Clinical implications

- Sperm concentrations in successive samples from one man, and aggregate data from many patients, are highly skewed and closer to a logarithmic distribution than a normal distribution
- The evidence for a long term decline in sperm concentrations, based on historical data, is unconvincing
- Lower reference values of normal (of 60×10^9/l or 20×10^9/l) should not be applied uncritically
- The pattern of individual variability means that averages may be poor measures of fertility
- Geometric means may be more appropriate clinical variables than arithmetic means but are unreliable and require validation

Similar reasoning applies to any sufficiently skewed distribution, so we would not expect improved data to change the general line of our argument. However, a decline that was considerably smaller than that reported by Carlsen *et al* could be consistent with our analysis and might be detectable with confidence, given better data. More extensive data are needed to establish with greater precision the probability distributions of sperm concentration in populations and in individuals.

It is standard to use arithmetic means of sperm counts and concentrations as clinical variables. However, if the hypothesis of near logarithmic distributions is confirmed, then the geometric mean would be a more appropriate statistic.

The level of significance ($P<0{\cdot}0001$) reported in the linear regression analysis of Carlsen *et al* represents only the confidence that the observed mean has changed. It does not indicate the cause of that change. It can be accounted for by a change in the lower reference value for normal sperm count, provided that the distribution for sperm production is sufficiently skewed towards lower values. In particular, a change in sperm concentration from 113×10^9/l to 76×10^9/l can be entirely accounted for in this way by using a logarithmic distribution, which is supported by the available data. The remaining discrepancy between 76×10^9/l and 66×10^9/l is unlikely to be significant.

Instead of confirming the apparent decline in sperm count, as Carlsen *et al* assert, the change in lower reference value may well be responsible for it.

1 Carlsen E, Giwercman A, Keiding N, Skakkebæk NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;**305**:609-12.
2 *Horizon* "Assault on the male" BBC2, 31 Oct 1993.
3 Feller W. *An introduction to probability theory and its applications*. New York: Wiley, 1957.
4 Moore DS, McCabe GP. *Introduction to the practice of statistics*. New York: Freeman, 1993.
5 Cohen J. The comparative physiology of gamete populations. In: Lowenstein O, ed. *Advances in comparative physiology and biochemistry*. Vol 4. New York: Academic Press, 1971:267-380.

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Commentary

Importance of empirical evidence

Niels Keiding, Aleksander Giwercman, Elisabeth Carlsen, Niels E Skakkebæk

Bromwich *et al* point out that the distribution of sperm count is skewed to the right and that if a differential selection of skewed distributions is applied over the years this will bias the observed time trends. Both of these assertions are correct; indeed, in all 16 of the 61 publications cited in our original overview for which both median and mean were given the median was smaller than the mean, confirming the skewness.[1]

Bromwich *et al* present some elaborate, although rather elementary, statistical points about skewed distributions and differential selection from these, but they fail to give any empirical reference that might support their suggestion of differential selection. One possibility is that they believe that the lower reference values for sperm counts of 60×10^6/ml in the 1940s and 20×10^6/ml at present had been used as truncation values for the reported distributions over the years. If Bromwich *et al* had actually studied the reports they would have found that there were plenty of values under these limits in even the oldest articles. The article by MacLeod and Gold in 1951, based on 1000 men, is particularly important in this respect.[2] This early paper is largely responsible for the high historical values and is thus responsible for a considerable part of the observed decline. However, the authors of this paper were surprised about the low values contained in it. This paper was presumably the first to explicitly mention that it is "obvious to many that this figure [60×10^6/ml] is too high."

There are many problems with historical overviews (meta-analyses), but the article by Bromwich *et al* amounts to discussing time trends detached from the relevant empirical evidence. Thus, the most cautious conclusion that can be drawn from the existing data is still that semen quality has declined significantly between 1940 and 1990. After several years of published evidence being ignored, the increasing incidence of abnormalities of male genital organs (including a highly significant increase in incidence of testicular cancer[3]) has finally attracted the attention of the scientific world. We hope that the paper of Bromwich *et al*, which is apparently based on wrong assumptions, will not bring confusion or divert attention from the urgent need for more research into the threat to male reproductive functions.[4]

Statistical Research Unit, University of Copenhagen, Panum Institute, DK-2200 Copenhagen, Denmark
Niels Keiding, *professor*

University Department of Growth and Reproduction, Rigshospitalet 5064, DK-2100 Copenhagen
Aleksander Giwercman, *senior registrar*
Elisabeth Carlsen, *research fellow*
Niels E Skakkebæk, *professor*

1 Carlsen E, Giwercman A, Keiding N, Skakkebæk NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;**305**:609-12.
2 MacLeod J, Gold RZ. The male factor in fertility and infertility. II. Spermatozoön counts in 1000 men of known fertility and in 1000 cases of infertile marriage. *J Urol* 1951;**66**:436-49.
3 Møller H. Clues to the aetiology of testicular germ cell tumours from descriptive terminology. *Eur Urol* 1993;**23**:8-15.
4 Skakkebæk NE. Giwercman A, de Kretser D. Pathogenesis and management of male infertility. *Lancet* 1994;**343**:1473-9.

Correction

Management of female prisoners with abnormal cervical cytology

An authors' error occurred in this paper by G P Downey *et al* (28 May, pp 1412-3). P Curtis, senior registrar in obstetrics and gynaecology at the Royal Free Hospital, was omitted from the list of authors. The authors of this paper are therefore G P Downey, G Gabriel, A R S Deery, J Crow, P Curtis, and P G Walker.