paracetamol. More than 100 different manufacturers were licensed to produce and market paracetamol elixirs at the time of this outbreak.[16] All seven of the eight manufacturers of brands of paracetamol found to contain diethylene glycol were small companies with little capacity for quality control which, together with 180 other small manufacturers, account for less than 10% of drug production in Bangladesh.[18] This proliferation of small pharmaceutical manufacturers is also occurring in other developing countries.[21]

Paracetamol is on the World Health Organisation's list of essential drugs[22] and is widely used in developing countries. The substitution of diethylene glycol for propylene glycol in paracetamol elixirs produced in two widely separated countries, Nigeria and Bangladesh, suggests that another such epidemic could happen elsewhere. The capacity of governments in developing countries to effectively monitor the importation, production, and sale of drugs will have to be improved if tragedies such as this are to be prevented.

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1 Windholz M, Budavari S, Blumetti RF, Otterbein ES, eds. *The Merck index.* 10th ed. Rahway, NJ: Merck, 1983:453.
2 Andrews LS, Snyder R. Toxic effects of solvents and vapors. In: Amdur MO, Doull J, Klassen CD, eds. *Casarett and Doull's toxicology.* 4th ed. New York: Pergamon, 1991:704-5.
3 Geiling EMK, Cannon PR. Pathologic effects of elixir of sulfanilamide (diethylene glycol) poisoning. A clinical and experimental correlation: final report. *JAMA* 1938;**111**:919-26.
4 Silverman M, Lydecker M, Lee PR. *Bad medicine: the prescription drug industry in the third world.* Stanford, CA: Stanford University Press, 1992:209-10.
5 Bowie MD, McKenzie D. Diethylene glycol poisoning in children. *S Afr Med J* 1972;**46**:931-4.
6 Some wine to break the ice [editorial]. *Lancet* 1985;ii:254.
7 Van Der Linden-Cremers PMA, Sangster B. Medical sequelae of the contamination of wine with diethylene glycol. *Ned Tijdschr Geneeskd* 1985;**129**:1890-1. (In Dutch.)
8 Van Leusen R, Uges DRA. A patient with acute necrosis of the renal tubules due to consumption of wine containing diethylene glycol. *Ned Tijdschr Geneeskd* 1987;**131**:768-71. (In Dutch.)
9 Cantarell MC, Fort J, Camps J, Sans M, Piera L. Acute intoxication due to topical application of diethylene glycol. *Ann Intern Med* 1987;**106**:478-9.
10 Pandya SK. Letter from Bombay: an unmitigated tragedy. *BMJ* 1988;**297**: 117-9.
11 Masland T, Marshall R. The pill pirates. *Newsweek* 1990 Nov 5:22-6.
12 Okuonghae HO, Ighogboja IS, Lawson JO, Nwana EJC. Diethylene glycol poisoning in Nigerian children. *Ann Trop Paediatr* 1992;**12**:235-8.
13 *The treatment and management of severe protein-energy malnutrition.* Geneva: World Health Organisation, 1981.
14 Task Force on Blood Pressure Control in Children, National Heart, Lung, and Blood Institute. *Pediatr* 1977;**59**(suppl):803.
15 People's Republic of Bangladesh, Director of Drug Administration. Memorandum no. VA/37-02/92/45 January 3, 1993. *Daily Inquilab* 1993 January 6.
16 Roy SK. *Drug testing laboratory, Dhaka, Bangladesh: assignment report.* Dhaka: World Health Organisation, 1993. (SEA/Drugs/98. World Health Organisation project BAN DSE 001.)
17 Grant JP. *The state of the world's children 1994.* Oxford: Oxford University Press, 1994:64.
18 Chetley A. *From policy to practice. The future of the Bangladesh national drug policy.* Penang, Malaysia: International Organisation of Consumers' Unions, 1992:53-4, 68-9.
19 Tiranti DJ. *Essential drugs: the Bangladesh example—four years on.* Oxford: International Organisation of Consumers' Unions, New Internationalist Publications, 1986:11.
20 Reich MR. Bangladesh pharmaceutical policy and politics. *Health Policy and Planning* 1994;**9**:130-4.
21 Castelo A, Colombo AL, Holbrook AM. Production and marketing of drugs in Brazil. *J Clin Epidemiol* 1991;**44**(suppl II):21-8S.
22 *The use of essential drugs. Model list of essential drugs (seventh list): fifth report of the WHO expert committee.* Geneva: World Health Organisation, 1992:22. (WHO technical report series No 825.)

