they will be entreating their clinical colleagues to undertake quality assurance would be tactless and foolhardy. Some of the annual reports that have been produced show signs of such an approach, and the Faculty of Community Medicine has established a working group to develop proposals.[5]

Might there be objections to the annual report being used in this way—on the grounds that improvements in the health of the population are not the sole responsibility of public health physicians nor are the interventions required always under their direct control? The answer is that public health doctors have a responsibility to provide realistic advice to health authorities about achievable goals. If annual reports achieve nothing more than dispelling such optimism as reducing mortality from heart disease by a third in five years, they will have made a major contribution to re-establishing realism in public health. For these reasons the reintroduction of annual reports is a welcome and potentially exciting step in the development of the subject. There is every sign that public health physicians intend to embrace it with enthusiasm.[6]

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1 Department of Health and Social Security. *Public health in England. The report of the committee of inquiry into the future development of the public health function.* London: HMSO, 1988. (Cmnd 289.) (Acheson report.)
2 Department of Health. *Health services management. Health of the population: responsibilities of health authorities.* London: Department of Health, 1988. (HC(88)64.)
3 Department of Health. *Annual reports on the health of the population.* London: DoH, 1989. (LEL (89) P/13.)
4 Secretaries of State for Health, Wales, Northern Ireland, and Scotland. *Working for patients.* London: HMSO, 1989. (Cmnd 555.)
5 Crown J. Audit in community medicine: ideas please. *Community Physician* 1989;**14**:6.
6 Gabbay J. The annual report: from idea to reality. *Community Physician* 1989;**13**:1.

Gall bladder lithotripsy

Investment decisions require sound evidence

The NHS has a poor track record for resisting pressure from manufacturers and politicians to invest in new technology. Clinicians are easily lured by a promise of prestige, and our hospitals contain many expensive machines that have never fulfilled their early promise. The many publications on technology assessment contrast with the few on the process by which a health authority decides to provide—or not—some new treatment. Gall bladder lithotripsy is a case in point.

Let us examine the process. The straightforward assessment of the machine and its use is covered by the manufacturer. Confident that the treatment is effective and safe and has minimal unpleasant side effects, the manufacturer moves rapidly into marketing—because he wants to keep ahead of the competition. It may be good business to donate a machine for a "clinical trial" and so to convert clinicians into advocates for the product. Before it knows what is happening the health authority may be on the defensive—having to explain why it is not offering this new invention to long suffering patients.

Yet the only fact established at that stage is the availability of a safe new treatment. We want to know more than that. Is the immediate benefit sustained? Is there a long term improvement in the patient's life? Who decides what is a better outcome? A patient may perceive this differently from a clinician.

Assessment of benefit should be based on properly designed studies. The health authority will want advice on the confidence it can place in such studies—the soundness of sampling methods, statistical analysis, and interpretation. It will wish to know the pattern of disease to be treated within its own population—or in any larger catchment it may wish to serve in these entrepreneurial days.

Another question that needs an answer is whether the authority actually wants to install this technology in one of its hospitals. Might the service be bought in? It might be easier to let someone else cope with teething troubles and face unforeseen disbenefits. Will the innovation fit into the existing service strategy? How does it fit with other priorities? Next, is installation feasible? If it is going to damage other departments the authority may want to think again. A district general hospital should have a site control plan based on perceptions of need and balance of services. This plan may not be immutable but it should not be ignored.

What are the implications for other services? The availability of clinic space, inpatient beds, back up tests, and the capacity to treat complications are all relevant. If the pathlogy department is already working near capacity the introduction of a new service based on a multidistrict catchment may cause an overload.

No one would buy a car or a dishwsher without knowing the price, but cost is a deceptively simple word. Capital cost comprises the equipment purchase price, plus the cost of installation, maintenance, and eventual replacement. The true revenue cost includes not only the salary of extra technicians but also the staff costs of all the increased functions described. These may be offset by a reduction in other activities—but it is a rare innovation that is not a cause of growth, hidden or otherwise. Any reduction in other services may occur outside the providing district. These other districts will deny to the last their falling activity, claiming it as quite impossible to cost with any useful degree of accuracy.

