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Left ventricular dysfunction in the diabetic population

Primary care provides an increasing proportion of the care for those with diabetes — a condition with a prevalence of up to 4% in those over the age of 45 years in the United Kingdom.[1] The major cause of death in such patients is cardiovascular disease, especially coronary artery disease. Diabetes also increases the risk of heart failure at least fourfold.[2] Hitherto, few data are available on how common left ventricular (LV) systolic dysfunction is in middle-aged diabetic patients in the United Kingdom, nor how best to identify such patients. A recently published primary care-based echocardiographic screening study reported a prevalence of LVSD of 7%, in a subset of 157 diabetic patients aged 45 years or older in the West Midlands.[3] These patients would benefit from angiotensin-converting enzyme (ACE) inhibitors, which delay the progression to frank heart failure.[4-5]

We wish to report the results of a preliminary study attempting to identify LV systolic dysfunction among diabetic patients in primary care in the North-east of Scotland. Sixty patients aged over 40 were identified from the diabetic register of one practice (list size = 4600) as suitable for invitation to undergo clinical examination and a transthoracic echocardiographic study at a nearby community hospital. Thirty-eight (63%) of these patients consented to take part in the study.

Eight patients had a history of coronary artery disease and two (25%) had clinically significant and symptomatic LV systolic dysfunction (ejection fraction <45%). One of these patients was on an ACE inhibitor already because the LV systolic dysfunction had been previously diagnosed. Of the 30 patients without a history of coronary disease, two (7%) had LV systolic dysfunction; both of these patients were asymptomatic.

It has been suggested that a normal electrocardiogram (ECG), or a normal plasma B-type natriuretic peptide (BNP) measurement, could guide the most efficient use of the limited echocardiographic resource in the UK to identify those with LV systolic dysfunction in primary care. Our pilot data support such recommendations (Table 1) with a high negative predictive value and moderate positive predictive value for both tests.

The prevalence of undiagnosed LV systolic dysfunction in middle-aged diabetic patients in primary care may be substantial (11% [95% confidence interval = 4 to 24%] in our series). These patients may have no symptoms but are likely to benefit from the introduction of ACE inhibitors to delay the progression to symptomatic heart failure. The best method for screening for LV systolic dysfunction in primary care remains to be determined. Our pilot study suggests that middle-aged diabetics with a history of coronary disease are at especially high risk of LVSD, but targeting only this group would miss other cases. Further studies are urgently needed.

Table 1. Clinical utility of using a normal ECG or plasma BNP result (measured using a near-patient assay [Biosite Diagnostics]) to exclude LV systolic dysfunction in middle-aged diabetic patients in a pilot study in primary care in the North-east of Scotland. NPV: negative predictive value; PPV: positive predictive value.

	EF ≥45%	EF <45%	Total
Normal ECG			
ECG normal	27	1	28
ECG abnormal	7	3	10
Total	34	4	38
Sensitivity = 75%	Specificity = 79%	NPV = 96%	PPV = 30%
Plasma BNP			
BNP <95 pg/ml	31	1	32
BNP ≥95 pg/ml	3	3	6
Total	34	4	38
Sensitivity = 75%	Specificity = 91%	NPV = 97%	PPV = 50%

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Predictive value of asthma medication to identify asthma sufferers

The article by Himmel *et al*[1] addresses an important concern — whether a prescription of particular drugs can act as a predictor of a clinical diagnosis of asthma. However, there are a number of serious flaws in the paper that should be acknowledged.

In the methods and the analysis, several terms are used wrongly, with important implications for the interpretation of the paper.

The 'specificity' of a prescription for the diagnosis of asthma is calculated as 'the number of prescriptions for patients with asthma in relation to all prescriptions of this drug class'. This is not specificity, which has a specific (*sic*) meaning, being, in this context, the proportion of patients without a prescription in a given drug class who do not have asthma. The measure proposed as specificity is, logically, the positive predictive value (PPV) of a prescription for a diagnosis of asthma.

