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Potential savings without compromising the quality of care

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SUMMARY

Aims: This study was designed to analyse the association between adherence to guidelines for rational drug use and surrogate outcome markers for hypertension, diabetes and hypercholesterolaemia. **Methods:** The study used a cross-sectional ecological design. Data from dispensed prescriptions and medical records were analysed from 24 primary healthcare centres with a combined registered population of 330,000 patients in 2006. Guideline adherence was determined calculating the proportion of the prescribed volume of antidiabetic agents, antihypertensives and lipid-lowering agents representing the 14 different drugs included in the guidelines for these three areas. Patient outcome was assessed using surrogate marker data on HbA1C, blood pressure (BP) and s-cholesterol. The association between the guidelines adherence and outcomes measures was analysed by logistic regression. **Results:** The proportion of guideline antidiabetic drugs in relation to all antidiabetic drugs prescribed varied between 80% and 97% among the practices, the ratio of angiotensin converting enzyme (ACE)-inhibitors to all renin–angiotensin drugs 40–77% and the ratio of simvastatin to all statins 58–90%. The proportion of patients reaching targets for HbA1C, BP and s-cholesterol varied between 34% and 66%, 36% and 57% and 46% and 71% respectively. No significant associations were found between adherence to the guidelines and outcome. The expenditures for antihypertensives and lipid-lowering drugs could potentially be reduced by 10% and 50% respectively if all practices adhered to the guidelines as the top performing practices. **Conclusion:** A substantial amount of money can be saved in primary care without compromising the quality of care by using recommended first-line drugs for the treatment diabetes, hypertension and hypercholesterolaemia.

What's known
- There are substantial price differences between branded and off-patent drugs for the treatment of diabetes, hypertension and hypercholesterolaemia.
- There is a wide variation in adherence to prescribe targets in primary healthcare.
- There is a limited knowledge on the relation between adherence to prescribing targets or guidelines, patient outcomes and potential savings that could be achieved.

What's new
- No significant associations were found at a practice level between adherence to the guidelines and outcomes in terms of patients reaching target levels for surrogate markers.
- A substantial amount of money can be saved in primary care without compromising the quality of care by using recommended off-patent drugs for the treatment of diabetes, hypertension and hypercholesterolaemia.

Introduction

A considerable number of guidelines and treatment recommendations are being developed by professional organisations, healthcare providers and authorities. In Stockholm, Sweden, regional guidelines for drug prescribing are developed by the Drug and Therapeutics Committees (DTCs) (1–3). These guidelines, called 'The Wise List', are produced by 20 expert groups with specialists in family medicine, hospital specialists, pharmacists and clinical pharmacologists. They consist of diagnosis-specific evidence-based recommendations with some 240 pharmaceutical products suggested as first-line choices for outpatient treatment of common diseases. The drugs in the Wise List are selected based on medical efficacy and safety preferably with data from randomised-controlled studies, pharmaceutical suitability, comparative cost-effectiveness, experience and environmental aspects (2,3). Substantial savings can be achieved using the drugs recommended in the guidelines, instead of the more expensive branded alternatives. Some examples include replacing atorvastatin with simvastatin for the treatment of hyperlipidaemia and replacing angiotensin receptor blockers (ARBs) with ACE-inhibitors (ACEi) for the treatment of hypertension and heart failure (4,5). Although certain differences in documentation and pharmacokinetic properties, these drugs have shown to be equally effective for a vast majority of all patients with hypertension and hyperlipidaemia respectively (6–12).