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Changes in body weight and incidence of hip fracture among middle aged Norwegians

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Lean body stature is an important risk factor for hip fracture.[1] We assessed prospectively the relation between intrapersonal change in body weight and the incidence of hip fracture.

Subjects, methods, and results

We followed up 21 510 women and 21 157 men born between 1925 and 1940 attending both the first (1974-8) and the similar second (1977-83) cardiovascular screening in three Norwegian counties (85·2% of all invited)[2] on average 11·3 (range 0·01-13·8) years after the second screening to study the incidence of hip fracture. We identified hip fractures (cervical or trochanteric) as described elsewhere[1] at all hospitals in the three counties. We calculated the observation time for each person from the second screening to hip fracture, emigration, death, or end of follow up (in that order). We matched the file to the cancer registry of Norway, which has information on all diagnosed cancers in Norway, and to the register of death and emigration form "Statistics Norway." Adjustment was made for potential confounders as described in a previous study of this cohort.[1]

During follow up we identified 227 hip fractures, excluding fractures associated with high energy traumas and metastatic bone disease. The mean age at fracture was 57·2 (range 46·7-65·9) years in women and 55·5 (42·9-65·0) years in men.

The mean weight in the total cohort increased by 1·3 (SD 4·3) kg between the first and second screening. The women losing more than 3 kg (1 SD from mean change) or gaining $\geq$5·6 kg (1 SD from mean change) had a distinctly higher risk of hip fracture (table). The same pattern, although not significant for those gaining $\geq$5·6 kg, was found in the men. Excluding all the subjects in whom cancer had ever been diagnosed and all those who died during follow up gave only minor changes in the relative risks. The same applied to additional adjustment for changes in physical activity and smoking habits between the first and second screening. If the whole study population had been exposed to the age adjusted rates of those gaining only 1·3-5·5 kg in weight then the incidence of hip fracture would have been reduced by 35% in the women and 26% in the men.

Comment

We found that both weight loss and excess weight gain, calculated from standardised weight measurements at two screenings of the same population, were strong predictors of hip fracture. This was in addition to body mass index, which is also a strong predictor of fracture.[1]

A relation between weight loss and hip fracture has previously been shown, and weight and bone loss is also associated with bone loss.[4] The raised risk of fracture in the

Rates and relative risks of hip fracture by change in body weight between first and second screening in 42 600 middle aged women and men in three Norwegian counties*

Change in weight (kg)	Mean change (kg)	No of subjects	Person years	No of fractures	Age adjusted analysis: Rate/10 000 person years	Age adjusted analysis: Relative risk	Multivariate relative risk (95% confidence interval)†
Women:							
Loss of >3	-6·7	2583	29 649	32	10·65	2·48	2·26 (1·41 to 3·65)
Loss of 3 to gain of 1·2	-0·6	8867	101 705	68	6–73	1·57	1·47 (0·98 to 2·20)
Gain of 1·3 to 5·5	3·1	7607	86 838	37	4·29	1·00	1·00 (reference)
Gain of ≥5·6	8·8	2453	27 413	25	8·85	2·06	2·33 (1·38 to 3·95)
Men:							
Loss of >3	-6·1	1735	19 335	13	6·77	3·37	2·12 (1·01 to 4·44)
Loss of 3 to gain of 1·2	-0·6	8860	100 717	25	2·44	1·21	1·05 (0·57 to 1·95)
Gain of 1·3 to 5·5	3·1	8022	90 184	18	2·01	1·00	1·00 (reference)
Gain of ≥5·6	8·3	2540	27 778	9	3·35	1·67	1·67 (0·73 to 3·81)

*Weight at second screening minus weight at first screening. Mean follow up after second screening was 11·3 years after first.
†By Cox proportional hazards regression, adjusted for the following variables at the second screening: height; body mass index (per kg/m^2); self reported physical activity at work and during leisure; diabetes mellitus (yes, no); disability pension (yes, no); marital status; smoking habits (current smoker yes, no); and age at screening.

subjects gaining ≥5·6 kg was unexpected. The mean weight in this group, however, was lower at the first screening and higher at the second compared with the subjects losing more than 3 kg. These people may be more prone to repeated weight changes (including weight loss) than those whose weight is stable, and a resulting fluctuation in bone mass may produce permanent micro-architectural damage. A relation—independent of obesity—between coronary heart disease, total mortality, and fluctuations in body weight has also been reported,[5] suggesting that among those with great fluctuations in weight different adverse health outcomes are overrepresented.