We may now at last begin to assess the cost, benefits, and realism of the proposal. We will have assessed the benefit to patients: we have a feel for disbenefits and can estimate total costs. With this better understanding of the implications, shall we now look at gall bladder lithotripsy?

Numerous non-comparative studies have described the progress of small numbers of patients.[1-4] The prevalence of gall stones is high (they are found in around 9% of the British population aged over 60), and untreated patients may suffer much pain and illness. Cholecystectomy is an established and safe procedure that gives good long term results. We should learn from the way renal lithotripsy was introduced and the arguments about its proper evaluation.[5-7] We need to be absolutely sure with comparative studies that gall bladder lithotripsy offers substantial advantages over conventional surgery. A full, prospective evaluation needs to be done—before clinicians' beliefs and public expectations are such that a true comparison is thought to be unethical. Once a new technology has become absorbed into medical and social folklore it is close to impossible to agree on the probity of a randomised trial.

The Department of Health together with Trent Regional Health Authority is presently funding a careful evaluation of lithotripsy with a randomised controlled trial.[8] Let us be patient and await its outcome.

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1 Hood KA, Keightley A, Dowling RH, Dick JA, Mallinson CN. Piezo-ceramic lithotripsy of gallbladder stones: initial experience in 38 patients. *Lancet* 1988;i:1322-4.
2 Sackmann M, Delius M, Sauerbruch T, *et al*. Shock-wave lithotripsy of gallbladder stones: the first 175 patients. *N Engl J Med* 1988;**318**:393-7.
3 Ponchon T, Martin X, Mestas JL, Cathignol D, Lambert R. Gallbladder lithotripsy: preliminary results in 13 patients. *Gastroenterol Clin Biol* 1987;**11**:832-3.
4 Bland KI, Jones RS, Maher JW, *et al*. Extracorporeal shock-wave lithotripsy of bile duct calculi. An interim report of the Dornier US bile duct, lithotripsy prospective study. *Ann Surg* 1989;**6**:743-53.
5 Challah LS, Mays NB. The randomised controlled trial in the evaluation of new technology: a case study. *Br Med J* 1986;**292**:877-8.
6 Charig CR, Webb DR, Payne SR, Wickham JEA. Comparison of treatment of renal calculi by open surgery, percutaneous nephrolithotomy, and extracorporeal shock-wave lithotripsy. *Br Med J* 1986;**292**:879-82.
7 Mays N, Challah S, Patel S, *et al*. Clinical comparison of extracorporeal shock-wave lithotripsy and percutaneous nephrolithotomy in treating renal calculi. *Br Med J* 1988;**297**:253-8.
8 Milner DC, Nicholl J, Westlake L, *et al*. The design of a randomized controlled trial for the evaluation of lithotripsy as a treatment for gallstones. *Journal of Lithotripsy and Stone Disease* 1989;**1**:122-32.

Breast cancer and a proto-oncogene

C-erbB-2 is a reliable prognostic marker

Proto-oncogenes encode proteins that have a normal function, but when these genes are altered or expressed abnormally they contribute to the pathogenesis of cancer. The proto-oncogene c-erbB-2 (neu, HER2, NGL) encodes a protein with a structure that indicates that it is a transmembrane growth factor receptor. Its amplification in human adenocarcinoma was reported in 1986,[1] and one year later Slamon *et al* reported that the gene was amplified in some 30% of carcinomas of the breast and that this amplification was associated with a poor prognosis.[2] Shortly afterwards Venter *et al* reported that gene amplification was associated with increased formation of the c-erbB-2 protein—shown immunohistochemically on frozen tissue sections.[3] How this knowledge might be used in managing patients with breast cancer is the subject of much current research.

Further studies using either DNA analysis or immunohistochemistry have reported the proportion of patients with c-erbB-2 amplification as between 10% and 30%, but until recently fewer than 200 patients had been included in any one study so confidence intervals were wide. Associations have been found with tumour size and tumour grade, amplification of the oncogene being most frequent in large,[4] poorly differentiated carcinomas.[5-7] Other reports relating to c-erbB-2 to recognised prognostic factors have been inconsistent.

