Explanations for variations in clopidogrel prescribing in England

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ABSTRACT

Background The National Audit Office (NAO) has produced prescribing indicators that Primary Care Trusts (PCTs) can use to judge their performance. One of the indicators is for the antiplatelet clopidogrel, measured as defined daily dose (DDD) per cardiovascular Specific Therapeutic Age Related Prescribing Unit (STAR-PU). Clopidogrel is used as an indicator because it is a more expensive medicine than the alternative (aspirin) and there may be scope for cost reduction. We aimed to establish if the NAO indicator for clopidogrel prescribing is a valid measure of prescribing performance.

Methods Prescribing data for 152 PCTs and a range of explanatory variables were obtained. Correlation between variables was determined. A regression analysis was conducted to compare the dependent variable (prescribing) with the explanatory variables identified.

Results The percentage of patients on the coronary heart disease register and Index of Multiple Deprivation explained 30% of the variation in prescribing (DDD/STAR-PU) between PCTs. Even though DDD/STAR-PU is adjusted for age and sex other measures of need still have an impact on prescribing.

Conclusions Using DDD/STAR-PU alone as a prescribing indicator might misidentify some PCTs, which are under- and over-using clopidogrel. Poor ranking against other PCTs using the NAO indicator should be fully explored taking into account other variables (cardiovascular morbidity and deprivation) before any corrective action is taken.

Keywords cardiovascular disease, economics, primary care

Introduction

The Department of Health (DH) has acknowledged that there is high variation in the cost of prescribing for certain therapeutic areas. In September 2006, the National Health Service (NHS) Institute for Innovation and Improvement launched a ‘Better Care, Better Value’ indicator for the prescribing of statins to show how financial improvements could be made if all Primary Care Trusts (PCTs) in England prescribed at the rate of the best performing PCTs.

Prescribing costs in primary care have also been identified by the National Audit Office (NAO), as an area in which the NHS could make savings and improve efficiency. The NAO has built on the ‘Better Care, Better Value’ statin prescribing indicator by developing other measures, in different therapy areas. One of the additional indicators is for the antiplatelet clopidogrel. Clopidogrel is included because it is a more expensive medicine than the alternative aspirin and there may be scope for cost savings. The measure used for clopidogrel is defined daily dose per 1000 cardiovascular STAR-PU's (DDD/STAR-PU).

The DDD is an analytic measure for a typical daily dose prescribed; the DDD for clopidogrel is 75 mg daily, or one tablet. The STAR-PU is the specific therapeutic group age–sex related prescribing unit. A STAR-PU is a PCT population figure adjusted to take into account expected prescribing variations in older people for particular therapeutic groups, in this instance cardiovascular medicines. It roughly measures how many prescriptions each PCT is expected to write, after adjusting for different age–sex profiles. The STAR-PU is used by the NAO as ‘a rough proxy measure for disease prevalence in a therapeutic area’.

The NAO ranking of PCTs by DDD/STAR-PU show a large variation in clopidogrel usage between PCTs, with the
lowest being Torbay Care Trust (61 DDD/1000 STAR-PUs) and the highest North Liverpool (341 DDD/1000 STAR-PUs) and the English average being (149 DDD/1000 STAR-PUs). The clopidogrel prescribing indicator makes the assumption that if variations in the age and sex of a population have been taken into account, then the usage should be the same in all parts of England. The NAO has made estimates of potential cost savings if all PCTs prescribed at the rates of the lowest quartile of PCTs. This assumes that STAR-PU values correspond to clinical need.

We aimed to establish if the NAO indicator for clopidogrel is a valid measure of prescribing performance.

**Method**

**Data sources**

Clopidogrel prescribing data in DDDs per 1000 STAR-PUs were obtained from the Prescription Pricing Authority for years 2004/5 and 2005/6 (www.PPA.nhs.uk).

