The content of this document is to be embargoed until Monday 22nd January 2001.

The report contains an independent audit of the York Nutritional Laboratory survey, conducted by the Department of Health Studies, University of York, on behalf of the British Allergy Foundation.

A copy of this report can be found on our website www.allergy-testing.com

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Audit of the York Nutritional Laboratory Survey

Background

Adverse reactions to food can cause a range of symptoms throughout the body. Some of these reactions are mediated through the immune system either by IgE (food allergy) or, more controversially, by IgG (food sensitivity). Over the last few years the York Nutritional Laboratory (YNL) have been conducting enzyme-linked immunosorbent assay (ELISA) tests on blood samples to detect raised food-specific IgG in the serum of people with one or more, usually chronic, symptoms.

YNL has conducted an extensive survey of people who have been tested and given dietary advice based on the results. The survey was distributed to a random sample of 4,200 individuals in the UK who had taken a 'pin prick' food sensitivity test between February 1998 and August 1999. A 42% response rate resulted in a total of 1761 questionnaires returned for analysis. Approximately 50% of all responders reported an improvement in symptoms at point 4 or 5 (relatively high improvement).

Whilst these results are encouraging, survey results are susceptible to several forms of bias including:

1) *Mistakes in data entry or data analysis*: Errors in transcribing data from the form to the computer.
2) *Responder bias*: Respondents may overstate improvements in their health because it is a company questionnaire.
3) *Non - response bias*: Those who do not respond to questionnaires are not representative of the general population and may be reluctant to report lack of benefit or lack of compliance with the diet. As a result, survey results which are based solely on those who respond are likely to be biased in favour of the interventions.

The Department of Health Studies, University of York was commissioned by the British Allergy Foundation to carry out an audit of the York Nutritional Laboratory in order be sure that the survey results are an accurate reflection of the views of food sensitivity test users.

Methods

The audit comprised 3 parts:

1) *Accuracy of data entry and analysis.*
A random sample of 100 cases was checked against the original questionnaires to verify the accuracy of data inputting and coding. An error rate of more than 5% would be regarded as significant.

2) *Validity of responses of responders and estimate of non-responders*
Two letters were developed inviting previous responders and non-responders to the YNL survey to participate in the audit. These were sent to a random sample of 150 responders and 450 non-responders, all of who had been sent the YNL survey within the last year. 70 people refused to participate in the audit, 9 responders and 61 non-responders. 3 people had moved, 1 had died, 4 had not included their name in the contact details, 2 had not yet started to eliminate the foods indicated.

The telephone interviews resulted in data for 46 responders (just under the 50 intended) and 90 non-responders. In order to increase the number of non-responders in the survey a second list of non-responders was obtained from YNL and letters were sent to a further random sample of 300 clients. (Unfortunately a YNL administrative error led to certain people being included on this list who had already been approached, 7 let us know). This second mailing resulted in data for a further 24 telephone interviews, resulting in data for 114 non-responders, less than the 150 intended. Due to shortage of time, we did not attempt to increase further the sample of non-responders.

As slips were returned agreeing or refusing to participate in the audit, names were checked against the YNL survey database to establish whether individuals were previous responders or non-responders to the original YNL survey.

Two phone questionnaires were devised, one for responders and one for non-responders. Responders were asked a subset of the same questions as in the original survey, to see if they would now respond in the same way. In addition interviewees were asked if the reported benefits (if any) were still present. Non-responders were asked the same subset of questions from the original survey but with a few changes. The question about benefit from the dietary changes was changed to include a ‘no benefit’ score, and the question on time taken to feel benefit was modified to allow an answer of ‘no benefit’

The return slips were distributed to the telephone interviewers in order to ensure both had an equal number of responders and non-responders. Telephone interviews took place at a time specified on the contact slip. Previous responder responses were coded and entered into an SPSS file alongside each interviewee’s original responses. Previous non-responder’s responses were coded and entered as new cases in an SPSS file.

3) Statistical analysis

The results from the re-surveying of responders were compared with original responses and the percentage showing a reduction in symptoms of 4 and 5 (a lot or quite a lot) estimated. This part of the study will enable us to report the proportion reporting relatively high benefit with a precision (95.0% confidence level) of approximately plus/minus 12% points and will allow us to test whether the results are significantly different from the YNL survey.

