their analyses seem at odds with the evidence that a small proportion of the population at high absolute risk can contribute a large proportion of all deaths from coronary heart disease.

Another paper in this issue, by Tunstall-Pedoe and colleagues (p 629), seeks to explain falling blood pressure levels in the MONICA study, which included 38 populations in 21 countries over four continents.¹⁰ The authors observed a similar decline at all levels of blood pressure and conclude this meant medication was unlikely to have made a significant contribution. They state this was unexpected and seem to infer that population prevention strategies are therefore superior to individual treatment strategies. However, there was almost no change in the proportion of people receiving drugs to lower blood pressure over the period of the study. Moreover, the analyses could not determine the potential population impact of blood pressure lowering treatment. Such analyses would need to have examined trends in treatment among the subgroup of patients at high absolute cardiovascular risk, who do not necessarily have high blood pressure levels. Nevertheless, the observed shift in the entire population distribution of blood pressure in so many populations is unexplained and needs further examination.

Population based prevention is the only sustainable strategy for reducing the burden of coronary heart disease.² But unless we also treat patients at high risk, we will have limited impact on morbidity and mortality from coronary heart disease in the short to medium term. Numerous effective interventions are now available for managing the risk of cardiovascular disease, and the recently proposed polypill is an exciting development.¹¹ Tools for risk assessment are also widely available to help target intensive interventions appropriately.¹²

This century, population strategies may have their greatest impact in low to middle income countries where relatively simple and cheap strategies, including high taxes on smoking and replacing saturated with unsaturated fats, have yet to be widely implemented. Nevertheless, individual strategies targeting patients at high risk should be introduced in parallel. If a cheap polypill delivers as expected and cuts risk by more than

half, then the impact of the developing epidemic of cardiovascular disease in low and middle income countries could be tempered while long term population strategies are put in place.¹³ Rose's population and absolute risk axioms are both relevant to cardiovascular disease prevention in the 21st century, although their applicability is likely to vary by country and by time.

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Nutritional supplements in cystic fibrosis

A new study suggests they're ineffective, but concordance may have been poor

People with cystic fibrosis and their caregivers know that the better the patient's nutritional status, the better their survival, lung function, wellbeing, and mental capabilities.¹⁻³ Poor nutrition is also associated with delayed puberty, a higher risk of pneumothorax, and a worse outcome after lung transplantation.^{4 5}

The increased demand for energy in cystic fibrosis is well recognised.⁶ Despite this, almost 20% of children with cystic fibrosis fall below the fifth centile for weight set by the Centers for Disease Control and Prevention,⁷ and their height and weight z scores often decline with age. Combating nutritional failure to ensure normal growth and weight gain is therefore a key challenge for

the entire team—doctors, nurses, dietitians, psychologists, and social workers.

Nutritional management in cystic fibrosis is difficult for several medical and psychosocial reasons. One priority is the optimal medical management of malabsorption from exocrine pancreatic insufficiency and deranged enterohepatic circulation of bile. Patients continuously have to adjust the dose of exogenous pancreatic enzymes they need to take to allow assimilation of ingested food. Meanwhile, patients often need lung clearance techniques and antibiotic treatments to reduce the increased energy demand from chronic pulmonary infection and inflammation and breathing difficulties. These toddlers, children,

Research p 632

BMJ 2006;332:618-9

adolescents, and adults have to integrate into “normal” life this huge burden of lifelong daily treatment.

Mealtimes can be psychological battlefields for such families, with eating often reflecting a child’s first experience of power struggles. Difficulties may recur in puberty, an age that may be critical for the further course of the disease; they are often exacerbated by the need for patients to conform to today’s ideal that “thin is beautiful.” Just as treating patients with anorexia nervosa needs more than simply prescribing supplements, efforts to clarify the underlying psychodynamic processes in cystic fibrosis may be critical for success.

In this issue (p 632) Poustie and colleagues present an important, well planned, and carefully conducted randomised multicentre study of oral supplements in cystic fibrosis patients.⁸ Concordance with the intervention was reinforced continuously by staff making regular home visits. Nevertheless, the prescription of extra oral supplements failed to improve the nutritional status of the patients.

The trial was conducted to detect a 10 point difference in centile for body mass index within one year of the intervention, comparing patients receiving dietary advice with patients who were also prescribed oral energy supplements. This means that the trial was powered to detect, for example, a difference in weight gain of 2 kg between two 9 year old girls allocated to the different treatment groups. This was a noble goal, but an over-optimistic end point for a clinical trial in cystic fibrosis.

The authors say that the intervention failed because of inconsistency or inaccuracy in the dietary records and, perhaps, because patients did not take the supplements they were prescribed. In addition, the appropriately used statistical method, intention to treat analysis, may have led to underestimation of the effects of the intervention, but a per protocol analysis was not possible in this trial because adherence to treatment was unknown. Therefore conclusions from the trial must be drawn very carefully.

Treatments for cystic fibrosis are time consuming, generally unpleasant, and potentially anxiety provoking, and this can be particularly problematic when patients are feeling generally healthy. Professionals often have to “sell” such medical options to patients. Powers and colleagues have reported how they successfully influenced the behavioural aspects of nutrition in children with cystic fibrosis by using a multidisciplinary approach.⁹ The “intention to feed” is certainly not enough.

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What sort of evidence do we need in primary care?

General practitioners need evidence from and about the patients they see

Research p 635

In this week’s *BMJ* (p 635), Mant and colleagues raise again the question of whether large scale randomised controlled trials provide evidence relevant to primary care.¹ In a cross sectional study they question whether the UK national clinical guidelines for stroke are applicable to primary care patients. These guidelines, largely based on the PROGRESS trial,¹ recommend a target blood pressure of 140/85 mm Hg, with further lowering beyond this target desirable through use of a thiazide diuretic and an angiotensin converting enzyme inhibitor.²

Mant and colleagues critiqued the applicability of these guidelines to primary care patients by comparing the characteristics of patients in English general practice who had confirmed stroke with participants in the PROGRESS trial. They concluded that these populations were not sufficiently similar to warrant

widespread use of the guidelines. Patients with stroke in English primary care were generally older, equally comprised men and women, and had had their cerebral events less recently than the trial participants. They may not necessarily benefit from the relatively aggressive treatment recommended in the national guidelines. Given that most chronic stroke patients are managed by general practitioners, Mant and colleagues are calling for more appropriate research to provide evidence applicable to primary care.³

Primary care has specific needs for research. This setting is contextually complex, with patients who present with a broad range of signs and symptoms. Therefore, practitioners need research evidence for the whole range of diagnostic, prognostic, interventional, and phenomenological questions that emanate from this contextual complexity.³ Well documented gaps in

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