Deprivation data were obtained from the 2004 Indices of Multiple Deprivation (IMD) (http://www.neighbourhood.gov.uk/page.asp?id=1057). The IMD are a measure of deprivation at 'super output area' level that combine indicators across seven domains (income, employment, health and disability, education skills and training, living environment and crime) into a single deprivation score. This was only available for the new PCT boundaries (i.e. the 152 PCTs that formed after mergers in 2006).

Deprivation data were provided with data about the age (in three bands) and sex of the PCT populations; and ethnicity (Afro-Caribbean and Asian). Since STAR-PUs are adjusted for age and sex, only ethnicity data were further utilized.

General Practitioners (GPs) in the UK are required to produce disease registers and outcome data for a number of long-term conditions, as part of their contract. This is known as the Quality Outcomes Framework (QOF). QOF data at PCT level, percentage of the population on the register, were obtained for coronary heart disease (CHD) and stroke for the year 2006 but this was only available for 152 new PCTs. These prevalence data are not standardized by age or sex, and its completeness relies on GP identification and reporting of relevant conditions.

Hospital Episode Statistics (HES) for indications for which clopidogrel could be prescribed was requested from the Information Centre for Health and Social Care (www.ic.nhs.uk) for NHS Hospital Trusts and (old n = 303) PCTs in England in 2004/5 and 2005/6. This HES included angina pectoris, acute myocardial infarction, subsequent myocardial infarction, chronic ischaemic heart disease, other ischaemic heart disease, unstable angina and percutaneous transluminal balloon coronary (and laser) angioplasty.

**Statistical analysis**

Correlation matrices were constructed to show the relationship between each pair of variables. Pairs of highly correlated variables cannot be used in regression analysis, and in such cases a decision was made about the best variable to take forward to the next stage of analysis. Regression analysis was conducted to compare the dependent variable (prescribing) with the range of potential explanatory variables identified. Potential explanatory variables (except those excluded on the basis of high correlation) were entered into a multiple linear regression model and excluded stepwise until a core set of explanatory variables remained. Model characteristics and diagnostic statistics were examined to assess the validity and explanatory power of each model.

**Descriptive models**

Graphs were drawn to illustrate the relationship between significant explanatory variables and PCT ranking by DDD/STAR-PU.

**Results**

HES reported very low numbers where high incidence of cardiovascular disease is known to exist. We believed that the data had been inconsistently collected and reported by hospitals. A decision was therefore made to omit it from the analysis.

The latest prescribing figure DDD/STAR-PU in 2005/6 was chosen for the analysis (DDDPU05). There is prior evidence to suggest under treatment of cardiovascular disease in ethnic minority groups, especially those of South Asian origin. There was a significant moderate positive correlation (0.406, P < 0.01) between the percentage of the PCT population that was Asian and Black. A combined variable was created for the percentage of the population that was Asian or Black (PCEthnic).

The two disease register (stroke and CHD) variables were strongly correlated and could not be summed (the same patients may be on both) therefore they could not be used together as independent variables in multi-variate analysis. CHD register data were used because it includes a larger number of conditions for which clopidogrel is indicated (PCCHD06).

Correlation between the final set of variables used in the regression model is summarized in Table 1. Possible explanations for the negative correlation between ethnicity and
CHD are the relative youth of ethnic populations (which raw population and ethnicity data supplied supports) and under diagnosis/reporting of CHD (for which we have no evidence in this case). Only prevalence of CHD and deprivation were left as significant predictors of prescribing in a parsimonious regression model (Table 2).

**DDD/STAR PU** adjusts prescribing need for age and sex. Nevertheless 30% of prescribing variation between PCTs is explained by CHD prevalence and deprivation. This suggests that the number of STAR-PUs on its own underestimates prescribing need. Figures 1 and 2 illustrate these relationships. In each figure DDD/STAR-PU ranking of data points (PCTs) is indicated by differently orientated triangles: up for quartile 4 (highest); right for quartile 3; left for quartile 2 and down for quartile 1 (lowest). Some data points are also numbered for illustration.