Data on the non-responders were analysed in the same way as the responders. We estimated the difference in response with the responders and then extrapolated this in order to estimate average results for all YNL users.

Results

1) *Accuracy of data entry and analysis.*

A random sample of 100 completed client questionnaires was requested from YNL for comparison with data recorded on their database. Data were imported from the SNAP database to an SPSS file.

143 questionnaires were received and the first 100 were checked. 12 of the questionnaires were duplicates and were omitted from the total.

Nine minor entry errors were found: one incorrect entry of presenting condition, two instances of omission of a second condition, one instance of omission of offending food, one instance of incorrect entry of client's name and sex, one omission of action following receipt of results, one misrecording of ease of dealing with laboratory ('difficult' recorded as 'easy'), one instance of misrecording of perceived benefit following modification of diet ('no benefit' recorded as 'no reply') and one instance of mis-recording of duration of condition.

The data entry was over 95% accurate in the checked sample.

2) *Validity of responses of responders and estimate of non-responders*

The distribution of results for the responders in this survey and the previous survey are shown below. 61% of the respondents to our phone survey said that they experienced, quite a lot or a lot of benefit, after changing their diet. This is the same percentage as in the postal survey (although the distribution between quite a lot and a lot differs slightly. The 95% confidence interval around this estimate is 47% to 74%. Thus this includes the 50% overall estimate for people reporting benefit in these two categories found in the YNL survey. Thus there is no statistically significant difference between the results of this phone survey and the larger postal survey (p= 0.2).

BENEFIT AS RECORDED IN PHONE SURVEY

	Frequency	Percent	Cumulative Percent
no benefit	6	13.0	13.0
low	4	8.7	21.7
a little	1	2.2	23.9
moderate	7	15.2	39.1
quite a lot	9	19.6	58.7
A lot	19	41.3	100.0
Total	46	100.0	

BENEFIT AS REPORTED IN ORIGINAL POSTAL SURVEY

	Frequency	Percent	Cumulative Percent
low	6	13.0	13.0
a little	2	4.3	17.4
moderate	6	13.0	30.4
quite a lot	11	23.9	54.3
A lot	17	37.0	91.3
no reply	4	8.7	100.0
Total	46	100.0	

Just over 70% reported that the benefits had been maintained since the test, over the last year, whilst around 20% said that symptom change had not been maintained or only partly over this period.

On the other hand, the results from the previous non-responders (shown below) are different. 36% of the 116 people responding to our phone survey reported improvements in the top two categories (95% CI: 28% to 45%). This is statistically significantly lower than those of the original YNL main survey result of 50% (p= 0.004). In addition, 31% reported little or no benefit. Thus non-responders who replied to our phone survey have a lower reported rate of benefit following the test. The rate of reduction of symptoms reported here may be a slight over-estimate given that only around 15% of previous non-responders contacted were included in the survey; most did not reply to the letter or declined to be interviewed. Thus these new respondents may not be a representative sample of all non-respondents.

PREVIOUS NON-RESPONDERS:
BENEFIT REPORTED IN PHONE SURVEY

	Frequency	Percent	Cumulative Percent
no benefit	33	28.4	28.4
low	3	2.6	31.0
some	8	6.9	37.9
moderate	23	19.8	57.8
quite a lot	21	18.1	75.9
A lot	21	18.1	94.0
N/A	7	6.0	100.0
Total	116	100.0	

The response rate in the YNL main survey was 42%. Therefore, we can get a better overall estimate of the proportion of clients likely to have experienced a reduction in symptoms by calculating a weighted average of those who responded and did not respond and the corresponding rates of improvement.

Average proportion with a lot or quite a lot of improvement in symptoms =
0.42 x 50% + 0.58 x 36% = 42%

Thus we can estimate that optimistically, around 40% of those having the YNL test may have experienced a lot or quite a lot of reduction in symptoms following the test.

3) *Association between reported benefit and adherence to diet*

In the YNL survey they found that whilst the proportion of clients showing relatively high benefit (quite a lot and a lot) was 50%, the proportion of those who stated that they rigorously adhered to the diet reporting substantial benefit was 58%. Only 33% not rigorously adhering to the diet reported relatively high benefit. We checked to see if this association was also true in the sample of people who previously were non-responders.

