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## Is fasting blood glucose a reliable parameter for screening for diabetes in hypertension

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### Record Status

This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

### Health technology

A stepwise approach to screening for diabetes in hypertensive patients was compared with a one-step approach. The stepwise approach consisted of the successive measurement of fasting plasma glucose (PG) and glycosylated haemoglobin (HbA1c), and the oral glucose tolerance test (OGTT). The one-step approach used the OGTT exclusively.

### Type of intervention

Screening.

### Economic study type

Cost-effectiveness analysis.

### Study population

The study population comprised patients with arterial hypertension. The primary inclusion criterion was a clinical systolic blood pressure (BP) of 140 mmHg, or a clinical diastolic BP of 90 mmHg. In addition, a 24-hour ambulatory BP measurement was performed, in which arterial hypertension was defined as a mean systolic BP of greater than 130 mmHg, or a mean diastolic BP of greater than 81 mmHg. Patients with a history of diabetes mellitus, or treatment with oral antidiabetics or insulin were not included. Additional exclusion criteria were evidence of impaired renal function, history of renal transplantation, evidence of chronic liver disease class B and C (Child classification), fever (>38 degrees C), and current treatment with steroids.

### Setting

The setting of the study was secondary care. However, the interventions examined could possibly have been performed in a primary care setting. The economic study was conducted in Vienna, Austria.

### Dates to which data relate

The effectiveness data were collected between January 1999 and July 2001. The resources used probably referred to the same dates, although this was not explicitly reported. The year to which the prices referred was not stated.

### Source of effectiveness data

The effectiveness data were derived from a single study.

### Link between effectiveness and cost data

The costing was carried out on the same patient sample examined in the study. Although not explicitly stated, it appears that the costing might have been carried out retrospectively.

### Study sample

All eligible patients who presented to the Hypertension Unit of the Department of Emergency Medicine in the General Hospital of Vienna between January 1999 and July 2001 were enrolled in the study, after informed consent had been obtained. No power calculations, to determine or assess the sample size, were performed either prospectively or retrospectively. There was also no evidence that the sample size was appropriate for the clinical study.

A total of 152 patients (77 men and 75 women) were enrolled. The median age of the patients was 60 years (25th to 75th interquartile range, IQR: 55 - 70). Laboratory values for renal function and serum electrolytes were within the normal range for all patients. The median body mass index was 28 (IQR: 25 - 31). The median duration of hypertension was 5 years (IQR: 1 - 10). The median clinical systolic BP was 150 mmHg (IQR: 140 - 161) and the median clinical diastolic BP was 87 mmHg (IQR: 81 - 92). The median values for ambulatory BP were 139 mmHg (IQR: 130 - 144) systolic and 81 mmHg (IQR: 74 - 88) diastolic. It was not reported that any patients refused to participate, or were excluded from the initial sample.

### Study design

This was a diagnostic cross-sectional study that was conducted in one hospital. The patients were screened for diabetes using a combination of screening tests, and then a 'gold' standard method was used to determine the diagnosis of diabetes. The follow-up lasted until the point at which the final diagnosis was confirmed (probably from a few hours to a few days). There were no losses to follow-up.

### Analysis of effectiveness

All the patients included in the study were accounted for in the analysis. The primary outcomes measured were the test characteristics of the screening methods evaluated (i.e. sensitivity, specificity, positive predictive value and negative predictive value). For the fasting PG test, the results were considered positive if the fasting PG was 7.0 mmol/L. The sensitivity and specificity of the HbA1c test to diagnose diabetes (i.e. predict a 2-hour PG of 11.1 mmol/L) were examined by receiver operating characteristic curve (ROC) analysis. The performance of HbA1c to diagnose diabetes was expressed as the area under the curve.