Some of the small studies have found a relation between c-erbB-2 and poor prognosis[7-9] and some have not.[4 5 10 11] Material from over 500 tumours, however, has now been examined by each of two groups.[6 12] Both found a correlation between c-erbB-2 and a poor outcome. Slamon *et al* have carried out the most comprehensive work so far, in which the oncogene and its products (RNA and protein) were examined in 526 patients.[12] Three hundred and forty five of the women had positive nodes, and in a multivariate analysis c-erbB-2 was found to be an independent negative predictor of both survival free of disease and overall survival. Unfortunately, the grade of tumour was not included in this analysis. No association between c-erbB-2 and prognosis was found in the 181 patients with negative nodes. The other study, on 602 patients with breast cancer, also showed that the presence of c-erbB-2 protein was an adverse prognostic factor.[6] The relation between amplification of c-erbB-2 and poor prognosis seems to be real, but the marker is only informative in the minority of women in whom the gene is amplified.

Immunohistochemical studies have several advantages over studies that examine oncogenes at the DNA level. Tumour tissue can be differentiated from surrounding stroma, and the expression of the oncogene product within specific parts of the tumour can be examined. At the end of 1988 van de Vijver *et al* showed that 42% (19) of samples from 45 in situ ductal carcinomas stained positively for the c-erbB-2 protein.[4] Strikingly, all the specimens that stained positively were of comedo type and were composed of large pleomorphic cells. A similar association between large cell size and amplification of c-erbB-2 has been reported for invasive carcinomas[13] and for Paget's disease of the nipple.[14] In most of the women with Paget's disease the in situ component of the underlying carcinoma was of comedo type, and the oncoprotein was present in 41 of 45 (91%) of them. This association between amplification of an oncogene and morphological type of carcinoma was predicted by Cardiff, who also foresaw that patterns of staining with antibodies against oncogene products could be a useful new way of classifying mammary carcinoma.[15]

The importance of c-erbB-2 has yet to be fully evaluated in comparison with existing prognostic factors in breast cancer. Will this marker be more useful than the best of the existing factors, such as tumour grade when consistently assessed and S-phase fraction measured by flow cytometry?[16 17] Although showing that an oncogene product is related to outcome is clearly exciting, it does not necessarily provide more information than that given by well established methods. The search for new and better prognostic factors must, however, continue so that optimal treatment can be selected for individual patients.

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1 Yokota J, Toyoshima K, Sugimara T, *et al*. Amplification of c-erbB-2 oncogene in human adenocarcinomas in vivo. *Lancet* 1986;i:765-7.
2 Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. *Science* 1987;**235**:177-82.
3 Venter DJ, Kumar S, Tuzi NL, Gullick WJ. Overexpression of the c-erbB-2 oncoprotein in human breast carcinomas: immunohistological assessment correlates with gene amplification. *Lancet* 1987;ii:69-72.
4 Van de Vijver MJ, Peterse JL, Mooi WJ, *et al*. Neu-protein overexpression in breast cancer: association with comedo-type ductal carcinoma in situ and limited prognostic value in stage II breast cancer. *N Engl J Med* 1988;**319**:1239-45.
5 Barnes DM, Lammie GA, Millis RR, Gullick WJ, Allen DS, Altman DG. An immunohistochemical evaluation of c-erbB-2 expression in human breast carcinoma. *Br J Cancer* 1988;**58**:448-53.
6 Lovekin C, Ellis IO, Locker A, *et al*. cERB2 oncogene expression in breast cancer: relationships and prognostic significance. *J Pathol* 1989;**158**:345.
7 Wright C, Angus B, Nicholson S, *et al*. Expression of c-erbB-2 oncoprotein: a prognostic marker in human breast cancer. *Cancer Res* 1989;**49**:2087-91.
8 Varley JM, Swallow JE, Brammar WJ, Whittaker JL, Walker RA. Alterations to either c-erbB-2 (neu) or c-myc proto-oncogenes in breast carcinomas correlate with poor short term prognosis. *Oncogene* 1987;**1**:423-30.
9 Berger MS, Locher GW, Saurer S, *et al*. Correlation of c-erbB-2 gene amplification and protein expression in human breast carcinoma with nodal status and nuclear grading. *Cancer Res* 1988;**48**:1238-43.