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Data collection should be integrated with patient care

EDITOR,—The editorial on making routine data adequate to support clinical audit mentions the high quality of data from the St Mary's maternity information system,¹ citing two recent papers on its validity.^{2,3} The editorial's authors, however, have missed the point about why this particular system has proved so successful. The basis of the system is that midwives enter the data themselves and then in turn use the system for practical purposes directly associated with patients' care—for example, it generates summaries and discharge letters. The system is thus integrally associated with patients' care and is not a separate task.

This experience strongly suggests that abandoning the normal practice of relegating the input of data to clerical staff results in better quality of data. This is both because the motivation of health care professionals is higher and, crucially, because of the reinforcing feedback loop involving the use of the information for patients' care.

The Department of Health has introduced an information management and technology strategy for the NHS in England, which has many positive features.⁴ Its potential Achilles' heel, however, is precisely this question of the quality of the data. Although it includes a data quality initiative, this is concerned mainly with administrative data (the postcode and codes for the provider, health authority, and general practitioner), the only clinical element being the code for the diagnosis.⁵ We suggest that a great deal could be learnt from the strengths and weaknesses of existing systems, especially successful ones like St Mary's maternity information system, and could then be used in the development of the future information technology for health care.

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Myths in medicine

EDITOR,—Richard Horton wishes to lay the Jenner myth to rest for the final time.¹ It was a common belief among farmers in the west country that previous infection with cowpox prevented smallpox. Acting on this, Benjamin Jesty, a farmer in Dorset, infected his wife and two sons with cowpox from a cow.² Twenty years later, on 14 May 1796, Jenner inoculated James Phipps with material from a sore on the hand of Sarah Nelmes, who had been infected with cowpox when milking Blossom.

Jenner thus showed that "true" cowpox could be transmitted from person to person. This was important, since an infected cow was not always available. Jenner then inoculated James Phipps with smallpox two months later and showed that inoculation with cowpox did prevent smallpox. Jenner repeated the experiments. He published his findings in a pamphlet entitled "An inquiry into the causes and effects of the variolae vaccinae . . . known by the name of the cow pox" in 1798. He spent much time answering questions and meeting criticism. He published further pamphlets. He once described himself as "the vaccine clerk of the world."

It is for this that Jenner received and deserves recognition. The bicentenary of Jenner's experimental proof of the effectiveness of vaccination will be celebrated next year.

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- 1 Horton R. Myths in medicine. *BMJ* 1995;310:62. (7 January.)
- 2 Perry CB. *Edward Jenner*. Bristol: University Press, 1983:21.

*Interestingly, the *BMJ* published the following letter and editorial footnote in October 1895 (*BMJ* 1895;ii:871).

SIR,—During my rambles in Dorsetshire a few weeks ago I noticed an inscription on a tombstone in the little village churchyard of Worth Matravers as follows: "Sacred to the memory of Benj. Jesty Downstay, who departed this life April 16th, 1816. Born at Yetminster in this county. A honest and upright man. He was the first person (known) that introduced cowpox with inoculation, who from great strength of mind made experiment from the cow on his wife and two sons in the year 1774."

I have since ascertained that there is no doubt as to the correctness of this statement, and the above was a farmer in that neighbourhood, and there remains no doubt that he performed vaccination, at least on his own family, several years before Jenner made the discovery.—I am, etc,

Bristol, Sept. 25th

G. C. PAULI, M.R.C.S.

The then editor added the footnote:

There is no reason to doubt the correctness of the statement made upon the tombstone. It was long a matter of traditional belief amongst the dairy farmers in England and in Holstein that cow-pox was protective against small-pox. The deliberate introduction of cow-pox may therefore well have been adopted by several independent minds. All great discoveries have been anticipated in a similar manner, but it detracts nothing from the greatness of him who first systematises or renders them available for the purposes of every day life.

Sudden infant death syndrome in Maoris

EDITOR,—Charles Essex's news item on the sudden infant death syndrome in New Zealand quotes the opinion of Dr Ed Mitchell, who coordinated the New Zealand cot death study from 1987 to 1990 and has continued to monitor baby care practices in New Zealand.¹ Essex points out the disproportionate rate of the syndrome among Maori babies. It must be appreciated, however, that a designated Maori can have any proportion of Maori blood. The New Zealand study called a baby Maori if either parent considered himself or herself to be Maori. But the Maori part was seldom full Maori. For some, it was as little as a quarter or less. Thus the relative rates of the sudden infant death syndrome for Maoris and non-Maoris vary according to the criteria that are used.