As the study involved only a single group of patients, comparability of the groups and adjustments for confounding factors were not an issue. However, the authors showed that, within the group, patients with a diagnosis of diabetes and those without such a diagnosis did not differ in age, body mass index, duration of hypertension, or systolic and diastolic DBP (both clinical and ambulatory). The only statistically significant difference was found in family history of diabetes mellitus, ( $p=0.019$ ), where 29% of patients with a diagnosis of diabetes had a family history of diabetes versus 12% of those with no diabetes diagnosed.

### Effectiveness results

Diabetes was diagnosed in 33 of the 152 patients (22%) by performing an OGTT (gold standard method).

For the stepwise approach, in the first step of screening all patients for fasting PG, 25 patients (16% of all patients, or 76% of diabetic patients) were identified as diabetic (all true positive).

Eight out of 152 patients would be falsely classified as nondiabetic individuals.

In the remaining 127 patients, HbA1c was measured to identify additional diabetic cases.

The cut-off for HbA1c, as determined by ROC analysis, was 6.1%.

The area under the curve was 0.87 (95% confidence interval: 0.79 - 0.95).

The identified cut-off of 6.1% revealed a sensitivity of 100% and a specificity of 75%.

The combined use of fasting PG and HbA1c identified all diabetic patients and revealed no false negative results (but it led to a number of false positive results).

The HbA1c test resulted in 38 patients being classified as positive. These were subsequently re-tested with OGTT to identify the true positive patients.

### **Clinical conclusions**

The combination of fasting PG and HbA1c was a reasonable alternative to the generally recommended OGTT for the screening of diabetes in hypertensive patients, as diabetes was correctly diagnosed in all patients by this stepwise procedure and the number of confirmatory OGTTs required was reduced.

### **Measure of benefits used in the economic analysis**

The benefit used in the economic analysis was the number of diabetic patients that were diagnosed either by the stepwise procedure or the comparator, out of the total number of patients screened. However, since the stepwise procedure was designed in such a way that all diabetic patients were ultimately diagnosed (100%), and as this was also the case with the 'gold' standard procedure that served as the comparator, the economic analysis was conducted in a manner that only considered the costs.

### **Direct costs**

The study perspective was that of a hospital. The costs consisted of those for screening only, for the identification of all patients with diabetes. The costs included were for physicians, nurses and laboratory procedures. The costs and the quantities were not reported separately. The costs were obtained from the finance department of the hospital in which the study took place. The total costs were estimated from actual data (i.e. the number of screening tests needed in the population examined) for the identification of all diabetes cases. Discounting was not carried out, which was appropriate since the costs were incurred during less than one year. The date to which the prices referred was not reported.

### **Statistical analysis of costs**

The costs were treated deterministically. No statistical analysis of the costs was performed.

### **Indirect Costs**

The indirect costs were not included in the analysis.

### **Currency**

The costs were expressed in both Euros (Euro) and US dollars (\$). The conversion rate was not reported.

### **Sensitivity analysis**

No sensitivity analysis was performed.

### **Estimated benefits used in the economic analysis**

The benefit used in the economic analysis was the number of diabetic patients diagnosed either by the stepwise procedure or the comparator, out of the total number of patients screened. The stepwise procedure was designed in such a way that all patients with diabetes were ultimately diagnosed from the study sample (33 of the 152 patients participating in the study (22%); 33 of the 33 diabetes cases within the study sample (100%)). The standard procedure also revealed all 33 diabetes cases.

### **Cost results**

The total cost of the stepwise screening procedure (152 fasting PG, 127 HbA1c, and 38 OGTT) was \$6,436.90 (Euro 6,569.54).

The total cost of OGTT to all 152 patients was \$11,153.76 (Euro 11,381.76). This resulted in a difference in total cost of \$4,716.86 (Euro 4,812.22).

The cost per patient screened was \$42.34 (Euro 43.22) for the stepwise screening procedure and \$73.38 (Euro 74.88) for the OGTT. The difference between the two of \$31.03 (Euro 31.66) per patient screened favoured the stepwise approach.