Of the 116 new respondents, 34 rigorously altered their diet of whom 47% reported quite a lot or a lot of improvement. Only 19% of those not rigorously altering their diet reported this level of benefit. Thus there is an association between stated adherence and reported benefit (p=0.008).

As above, we can get a better overall estimate of the proportion of clients *who rigorously altered their* diet who were likely to have experienced a substantial reduction in symptoms by calculating a weighted average of those who responded and did not respond and the corresponding rates of improvement.

Average proportion of those who rigorously altered diet reporting a lot or quite a lot of improvement in symptoms = 0.42 x 58% + 0.58 x 47% = 52%

Thus we can estimate that around 52% of those having the YNL test who rigorously altered their diet may have experienced a lot or quite a lot of reduction in symptoms following the test.

Conclusions

This audit has shown that:

1) Data entry from the YNL original survey was carried out at a high level of accuracy and so their results reflect the data collected.
2) The responses by YNL clients given in the postal survey are supported by the results of an independent phone survey. In particular, that around 50% of clients report a lot or quite a lot of reduction in symptoms after dietary change following the test results.
3) Around 70% of clients reported in the phone survey that these improvements have been maintained subsequently.
4) Non-responders experienced a lower rate of reduction in symptoms with 36% (95% CI: 28% to 45%) reporting a lot or quite a lot of reduction.
5) A weighted average of the proportion experiencing a lot or quite a lot of reduction in symptoms is 42%. This may however, be a slight over-estimate.
6) A higher proportion of those stating that they rigorously altered their diet reported a lot or quite a lot of symptom reduction – 58% in the responders and 47% in the previous non-responders (a weighted average of 52%).
7) The YNL survey form is flawed by not including a 'no benefit' option. Though this does not appear to affect the proportion of clients reporting 'a lot' or 'quite a lot' of benefit, it does distort the results lower down the scale. This should be amended in future surveys by the company.

This study has validated the results of the YNL survey. In general (taking into account the issue of non-responders) the YNL survey accurately reflects the reported experience of their clients.

It is important to note, however, that this does not mean that the reported improvement in symptoms is the result of or can be directly attributed to either the ELISA test or the dietary modification. Chronic symptoms do fluctuate, often randomly, and it is likely that on average, if people sought the food sensitivity test during a period of severe symptoms, then this would be followed by a reduction in symptoms (regression to the mean). In addition, there is the well-known phenomenon of the placebo effect, which may also account for some or all of the symptom reduction reported.

The association between rigorous adherence to dietary changes and reported benefit in both samples is a necessary finding if there is any causal association between the intervention and symptom reduction. However, it is

not proof of causality since one would expect a higher placebo effect amongst compliers. In addition, the causality could be working in the reverse direction those experiencing a reduction in symptoms (for whatever reason, including regression to the mean) may be more motivated to adhere to a new diet.

On the other hand, over 70% of clients reported that the benefits had persisted and given that many of these people came to YNL with long histories of chronic symptoms, this is important. Thus whilst the survey results cannot be taken as proof of the benefit of the ELISA test and/or subsequent dietary modification, they are sufficiently suggestive to justify further evaluation by means of properly conducted randomised controlled trials (RCTs). These could be undertaken with patients reporting those symptoms for which people most commonly sought food sensitivity testing – gastrointestinal (e.g. irritable bowel syndrome), dermatological (e.g. eczema), and neurological (e.g. migraine).

A further argument for rigorous evaluation is the potential cost-effectiveness of this health technology if such symptom reductions are indeed the direct result of the dietary changes based on the test results. In addition to the potential individual health benefits, significant societal benefits and cost reductions could possibly be achieved if this is effective because the test is a one off intervention and cheap for the NHS (though not for individuals) relative to the costs of these chronic conditions. In order to estimate the potential cost savings to the NHS we carried out a brief review of studies of the economic impact of these three common conditions. (See appendix).

In all of these three common conditions, a test and food elimination diet which costs no more than £200 would be cost saving to society within one year and cost saving to the NHS within 2-3 years assuming a 40% effectiveness sustained for these periods (i.e. 40 % of patients had a significant reduction in symptoms which resulted in a pattern of doctor consultation and work absence similar to people of the same age and sex without these symptoms). The cost-effectiveness of the test, if effective at these levels, would of course be significantly greater if the price was lower. Studies of cost effectiveness would also need to take into account the cost of any specialist nutritionist support to help maintain dietary change in patients who, unlike many of the YNL clients, were .not self referred and might need more motivation and support.