The article is accompanied by a photograph of a Maori woman in a flax skirt who is holding a baby and standing in front of the traditional meeting

Maoris today live like other New Zealanders

house. This gives the impression that this is the manner in which Maoris live in New Zealand. Nothing could be further from the actuality. The situation depicted in the photograph is one used for tourist publicity. Maoris today live like other New Zealanders. Their education is equal, and most of them live in similar houses, enter the same professions and occupations, and are just as familiar with late 20th century technology (figure).

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- 1 Essex C. Cot deaths. New Zealand: campaign falters over bed sharing. *BMJ* 1995;310:8-9. (7 January.)

We apologise for the unintended offence caused in New Zealand by our use of an old picture, and we are grateful to the New Zealand Cot Death Association for supplying us with modern pictures that we can use in the future.—ED, *BMJ*

n of 1 trials in osteoarthritis

Study was conceptually and statistically biased

EDITOR,—Lyn March and colleagues' study comparing a non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis displays conceptual and statistical bias towards paracetamol.¹ The conceptual bias—that non-steroidal anti-inflammatory drugs are illogical when there is little inflammation—would not arise if these drugs were called potent pain killers. After all, paracetamol has antipyretic activity but is used in the absence of fever. Statistical bias arose by the authors' designation of paracetamol as the drug of choice if differences from diclofenac did not reach significance. It was impossible, however, for diclofenac to be significantly better on a global rating: when all preferences were for diclofenac the P value was only 0.06. In fact, 12 patients showed more preferences for diclofenac (compared with one with more preferences for paracetamol); nine patients had more pain and eight more stiffness when taking paracetamol (compared with one and two, respectively, when taking diclofenac); and 12 needed more escape analgesia when taking paracetamol (compared with one when taking diclofenac (median 7.5 tablets v 1, P=0.13)). Eight patients reported more side effects while taking paracetamol compared with five while taking diclofenac; median number six v three, P=0.17). These results suggest that paracetamol was relatively ineffective and poorly tolerated.

Other studies in osteoarthritis also show that paracetamol is less effective than non-steroidal

anti-inflammatory drugs. Dieppe *et al.*² together with Brandt and Bradley,³ reviewed all identifiable controlled studies, which showed that "paracetamol reduced pain and tenderness significantly" compared with placebo; "Voltarol significantly improved mobility score" compared with Distalgesic; "ibuprofen improved pain at rest significantly" compared with paracetamol; "diclofenac 100 mg daily produced significantly greater improvement in pain and mobility than ... dextropropoxyphene 180 mg and paracetamol 1.95 g daily"; and there was "strong patient preference for ketoprofen rather than paracetamol/propoxyphene." Brandt and Bradley concluded that paracetamol was as good as ibuprofen in osteoarthritis since scores obtained with the health assessment questionnaire showed no difference even though pain on walking ($P=0.10$) and at rest ($P=0.05$) did.⁴

Because of these data I believe that it was wrong to conclude that "the assertion that [non-steroidal anti-inflammatory drugs] are more effective ... than paracetamol is not yet substantiated."² The inadequacy of paracetamol is further supported by a recent survey in Nottingham of 1137 patients receiving non-steroidal anti-inflammatory drugs in general practice; 51% named their current non-steroidal anti-inflammatory drugs as the most effective treatment they had received, compared with only 6% favouring other analgesics that were not non-steroidal anti-inflammatory drugs.⁵

While anxiety about the gastrointestinal toxicity of non-steroidal anti-inflammatory drugs is legitimate, this accounts at most for one admission to hospital per 45 patient years in elderly people.⁶ Paracetamol is a relatively poor analgesic with imperfectly assessed gastrototoxicity that is likely to make no more than a minor contribution to reducing the problems of complications associated with non-steroidal anti-inflammatory drugs.

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- 1 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. (22 October.)
- 2 Dieppe PA, Frankel SJ, Toth B. Is research into the treatment of osteoarthritis with non-steroidal anti-inflammatory drugs misdirected? *Lancet* 1993;341:353-4.
- 3 Brandt KD, Bradley JD. Simple analgesics versus NSAIDs for osteoarthritis. *Lancet* 1993;341:770-1.
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- 5 Cullen DJ. Suitability of ibuprofen for widespread ulcer sparing use in the community. *Gastroenterology* 1994;106:A6.
- 6 Silverstein FE, Geis GS, Struthers BJ, and the MUCOSA study group. NSAIDs and gastrointestinal injury: clinical outcome, the musosa trial. *Gastroenterology* 1994;106:A180.

Caution in interpretation needed

EDITOR,—Considerable caution must be exercised in interpreting the results of Lyn March and colleagues' n of 1 trials in osteoarthritis.¹ For example, the authors observe that "seven of he eight patients who changed treatment from baseline changed to paracetamol ($P=0.07$, exact binomial)." Of the 20 patients analysed, 16 were taking a non-steroidal anti-inflammatory drug and only three were taking paracetamol. Therefore, at most three patients could have changed their treatment from paracetamol.