### **Synthesis of costs and benefits**

The benefits considered were reported as the cost per patient screened, (and not the cost per case detected). The difference between the ratios was reported. An incremental analysis was not performed, but it was not applicable since the two strategies compared aimed to identify all cases of diabetes. The cost per patient screened has been reported already (see Cost Results).

### **Authors' conclusions**

The combination of fasting plasma glucose (PG) and glycosylated haemoglobin (HbA1c) was a reasonable alternative to the oral glucose tolerance test (OGTT) for the screening of diabetes in hypertensive patients. This was because diabetes was correctly diagnosed in all patients by this stepwise approach, and the number of confirmatory OGTTs needed was reduced. Moreover, this approach demonstrated a cost-saving effect.

### **CRD COMMENTARY - Selection of comparators**

The selection of the comparator was justified since it was considered the widely recommended, 'gold' standard method for identifying diabetes. You should consider whether this technology reflects current practice in your own setting.

### **Validity of estimate of measure of effectiveness**

The basis of the analysis was a cross-sectional study. This was an appropriate study design for the study question, which was the estimation of test characteristics of a stepwise screening approach and, ultimately, the determination of the optimal screening pathway. Appropriately, another one-step screening method with known characteristics was used to confirm the diagnosis, serving as the 'gold' standard comparator. The study sample was representative of the study population. However, no power calculations appear to have been conducted and the sample size was small. Hence, it might have been inadequate. Statistical analyses were performed to compare baseline characteristics between those with a diagnosis of diabetes and those without, within the study sample. However, no statistical analysis of the results was performed to test their statistical significance.

### **Validity of estimate of measure of benefit**

The analysis of benefits was based upon the diagnostic equivalence of the two screening strategies compared. Therefore, the economic analysis included, in practice, only the costs.

### **Validity of estimate of costs**

The perspective adopted was that of a hospital. All the relevant costs appear to have been included in the analysis. The costs and the quantities were not reported separately. No statistical analysis of the costs or sensitivity analysis was conducted. This may limit the interpretation of the study findings. The authors presented their results in both US dollars and Euros, but the conversion rate used was not provided. Discounting was not carried out, which was appropriate since the costs were incurred during less than one year. The date to which the prices referred was not stated.

### **Other issues**

The authors made appropriate comparisons of their findings for the effectiveness outcomes with those of other studies. The issue of generalisability of the results to other settings was not addressed. The results of the study were adequately

reported. Although the effectiveness outcomes were equivalent, the economic results were presented as ratios, expressing the cost per patient screened by each method. However, these ratios depended also on the prevalence of the disease in the investigated population. A different prevalence of diabetes would change the number of tests required with the stepwise approach and would, in all probability, alter the ratio related to this strategy. Thus, the ratios presented (and the difference between them) cannot be generalised to populations with a different prevalence of diabetes. The authors were aware of this limitation. They stated that the results referred to a population of hypertensive patients with a specific prevalence of diabetes, and not to the general population. The prevalence of diabetes in the study population was reported to be similar to that of other populations of hypertensive patients reported elsewhere. Thus, the results may be generalised to the population of hypertensive patients generally.

The authors acknowledged another limitation. A single OGTT was used as the 'gold' standard for the diagnosis of diabetes, although concerns had been expressed about the reproducibility and validity of a single OGTT. Further, the authors admitted that the definition of diabetes (fasting PG of 7 mmol/L) might be considered arbitrary. However, the results obtained by the stepwise approach were confirmed by performing an OGTT on all patients.

Despite the limitations highlighted, the authors' conclusions reflected the scope of the analysis.

### **Implications of the study**

Based on the study results, the authors suggested that recommendations concerning the screening of hypertensive patients be re-evaluated. They considered the stepwise combination of fasting PG and HbA1c as a reasonable method for diabetes screening in hypertensive patients.

### **Source of funding**

None stated.

### **Bibliographic details**

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