However, guidelines are poorly adopted in healthcare because of various barriers at an organisational and professional level (13). Furthermore, many physicians are facing the challenge to comply with an

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ever increasing number of different guidelines (14). Consequently, guideline implementation needs to be supported by the use of indicators to monitor healthcare performance against agreed targets. Traditionally, these indicators focused on quality and were developed by professional organisations to stimulate learning and promoting adherence to guidelines (15–17). In recent years, there has been an ongoing trend in many countries towards linking quality indicators to financial incentives and paying the doctors for reaching certain targets (17–21). The most comprehensive system is probably the Quality and Outcomes framework in the UK, whereby 30% of the payment in general practices is linked to a sophisticated system of quality indicators covering different aspects of care ranging from practice management, record keeping and continuous education to patient satisfaction, clinical outcomes and adherence to guidelines for the treatment of 10 common chronic diseases (17–19). Similar programmes have also been introduced in Germany where physicians receive payment for monitoring patients with chronic illnesses using specific forms including outcome measurements under the Disease Management Programme initiative (20,21).

Indicators can be classified in structure, process or outcome depending on which aspect of care is being assessed (22). The structure comprises the organisational factors that define the health system under which care is provided; the process is the interaction between users and the healthcare structure; and the outcome is the consequences. Although outcome measures are important as they reflect all aspects of care, they are difficult to apply in quality improvement activities (23,24). Healthcare is only one determinant of health and differences in outcome may be because of case mix, how the data were collected, chance, or quality of care. Process measures are more sensitive to differences in the quality of care. They are readily measured and they can directly indicate deficiencies of care which need to be remedied (23,24). However, concern has been raised that a too strict focus on performance measures and prescribing guidelines as currently being undertaken in many countries may have negative effects on the quality of care provided. We therefore analysed to what extent our DTC guidelines were followed in primary healthcare and the potential association between adherence to guidelines and the surrogate outcome markers – blood pressure (BP), HbA1C and s-cholesterol.

Methods

This cross-sectional, ecological study was undertaken in 24 primary healthcare centres (PHCs) in the south-western part of Stockholm County, Sweden. Primary healthcare is the basis of the Swedish healthcare system, although PHCs lack a gatekeeper function and patients are generally allowed to seek care from specialists without referral. All the participating PHCs were group practices of varying size from five general practitioners up to 20. The combined registered population was 330,000 patients in 2006. All the PHCs are part of a voluntary quality collaboration administered by the south-western DTC. This collaboration has included agreements on how to register diagnosis and quality parameters in the electronic medical records.

'Adherence to guidelines (drug formulary recommendations)' was determined using data on dispensed prescriptions collected from the Swedish National Prescription Register administered by the National Corporation of Swedish Pharmacies. The register was introduced in 1997 and consists of aggregate data from all prescriptions dispensed at Swedish pharmacies regardless of reimbursement status. We included all prescriptions dispensed in 2006 issued from the participating PHC centres. As all prescriptions are valid for 1 year, the dispensing data reflected the prescribing for a period up to 1 year before the dispensing.

Drug utilisation (DU) was expressed in defined daily doses (DDDs) (25) and expenditure in Swedish Crowns – SEK; 100 SEK = 10.4 Euro (10 February 2009). The extent of potential savings with physicians switching to less expensive but similarly effective choices such as generic simvastatin vs. atorvastatin and an ACEi vs. ARBs was calculated on a DDD basis assuming all practices could adhere similarly to the guidelines as the top performing practices. The average cost/DDD for simvastatin and atorvastatin was 0.72 and 5.90 SEK/DDD (0.075 and 0.61 €/DDD) respectively in 2006. The average cost for ACEi and ARB was 0.84 and 6.77 SEK/DDD (0.087 and 0.70 €/DDD) respectively.

The global adherence to drug recommendations (not capturing data on diagnosis) was determined for antidiabetic drugs (ATC A10), antihypertensives (C03, C07, C08 and C09) and lipid-lowering agents (C10A) using three different drug-specific indicators (15,16):

- Proportion of the overall volume in DDDs representing drugs included in the guidelines – antidiabetic agents and lipid-lowering drugs.
- Drug Utilisation 90% focusing on the number of drugs constituting 90% of the volume expressed in DDDs and the adherence to recommendations within this segment (26) – antihypertensive agents.
- Ratios between different treatment alternatives (share of recommended drugs in DDD within a

pharmacologic group) – % of simvastatin of all statins and % ARBs of all renin–angiotensin drugs.