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Appendix

Studies on the direct and indirect costs of relevant chronic conditions

Migraine

The economic burden of migraine falls predominantly on patients and their employers in the form of bedridden days and lost productivity as the condition predominantly affects people during their working lives (Hu et al, 1999; Solomon and Price, 1997; Lipton et al, 1997)). People with migraine require around 4-6 bed rest days per year (Solomon and Price, 1997; Roijen et al 1995). Medical expenses in the USA came to about $100 per year per patient, however, the productivity loss per patient was greater at between $700 to $1,100 per year on average given the proportion who are employed. European studies showed an annual direct cost of around £50 million (1993 costs) in the UK or around 0.1% of NHS costs. This is likely to increase with better disease recognition and new more expensive treatments. Indirect costs of around £500 million have been estimated (Ferrari, 1998).

Irritable Bowel Syndrome

It has been conservatively estimated that IBS is the cause of 850,000 consultations in the UK per year costing nearly £50 million (1995 prices), including GP prescribing (Camilleri & Willims, 2000). Wells et al (1997) using market research estimated that total prescribing costs in 1995 for IBS were about £12.5 million a year, which with costs of GP visits and hospital services rises to around £46 million a year. US studies have shown that patients with IBS symptoms have double the medical costs of age and sex matched people without these symptoms (Talley et al, 1995). The development of new drugs for treating IBS is likely to raise these costs considerably in the near future. In addition there are considerable indirect costs due to nearly double the rate of absence from work than people without IBS (Donker et al, 1999). The direct cost of IBS has been estimated to account for between 0.1% and 0.5% of NHS expenditure, the indirect costs are as least as great, resulting in estimates of a total societal cost of IBS of around £250 per year.

Eczema

Atopic dermatititis is a common disease which affects over 10% of children and over 2% of the whole population in Western communities. Treatment costs in Australia have been estimated at between $A1,000 and $A6,000 per child per year (Kemp, 1999) with personal costs at around $A800 per year depending on severity . In the 1995 a British study reported that the annual costs to the NHS exceeded £125m and personal costs due to days of lost salary etc were around £300m (Herd et al, 1996).

References

Camilleri M, Williams DE. Economic Burden of irritable bowel syndrome. Pharmaco-economics, 2000;17:331-338.

Donker, Foets M, Spreeuwenberg P. Patients with irritable bowel syndrome: health status and use of health care services.Br J Gen Practice 1999;49:787-792.

Ferrari M D.. The economic burden of migraine to society. Pharmacoeconomics, 1998, 13(6), pp.667-676.

Herd RM, Tidman MJ, Prescott RJ, Hunter JAA. The cost of atopic eczema British Journal of Dermatology, 1996, 135(1), pp. 20-23.

Hu X H, Markson L E, Lipton R B, Stewart W F, Berger M L. Burden of migraine in the United States:disability and economic costs. Archives of Internal Medicine 1999; 159: 813-818.

Kemp A S. Atopic eczema: its social and financial costs. Journal of Paediatrics & Child Health 1999; 35(3): 229-231.

Lipton R B, Stewart W F, Von Korff M.. Burden of migraine: societal costs and therapeutic opportunities. Neurology, 1997, 48(3 Suppl 3), pp. S 4-S 9

Solomon G D, Price K L. Burden of migraine: a review of its socioeconomic impact PharmacoEconomics, 1997, 11(Suppl. 1), pp.1-10

Su J C, Kemp A S, Varigos G A, Nolan T M.. Atopic eczema: its impact on the family and financial cost. Archives of Disease in Childhood, 1997, 76(2), pp. 159-162

Talley NJ, Gabriel SE, Harmsen WS, Zinsmeister AR, Evans RW. Medical costs in community subjects with irritable bowel syndrome Gastroenterology, 1995, 109(6), pp. 1736-1741

van Roijen L, Essink-Bot M-L, Koopmanschap M A, Michel B C, Rutten F F.. Societal perspective on the burden of migraine in the Netherlands. PharmacoEconomics, 1995, 7(2), pp. 170-179.

Wells N E J, Hahn B A, Whorwell P J. Clinical economics review:irritable bowel syndrome. Alimentary Pharmacology & Therapeutics 1997; 11(6): 1019-1030.