The analysis section defines 'odds ratios' (ORs) as the ratio of the 'likelihood of predicting the diagnosis of asthma and the likelihood of having any other diagnosis'. This is not the odds ratio, which is the ratio of the odds of having asthma given a prescription of a particular drug to the odds of not having asthma. The definition given of 'odds ratio' is very close to what would be the likelihood ratio for a positive diagnosis of asthma given a prescription of a drug, but is rendered confusing by two facts. First, it is not clear what the 'likelihood of predicting' means and secondly, likelihood ratios calculated from the data given in the paper are quite different from those presented in the tables of results.

We have tried to replicate the calculation of odds ratios presented in the paper without success. As an example, we believe that for the association between prescriptions of inhaled β-2 agonists and asthma diagnosis in general practice (i.e. asthma or asthma and chronic obstructive pulmonary disease), the 2 x 2 contingency table should be as shown above.

	Diagnosis of asthma		Total
Prescription of β-2 agonist	+	–	
+	65	16	81
–	141	175	316
Total	206[a]	191	397[b]

[a]From Himmel *et al* Table 1: diagnosis of asthma or asthma + COPD. [b]From Himmel *et al* Table 1: 429 patients in total, minus 32 excluded from the analysis.

From this table:

- the PPV is 0.802, which is close to the 'specificity' reported;
- the specificity of a β-2 agonist prescription is 0.92; in other words, 92% of patients who don't have asthma don't have a prescription for β-2 agonists;
- the sensitivity is 0.32; in other words, 32% of patients who have asthma have a prescription of β-agonists.
- the odds ratio for a diagnosis of asthma given a prescription of β-2 agonist is 5.0.
- The likelihood ratio (sensitivity/1–specificity) for a positive diagnosis given a prescription of asthma is 3.8. In other words, a patient with a prescription of a β-2 agonist is 3.8 times more likely to have asthma than not to have it.

It is not clear how the reported OR of 2.02 has been calculated and what its interpretation should be, given the mistaken definition. Indeed, back-calculation of the OR of 2.02 does not yield any numbers that are recognisable from the data presented in the paper.

A further important flaw in the study is the absence of an attempt to identify patients with asthma from other than prescribing information. We therefore have no information on the true number of people who have asthma but no prescription of a β-2 agonist. Instead, we have the number of people with asthma who have prescriptions for drugs other than β-2 agonists; in other words, a subset of the actual 'false negatives'. This infers that the sensitivity of β-2 agonists for a diagnosis of asthma would be lower than the data suggest.

The correct definition and application of epidemiological measures is essential and it is a pity that this potentially important paper appears to have fundamental errors.

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1. Himmel W, Hummers-Pradier E, Schumann, Kochen M. The predictive value of asthma medications to identify individuals with asthma — a study in German general practices. *Br J Gen Pract* 2001; **51:** 879-883.

Authors' response

The letter from Dr Stein and colleagues from Exeter gives us an opportunity to clarify the aims and methods of our study:

Dr Stein's definition of 'specifity' is of course correct. But the calculation of this 'epidemiological' measure requires the knowledge of the prevalence of asthma, i.e. the exact number of asthma patients. This is a problem of pharmacoepidemiology in a (German 'no-list') general practice setting, since we cannot know whether or not all asthma patients receive a prescription (especially in stages I and II) and are thus identified.

Our focus, however, was not an epidemiological one. Our starting point was the complete knowledge of all medicines prescribed in a defined sample of general practices. These data (which can be obtained, for example, from the British PACT database or from German health insurance records) are usually not linked with diagnoses. Before any conclusions regarding doc-

tors' performance were drawn on the basis of their prescriptions, we wanted to know how exactly a prescription for an asthma drug predicts the diagnosis of asthma. This is what we called the 'specificity of a prescription'. We admit that the use of this term in a manner different to its epidemiological definition may cause some misunderstanding. However, since we defined the term in our paper, there should be no reason for misunderstanding our intention.