Furthermore, the authors implicitly assume that

failure to find a significant difference in favour of diclofenac in the n of 1 trials considered constituted adequate grounds for preferring paracetamol. In drug development generally it is many years since failure to find a significant difference has been accepted as "proof" of equivalence. For fixed effects an n of 1 trial with three pairs of treatment periods has roughly the same power as a two period crossover with three patients; this is inadequate to establish treatment effects in osteoarthritis. We have reconstituted the variances of the individual estimates of the differences between treatments from the authors' table and find an average variance of 33 for pain scores. If the clinically relevant difference (between paracetamol and diclofenac) was 10 mm the power to detect a significant difference would be only 33%; thus, using a significance test under such circumstances one would, on average, incorrectly designate two thirds of patients as "adequately controlled" with paracetamol.

It is true that when the data are examined with a random effects model there is clear evidence of heterogeneity. Whether a random or fixed effects model is used, however, the overall treatment effect is significant and in favour of diclofenac ($P=0.04$ and $P<0.0001$, respectively).

"Peering at P values" is not an appropriate way to use data from n of 1 trials.² Strategies for combining information from individuals with information from groups are needed.² In this series of n of 1 trials flaws in the methodology will have biased downwards the estimate of the proportion of patients responding better to diclofenac.

We also consider that, whereas a small series of trials in selected patients (essentially a "convenience" sample) might be suitable for showing the capability of one drug to prove superior to another (which is the case here for diclofenac), it could never, and particularly if analysed in this way, support the generalisation that "in osteoarthritis many patients currently receiving or being considered for non-steroidal anti-inflammatory drugs may achieve adequate control with paracetamol."

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- 1 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. (22 October.)
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Authors' reply

EDITOR,—We regard n of 1 trials as a useful tool to help a patient and practitioner decide whether non-steroidal anti-inflammatory drugs offer appreciably better relief than paracetamol. Only then do we think it worth using non-steroidal anti-inflammatory drugs, given their risk of serious side effects. The conceptual bias discussed by C J Hawkey is not a bias but rather our view of sensible decision making. Nor is statistical bias an issue because the decision about treatment was made not by "peering at P values" but rather by the patient and general practitioner viewing their individual plots of pain and stiffness scores and side effect profiles. We agree with Stephen Senn and colleagues that few patients could have changed from paracetamol. The real issue, however, was that seven of 16 who were previously taking non-steroidal anti-inflammatory drugs thought that these drugs did not offer appreciable relief over paracetamol and six of these seven thought that

paracetamol continued to relieve symptoms adequately three months later.

We agree that failure to find a difference should not be regarded as proof of equivalence, and we at no stage claimed that it was. We were not addressing drug development, nor were we making statements about which drug in general is better for the treatment of osteoarthritis. Rather, as we made explicit in the evaluation of efficacy in our paper, in a setting in which one of the possible treatments (non-steroidal anti-inflammatory drugs) may have hazardous side effects we asked the patients and their general practitioner to decide whether there was any appreciable difference in response. The table in our paper shows clearly that most subjects' responses were more favourable during the diclofenac periods, yet many elected to continue taking paracetamol.

Our primary aim was to analyse individual patients' responses, whereas an overall effect seems to be the primary focus of interest of all the authors commenting on the article, including K B Saunders.¹ We agree with Senn and colleagues that there is heterogeneity, as shown in the plot of individual treatment effects in our paper, and consider that this makes n of 1 trials particularly important. To evaluate overall group effects there is no substitute for randomised controlled trials, and we were surprised to find so few comparing non-steroidal anti-inflammatory drugs with paracetamol alone. We stand by our claim that n of 1 trials are acceptable and clinically useful in osteoarthritis.

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- 1 Saunders K. n of 1 trials. *BMJ* 1994;309:1584. (10 December.)

Childhood antecedents of schizophrenia

EDITOR,—Brian Martindale presents selective evidence to suggest that the environmental contribution to schizophrenia is considerable,¹ neglecting to mention recent strong evidence supporting genetic transmission of schizophrenia based on the biological relatives of schizophrenic adoptees.² The diagnoses and analysis of this supportive study have, furthermore, been independently replicated.³

Moreover, a more recent report of the Finnish adoptive family study than that cited by Martindale has been published.⁴ This states that schizophrenia (according to the definition in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised) was diagnosed in nine adoptees, eight of whom were in the group whose biological mothers had either schizophrenia or "spectrum psychoses" ($n=155$) while just one was in the control group with normal biological mothers ($n=186$). Martindale's assertion that adopted offspring of schizophrenic mothers had