The chosen guideline for comparison was the list of drugs recommended in the county of Stockholm 2006 (Kloka Listan – 'the wise drug list') (1–3). The drugs recommended in diabetes, hypertension and hyperlipidaemia are listed in Table 1. They are selected on the basis of medical efficacy, safety and comparative cost-effectiveness. A high proportion of these drugs or a high proportion of low cost generic ACEi compared with expensive brand ARBs is considered to be legitimate targets to enhance prescribing efficiency based on their current acquisition costs vs. alternatives and the wealth of available published evidence reviewed by the expert groups.

Patient outcome was assessed using surrogate marker data captured from electronic medical records. We included all patients who visited any of the 24 PHC centres between 1 January 2005 and 31 December 2006. A 2-year period was selected to include also those patients visiting the practice once a year being prescribed a sufficient supply of drugs for 1 year. All patients with recorded diagnoses of hypertension (ICD-codes I10-, I13-P, I15-) diabetes mellitus (E108P, E109, E118P, E119 and E14-P) and/or ischaemic heart disease (IHD) (I200, I209P, I21-P and I25-P) were included. Data on age, systolic and diastolic BP, HbA1C and s-cholesterol were analysed with the outcomes indicators below, each of them based on last recorded value during the period for each patient. The targets include the:

- Proportion of patients with diabetes mellitus with an HbA1C ≤ 6.
- Proportion of patients with hypertension having a recorded BP ≤ 140/90.
- Proportion of patients with IHD with s-cholesterol ≤ 5 mmol/l.

Table 1 Drugs included in the guidelines (the Wise Drug List)

Antidiabetic agents	Antihypertensives	Lipid-modifying agents
Metformin	Hydrochlorothiazide	Simvastatin
Glibenclamide	Bendroflumethiazide	
Insulin (human)	Enalapril	
Insulin lispro	Ramipril	
Insulin aspart	Amlodipine	
	Metoprolol*	
	Losartan*	
	Candesartan*	

*Recommended as second-line drugs in the guidelines.

These targets were chosen from 'The Wise List 2006' and from national guidelines for the prevention of IHD and diabetes from the National Board of Health and Welfare (27,28).

All data were extracted using RAVE software (Stockholm, Sweden) (29). The RAVE software extracts data from the medical record database in a reliable and systematic way making it possible to link most of the recorded data such as diagnosis, laboratory findings and text registered in the medical record. If quality parameters are recorded under specific key words, they will be found in the extraction and included. There is no regulation in Sweden requiring diagnoses to be recorded at the consultation. Nevertheless, in 85% of all consultations performed in these PHCs in 2006, a diagnosis had been registered in the medical record following established standards (30).

The association between the proportion of patients reaching target levels in each age group in different PHCs and the proportion of DDDs following recommendations in the corresponding groups was analysed by logistic regression. The models including the proportion following recommendations divided by age groups (40–64, 65–79 and 80+) displayed substantial over-dispersion; consequently, the p-values and confidence intervals were subsequently adjusted by scaling for heterogeneity. Results were presented as odds ratios per 10 percentage units of the 'prescriptions' following recommendations together with 95% confidence intervals and p-values for a log-linear trend.

Results

A total of 1.3 million prescriptions (all drugs) were dispensed in 2006 that had been issued by the 24 PHCs. The total drug expenditures were 243 million SEK (25.3 million €).

The mean number of prescriptions per practice was 54,000 (variation 24,000–118,000) with a mean total cost of 10.1 million SEK (1.05 million €) (variation 5.3–20.4 SEK, 0.55–2.12 €).

The total number of DDDs dispensed for antidiabetics, antihypertensives and lipid-lowering agents during the year was 2.9, 16.4 and 5.1 million respectively (Table 2). In 2006, metformin and glibenclamide were recommended as first-line peroral agents, while various fast- and intermediate-acting insulins were recommended for parenteral use. The average adherence to the DTC guidelines was 91%, with variation seen between practices (Table 2).