In Fig. 1, the lowest quartile (‘good prescribers’ by the NAOs preferred indicator) shows no increase in prescribing as morbidity rises (SE quadrant). The NE and SW quadrants show prescribing in proportion to morbidity. The NW quadrant (which is not densely populated) shows high prescribing with low morbidity.

In Fig. 2, ‘bad prescribers’ (highest quartile) have the highest levels of deprivation. The indicator should perhaps lead us to ask more questions of high prescribing PCTs with low levels of deprivation (e.g. 86 = Northern Lincolnshire; 115 = Hillingdon) than those with higher levels.

**Discussion**

**Main findings**

STAR-PUs provide a weighting for age and sex, since it is expected that increasing age and male sex reflect increased need. We found that using clopidogrel DDD/STAR-PU alone as a prescribing indicator might misidentify some PCTs, which are under- and over-using clopidogrel. When judging PCTs prescribing performance, all readily available indicators, such as deprivation measures and incidence of

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**Table 1** Correlation matrix for variables in regression model

<table>
<thead>
<tr>
<th></th>
<th>DDDSU05</th>
<th>PCEthnic</th>
<th>PCCHD06</th>
<th>IMD04</th>
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<tr>
<td>DDDSU05</td>
<td>1</td>
<td>0.166b</td>
<td>0.248b</td>
<td>0.531c</td>
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<tr>
<td>PCEthnic</td>
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<td>1</td>
<td>-0.594c</td>
<td>0.457c</td>
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<tr>
<td>PCCHD06</td>
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<td>1</td>
<td>1</td>
<td>0.080</td>
</tr>
<tr>
<td>IMD04</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Percentage of the total population.

*bCorrelation significant at the 0.05 level (2-tailed).

*cCorrelation significant at the 0.01 level (2-tailed).

**Table 2** Parsimonious regression model

<table>
<thead>
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<th>Variable</th>
<th>Coefficient</th>
<th>Standard error</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>431.441</td>
<td>141.803</td>
<td>0.003</td>
</tr>
<tr>
<td>PCCHD06</td>
<td>103.208</td>
<td>33.635</td>
<td>0.003</td>
</tr>
<tr>
<td>IMD04</td>
<td>24.913</td>
<td>3.274</td>
<td>0.000</td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Standard error of estimate</td>
<td>391.225</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model F</td>
<td>35.747 (P &lt; 0.01)</td>
<td></td>
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</tr>
</tbody>
</table>
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cardiovascular disease, should be considered. Alternatively the basis of cardiovascular STAR-PUs could be reconsidered.

What is known already

A previous study has found that prescribing rates for cardiovascular drugs are generally positively related to CHD hospital diagnosis and procedures up to the age of 74. However, from 75 years and above there was a negative relationship with statins and ACE inhibitors but not with aspirin. This perhaps reflected a less interventionist approach in the elderly for coronary artery bypass grafts or statin prescribing for example. Age, ethnicity and socio-economic status are all important factors for predicting CHD epidemiology. CHD, HES and deprivation were found to explain 33 and 10% respectively, of aspirin prescribing. In total, 50–90% of aspirin prescribing could be explained by hospital episodes, deprivation and age. So, although age was an important predictor of need, it only partly explained prescribing.

What this study adds

Our findings suggest that the prevalence of deprivation has an additional effect on prescribing need over and above the prevalence of CHD on general practice registers. This suggests GPs CHD registers under-identify CHD. Previous work has shown increased cardiac mortality to be significantly associated with increased deprivation. Making comparisons between PCTs on the indicator clopidogrel DDD/STAR-PU does not take into account the level of case mix and ‘risk adjustment’ for which clopidogrel is indicated. In other words, the background incidence, within each PCT, for which clopidogrel is indicated in its license needs to be known before comparisons between organizations can be made. Once these have been established other variations may be explained by factors such as doctors prescribing behaviour, e.g. using clopidogrel first line before less expensive alternatives such as aspirin and having a low threshold for using clopidogrel rather than aspirin for patients who complain of dyspepsia. PCTs and individual general practices which have a high use of clopidogrel should audit their use to ensure that this is not happening.