Far more interesting — and open for debate — is the following issue: The different values of the odds ratios (ORs) reported by the two study groups are not caused by erroneous calculations (the definition of the OR given by Dr Stein is exactly the formula we used in our analyses). They result from a different unit of analysis. Dr Stein and his colleagues used the *patient* as the unit of analysis. Since we were interested in the marker function of individual drugs (rather than treatment patterns) we used the *prescription* as the unit of analysis. Our 2 x 2 table for betamimetics is as shown below.

As our analysis was based on prescriptions from a three-month period only, multiple prescriptions of the same drug for one patient were, as should be expected, rare. It should be emphasised that Dr Stein's OR (5.0) and likelihood ratio (3.8) give a similar indication to our calculated OR (2.02) based on the prescription as the unit of analysis. Thus, both values confirm that inhaled betamimetics were a marker for the diagnosis of asthma. Vice versa, inhaled steroids were not.

The lesson from that debate might be that epidemiological terms should not be used without looking to study design and methodology. Furthermore, we should be aware that problems in general practice might be looked at from different angles by epidemiologists and general practitioners. We were interested in the marker quality of single groups of drug so that the usefulness of global prescribing indicators (for example, the ratio of inhaled steroids to bronchodilator drugs) for general practitioners' prescribing performance can be assessed. To use the single drug as the unit of analysis instead of patients was, therefore, a logical consequence.

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	Diagnosis of asthma		Total
Prescription of β-2 agonist	+	–	
+	65	16	81
–	398[a]	198[b]	596
Total	463	214	677

[a]From Himmel *et al* Table 1: total number of prescriptions other than β-2 agonists for patients diagnosed as asthmatics. [b]From Himmel *et al* Table 1: total number of prescriptions other than β-2 agonists for patients not diagnosed as asthmatics (most often diagnosed with COPD).

Melleril: gone forever!

Following guidelines from the Committee on Safety of Medicines (CSM), thioridazine is now limited to use in second-line treatment of schizophrenia under the supervision of a consultant psychiatrist. With particular relevance to primary care it is no longer indicated for the management of anxiety, agitation, and restlessness in the elderly. We recently sought the views of all 296 general practitioners within two health authorities (North West Lancashire and West Pennine Health Authority) about the recent introduction of these guidelines in relation to their patients over the age of 65. The response rate for a postal questionnaire was extremely high with over 90% of GPs responding, perhaps reflecting that the recent advice was of some relevance and interest within primary care. Of the 98% who were aware of the guidelines, just over three-quarters (81%) chose to discontinue medication in some of their patients. Just under one-fifth (18%) chose the option of dose reduction as a management strategy. Not surprisingly, under 5% were prepared to monitor their elderly patients with serial ECGs. When choosing a replacement therapy, side-effect profile was of major importance in choosing the new treatment (65%).

Many practices (27%) had a protocol in place to deal with the guideline. It was an interesting finding that over 40% felt that they were not provided with enough information to manage their patients during the immediate period following withdrawal, an issue that may well need addressing by the CSM on dissemination of future guidelines.

With regard to the choice of an alternative treatment, risperidone was the most popularly prescribed drug, used by over 50% of responders. The next most popular choice was chlorpromazine, perhaps reflecting its cost, the same dose-for-dose prescribing as melleril, and its familiarity. It was pleasing to see that many GPs are now becoming confident in prescribing newer neuroleptics for their elderly patients which, owing to their lower side-effect profile and increasing evidence base, are now well accepted as the treatment of choice in management of the behavioural and psychological manifestations of patients with dementia illnesses.

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Correction

We would like to point out that the letter by Dr Denise Wawman, entitled 'Access to primary care and distance from PCC' (December 2001 *BJGP*, page 1013), was published with an incorrect correspondence address. The correct correspondence address is as follows: Dr Denise Wawman, Warden Road Surgery, 11 Warden Road, Minehead, Somerset TA24 5DS. We would further like to affirm that Dr Wawman has never had any connection with the University of Edinburgh. We apologise for the error and for any confusion this may have caused.