involved, to generate items for inclusion in a mode of enquiry relevant to that group. The result would be a set of questions, some common to all study groups and some group specific. Such a procedure would allow for comparisons within groups over time and between groups for the shared items.

Translators should be trained to advise both on the target language and the cultural acceptability of the questions to be asked. Unless requested to do so translators may not regard it as part of their task to comment on the salience or sensitive nature of the questions asked.

Researchers doing research with ethnic minorities should be cognisant of the customs, values, and beliefs of the target group(s) before designing any project. Issues of cross language data collection should be seen as a challenge and not as an obstacle, a stimulus to innovative thought and the development of new techniques of investigation. This is no small task. In London alone over 300 languages are represented,[9] and the research implications of this are enormous, not least in the decision about which languages to address initially.

Cultural and linguistic differences have yet to be incorporated as fundamental to sound public health, primary and secondary care, and health promotion. Health and social services would achieve their goal of equitable services for Britain's diverse populations faster were the cultural dimensions of self report given more attention than hitherto.

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Anti-inflammatory drugs and Alzheimer's disease

Evidence implying a protective effect is as yet tentative

The first inkling that anti-inflammatory drugs might lessen the risk of Alzheimer's disease came from an observation that people with rheumatoid arthritis had an unexpectedly low prevalence of dementia.[1] It was an imaginative idea, but the evidence that gave rise to it was far from secure. More data have now accumulated, but the matter remains unsettled. Surveys in France and Australia, for example, failed to find any protective effect from non-steroidal anti-inflammatory drugs. On the other hand, the Rotterdam study, a longitudinal, population based investigation of nearly 7000 middle aged and elderly people, reported a considerable reduction in risk of Alzheimer's disease in those who had taken these drugs for two years or longer, although the reduction in risk was less and did not reach statistical significance for people who had used them for shorter periods.[2]

A systematic review, published recently, identified nine observational studies that have addressed the question.[3] The pooled estimates of risk from these studies suggested that non-steroidal anti-inflammatory drugs do offer some protection against Alzheimer's disease, particularly when taken long term. But this optimistic conclusion must be set against the results of a recent randomised controlled trial that showed no benefit from one year's treatment with either naproxen or rofecoxib in patients with mild to moderate Alzheimer's disease.[4]

A prime suspect in the pathogenesis of Alzheimer's disease is the 42 residue β amyloid peptide. This peptide is a fragment of a much larger molecule, the amyloid precursor protein—a membrane protein whose function is as yet unknown. The proteolytic processing pathways of amyloid precursor protein are complex, but it seems fairly clear that in Alzheimer's disease overproduction of the 42 residue β amyloid fragment occurs relative to other cleavage products.[5] This β amyloid peptide is the principal component of extracellular amyloid plaques, which are a characteristic histological feature of Alzheimer's disease. Activated microglia and reactive astrocytes surround these plaques, and evidence of a local increase in pro-inflammatory mediators exists. Whether this inflammatory response contributes to the progressive neurodegeneration of Alzheimer's disease is not known, but it is generally assumed to do more harm than good.[6]

The anti-inflammatory activity of non-steroidal anti-inflammatory drugs resides in their ability to inhibit isoforms of the enzyme cyclo-oxygenase, which

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converts arachidonic acid to prostaglandins. So the straightforward explanation of how these drugs might reduce the risk of Alzheimer's disease is that they attenuate pro-inflammatory prostanoid synthesis. There is, however, another possibility. In cell lines and mouse models of Alzheimer's disease, a subset of non-steroidal anti-inflammatory drugs including ibuprofen, indomethacin, and sulindac has been found to reduce production of the 42 residue β amyloid peptide independently of changes in cyclo-oxygenase activity.[7] Instead the effect seemed to be mediated through changes in the proteolytic processing of the amyloid precursor protein.

One reason then for the discrepancy between the conclusions of the systematic review of observational studies and the results of the randomised controlled trial might be that the trialists chose the wrong anti-inflammatory drugs. Another is that although these drugs are ineffective in established disease, they do exert a beneficial effect in the presymptomatic stage of the illness. A trial in progress may resolve both of these points: ibuprofen and the selective cyclo-oxygenase-2 inhibitor celecoxib are being compared with placebo in a group of people who, because of their family history, are at high risk of Alzheimer's disease.[8]

We also have to face the possibility that, despite the best efforts of the investigators, the results of the observational studies that reported a protective effect were distorted by some unmeasured confounding variable. After all, it is not hard to imagine that the sort of people who need to take non-steroidal anti-inflammatory drugs in the long term have a way of life or a genetic constitution that reduces their susceptibility to Alzheimer's disease—even if it is impossible to say precisely what the protective factor might be. If this view seems unnecessarily bleak, remember the story of hormone replacement therapy. Here too, the observational studies indicated that it protected against cognitive decline. Plausible mechanistic explanations were invoked.[9] But the results of a large randomised controlled trial, the women's health initiative memory study, showed that women taking a combination of oestrogen and progestogen actually experienced higher rates of dementia and cognitive decline than those taking placebo.[10 11]

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Treatment of anal fissure

Medical treatments are only marginally better than placebo, but surgery may cause incontinence

Anal fissure is one of the most common lesions to consider in the differential diagnosis of anal pain. This is an ulcer in the squamous epithelium of the anus located just distal to the mucocutaneous junction and usually in the posterior midline. It typically causes episodic pain that occurs during defecation and for one to two hours afterwards.[1] This feature uniquely distinguishes anal fissure from other causes of anal pain such as thrombosed haemorrhoids, abscess, viral ulcers, and others. Atypical fissures may be multiple or off the midline, or be large and irregular. These may be caused by inflammatory bowel disease, local or systemic malignancy, venereal infection, trauma, tuberculosis, or chemotherapy. The cause of the typical or benign fissure is not clear nor are there accepted methods for the prevention of fissures—both fertile areas for research.

The most consistent finding in typical fissures is spasm of the internal anal sphincter, which is so severe that the pain caused by the fissure is thought to be due to ischaemia of the sphincter.[2] Relief of the spasm has been associated with relief of pain and healing of the fissure without recurrence. Historically the most common approach for relieving the pain associated with spasm of chronic adult anal fissure is surgical, though no placebo controlled surgical trials have been undertaken. Morbidity from operative procedures, mainly incontinence, was once thought to be extremely rare[3] but has been substantial in some recent reports.[4] So by the late 1990s when alternatives to surgery were sought because of cost, time for recovery, and risk of incontinence, rather than turn back to older treatments, such as lubricants and numbing agents, newer medications were investigated—in each case a medication that was known to relax muscle spasm. These have included nitroglycerin ointment, injection of botulinum toxin, and calcium channel blockers either given as tablets or applied topically.

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