Clopidogrel is indicated for the prevention of atherothrombotic events, which lead to listing on the stroke register and CHD register. The National Institute for Clinical Excellence (NICE) have recommended that clopidogrel in combination with low-dose aspirin should be continued for up to 12 months after the most recent acute episode of non-ST-segment elevation acute coronary syndrome. NICE have also recommended clopidogrel alone (within its licensed indications) for people who are intolerant of low-dose aspirin. Clopidogrel use following angioplasty with stenting is supported by clinical trial data and widely prescribed in the UK for this indication. There is currently a lack of consensus on the period of preventive anti-platelet therapy necessary to avoid later thrombosis. Suggested periods range between 3 months and lifetime. There is some evidence that risks may be greater after drug-eluting stent implantation. A recent HTA assessment of drug-eluting stents suggests a 12 month period for clopidogrel use with aspirin. Clopidogrel, therefore, has some clearly defined indications. It is reasonable to assume that the incidence of these is proportional to the number of patients on CHD registers. However, there is also a possibility for wasteful prescribing such as continuing beyond 12 months in acute coronary syndrome or prescribing first line before trying aspirin. Again audit should be used to ensure that these are not happening.

Prescribing indicators should be used as a starting point for reviewing progress. Prescribing indicators should not be definitive and should be used with other sources of information. The DH, in its productivity metric for statins, has suggested that the ‘bottom’ 75% (highest cost) PCTs should aim to reach the cost of prescribing achieved by the ‘top’ 25% (lowest cost). It should be noted that when this productivity metric was developed that there was no intention for it to become a ‘target’ but targets have been quickly adopted by Strategic Health Authorities and PCTs. The NAOs have similarly based their assumed cost savings on the possibility of PCTs achieving values of the top 25% of PCTs. Using DDD/STAR-PU alone may be misleading and should not be used as a ‘league table’. Deprivation and the prevalence of CHD (both of which are readily available data sets for PCTs) are also important independent indicators of clopidogrel use and should be used in conjunction with DDD/STAR-PU.

Limitations of this study

Ideally, we would like to have had data on indications for which clopidogrel is clearly indicated. However, hospital HES data were incomplete, meaning the data sets were inaccurate. In addition, we could not relate hospital episodes to PCTs. Hospital episodes are a measure of activity whereas CHD registers are a measure of potential need. It could be argued that the later are a more appropriate measure of prescribing need.

We used data on morbidity from general practices QOF registers. These registers may under-identify CHD. There is evidence that general practices’ prescribing of cardiovascular drugs do not always correlate with CHD mortality, which
suggests some practices fail to identify and therefore treat CHD patients. In addition, CHD registers may under-represent patients in deprived communities and it is known that the prevalence of CHD in England is positively associated with deprivation. A more definite measure would have been to use mortality from all circulatory diseases.

PCT boundaries changed during the period, when data were collected. This meant that available data had different PCT denominators. The old PCT areas, of which there were more and who had smaller populations, may have provided more accuracy in identifying specific areas that under or over use clopidogrel.

Conclusions

Using DDD/STAR-PU alone as a prescribing indicator might misidentify some PCTs which are under- and over-using clopidogrel. Poor ranking against other PCTs using the NAO indicator should be fully explored taking into account other variables (cardiovascular morbidity and deprivation) before any corrective action is taken.

Acknowledgements

We are very grateful to Dr Nagpal Hoysal (Consultant in Public Health Medicine, Bradford Airedale PCT) for reviewing this article and providing comments.

Funding

D.P. and J.S. approached Pharmacomm Ltd to source funding from Sanofi-Aventis for this study. There has been no contact between the authors and educational grant providers for this study and no input into the data collection or study design. Sanofi-Aventis have not been provided with any drafts of this paper prior to publication.

Ethical approval

Not required.

Supplementary data

Supplementary data are available at Journal of Public Health online.

References

2 Institute for Innovation and Improvement. http://www.institute.nhs.uk