;265:308-10.
- 6 Keiding N, Giwercman A, Carlsen E, Skakkebaek NE. Importance of empirical evidence. *BMJ* 1994;309:22.
- 7 Carlsen E, Giwercman A, Skakkebaek NE, Keiding N. Decreasing quality of semen. *BMJ* 1993;306:461.
- 8 Keiding N, Giwercman A, Carlsen E, Skakkebaek NE. Falling sperm quality. *BMJ* 1994;309:131.
- 9 Auger J, Czyglik F, Kunstmann JM, Jouannet P. Significant decrease of semen characteristics of fertile men from Paris area during the last 20 years [abstract]. *Hum Reprod* 1994;9(suppl 4):72.
- 10 Van Waelegheem K, De Clercq N, Vermeulen L, Schoonjans F, Comhaire F. Deterioration of sperm quality in young Belgian men during recent decades [abstract]. *Hum Reprod* 1994;9(suppl 4):73.
- 11 Irvine DS. Falling sperm quality. *BMJ* 1994;309:476.
- 12 Skakkebaek NE, Giwercman A, De Kretser D. Pathogenesis and management of male infertility. *Lancet* 1994;343:1473-9.
- 13 Adami H-Q, Bergström R, Möhner M, Zatonski W, Storm H, Ekblom A, *et al.* Testicular cancer in nine Northern European countries. *Int J Cancer* 1994;59:33-8.
- 14 Henderson BE, Ross R, Bernstein L. Estrogens as a cause of human cancer: the Richard and Hinda Rosenthal foundation award lecture. *Cancer Res* 1988;48:246-53.
- 15 Colborn T, vom Saal FS, Soto AM. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environ Health Perspect* 1993;101:378-84.
- 16 White R, Jobling S, Hoare SA, Sumpter JP, Parker MG. Environmentally persistent alkylphenolic compounds are estrogenic. *Endocrinology* 1994;135:175-82.
- 17 Sharpe RM, Skakkebaek NE. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? *Lancet* 1993;341:1392-5.
- 18 McLachlan JA. Functional toxicology: a new approach to detect biologically active xenobiotics. *Environ Health Perspect* 1993;101:386-7.

European directive on training for general practice

Doctors, patients, or profession—someone is going to lose out

Widespread anxiety exists about fully implementing the European Union directive on specific training for general practice. Training for general practice has been mandatory in Britain since 1981, with the legislation embodied in the NHS Vocational Training Regulations.¹ These regulations apply to the training of principals in general practice in the NHS, but other categories of doctors, such as locums and assistants, have not needed to comply.

In 1986 the European Community introduced legislation to make specific training for general practice mandatory in all member states.² This directive was consolidated with previous directives in 1993 to become Directive 93/16/EEC³; member states must fully implement it by 1 January 1995. The directive provides for the mutual recognition of diplomas and periods of training and defines the minimum acceptable length of specific training. It also requires that each member state ensures that "the exercise of general practice under national Social Security schemes" from next January should be conditional on doctors having undergone a period of specific training or on having been exempted from that training by the issue of an acquired right.

The problem now facing Britain is what to do about the many doctors who have been working as locums or assistants within the NHS but have never been principals and have not previously been required to complete training under the vocational training regulations. Member states are empowered to grant acquired rights to practise to whomsoever they choose, but once granted that acquired right will permit a doctor to practise as a general practitioner within the social security system in any member state within the European Union. The purpose of granting acquired rights is to enable doctors who have been practising since before training was introduced to continue to practise. A similar situation existed in 1981 when categories of doctors working as NHS principals were granted permanent exemption from the vocational training regulations when they became fully operational.

Several important questions arise. Firstly, locums and assistants who have not been vocationally trained have been allowed to practise in Britain. Should this continue or should such doctors have to undergo a period of training at this stage in their careers; if so, how is this to be arranged and financed? Secondly, is it acceptable for patients to be