Adjustment for self reported physical activity did not have any substantial impact on the estimates of weight changes. Increase in weight was related, however, to a decrease in physical activity from first to second screening,[2] and thus may indicate low levels of physical activity during follow up.

People with chronic diseases might be more exposed to dramatic weight changes than more healthy people. Additional analyses that took account of this as far as our data permitted, however, did not substantially influence the strong association between weight change and hip fracture found in this cohort.

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1 Meyer HE, Tverdal A, Falch JA. Risk factors for hip fracture in middle-aged Norwegian women and men. *Am J Epidemiol* 1993;**137**:1203-11.
2 National Health Screening Service. *The cardiovascular disease study in Norwegian counties. Results from second screening.* Oslo: NHSS, 1988.
3 Cumming RG, Klineberg RJ. Case-control study of risk factors for hip fractures in the elderly. *Am J Epidemiol* 1994;**139**:493-503.
4 Reid IR, Ames RW, Evans MC, Sharpe SJ, Gamble GD. Determinants of the rate of bone loss in normal postmenopausal women. *J Clin Endocrinol Metab* 1994;**79**:950-4.
5 Lissner L, Odell PM, D'Agostino RB, Stokes J, Kreger BE, Belanger, AJ *et al.* Variability of body weight and health outcomes in the Framingham population. *N Engl J Med* 1991;**324**:1839-44.

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A MEMORABLE PATIENT

A heart lift patient

Most doctors recognise heart sink patients in whichever branch of medicine they practise. Ellen was a heart life patient. She joined my practice at the age of 83. She had retired as a headmistress over 20 years before and enjoyed an active retirement. She had decided to move to a bungalow in the grounds of a residential home nearer her family and friends because of ill health, emphysema, and mild heart failure.

Over the 10 years that I cared for her she had shingles and post-herpetic neuralgia, an unexplained peripheral mononeuropathy, a myocardial infarct, cataracts, and deteriorating vision as well as repeated chest infections leading to her ever worsening lung function. During this same 10 years she continued to entertain her friends, made new friends, and rediscovered pillow lace making, becoming an accomplished lace maker.

After the death of a younger friend's wife from cancer she started raising money for the local cancer group by selling her lace, having botanical water colours which she had painted earlier in her life printed as postcards to sell, and eventually selling the beautiful original water colours. She raised over £12 000. A memory of mine is of entering her bungalow to see her bowed grey head intent on the dozen bobbins attached to her work pillow, with the lace and pins as a centre piece.

She was an astute observer of behaviour. After a domiciliary visit by a neurologist for her mononeuropathy she observed that "he lost interest once he made the diagnosis." She would regularly comment on my behaviour, and never lost her headmistress's sharpness or her wry sense of humour. She had a keen interest in the younger family members, friends, and carers. In spite of extreme ill health she was always a clear historian and a compliant patient who would discuss the relative advantages and disadvantages of treatment or non-treatment and fought every illness and set back with a joi de vivre that was insurmountable. Her repeated chest infections often brought her near to death, only to recover after a few weeks and to plan her latest fund raising, to visit relatives, or to discuss the controversy of the day.

As it became obvious that she was failing, her only complaint was that she could not finish the lace for the local abbey altar cloth. Yet she still rang to cancel a planned visit I was to make, as she had convinced a friend to load her, her wheelchair, and her oxygen bottle into a small car to visit Teesdale (over 20 miles of moorland roads) to see the wild gentian flowers that she had read were again flowering.

As with heart sink patients, I visited Ellen regularly often when it was not strictly necessary, medically, but the initiator of the visit and the reason for the visit differed. I visited on a Friday afternoon to have my spirits lifted by this inspirational character. I may have seen three heart sink patients that morning but one visit to Ellen was more than equal to that.

Ellen died of a myocardial infarct in October 1994, aged 93. On the afternoon of her death she said, "Hold my hand." It was the only time she ever asked anything of me.—TIM CARNEY *is a general practitioner in Hexham*