A total of seven different antihypertensive agents were recommended in the DTC guidelines – hydrochlorothiazide, bendroflumethiazide, enalapril, ramipril, amlodipine, metoprolol, losartan and candesartan

(Table 1). The range of drugs used varied between the practices with on average 16 drugs accounting for 90% of the volume, i.e. DU90% (Table 2). The adherence varied between 64% and 81%. There was a wide variation in the use of ARBs, and the proportion of ACEi to all renin–angiotensin drugs varied between 40% and 77% (Table 2).

The DTC guidelines included only one lipid-lowering agent, simvastatin, recommended for cardiovascular prevention after IHD, stroke and for patients with a high cardiovascular risk. The ratio of simvastatin to all statins varied between 58% and 90% among the practices (Table 1).

The number of patients with diagnoses of diabetes, hypertension or IHD who had visited the practices in 2005–2006 was 9150, 21,175 and 4449 respectively. However, data on surrogate outcomes markers were not recorded for all patients. Information about HbA1C was recorded for 92%, BP for 87% and s-cholesterol for 69% of all patients with a diagnosis of diabetes, hypertension and IHD respectively.

The proportion of patients reaching targets for the surrogate markers HbA1C, BP and s-cholesterol varied among the practices between 34% and 66%, 36% and 57% and 46% and 71% respectively. The variation is illustrated by age in Figure 1.

No significant associations were found between the process indicators measuring adherence to the guidelines (or guidance) and the outcome indicators measuring the proportion of patients reaching surrogate targets (Figure 2 and Table 3).

The total expenditures in 2006 for the prescribing of antidiabetics, antihypertensives and lipid-lowering agents from the 24 PHC centres were 14, 35 and 10 million SEK (1.46, 3.64 and 1.04 million €) respectively. The renin–angiotensin drugs accounted for 15 million SEK (1.56 million €) of the total expenditures for antihypertensives. The estimated savings if all practices adhered to the guidelines as the top performing practices were 3.6 million SEK (0.37 million €) by increasing the proportion of ACEi to 77% and 5.4 million SEK (0.56 million €) by increasing the proportion of simvastatin to 90%.

Table 2 Total volumes (DDD) and adherence to DTC guidelines

Indicator	Total	Mean/practice	Variation
Antidiabetic agents			
Number of DDDs × 1000	2900	121	56–292
% Recommended drugs	91	91	80–97
Antihypertensives			
Number of DDDs × 1000	16,400	684	343–1267
DU90% (no of drugs)	–	16	13–20
DU90% adherence	–	75	64–81
DDD ACEi/ARB × 1000	5600	234	112–441
Ratio of ACEi to ACEi/ARB (%)	66	66	40–77
Lipid-lowering agents			
Number of DDDs × 1000	5100	213	110–394
% Recommended drugs	78	78	54–90
Ratio of simvastatin to statins (%)	79	79	58–90

Prescriptions dispensed in 2006, issued from 24 PHC centres in south-west Stockholm. DDD, defined daily dose; DTC, Drug and Therapeutics Committee; PHC, primary healthcare centre; DU90% drug utilisation 90%; ARB, angiotensin receptor blocker; ACEi, ACE-inhibitors.

Table 3 Association between the adherence to guidelines and the proportion of patients reaching target levels in each age group in different primary care centres

Effect	OR	Low 95% CI	Up 95% CI	p-Value
% Recommended antidiabetic agents	1.03	0.84	1.26	0.79
% Recommended lipid-lowering agents	1.02	0.92	1.12	0.75
% Simvastatin to all statins	1.00	0.91	1.10	0.99
% ACE-inhibitors of all RAAS	0.95	0.90	1.01	0.07
DU90% adherence antihypertensives	0.94	0.84	1.05	0.31

Presented as odds ratios (OR) per 10 percentage units of the 'prescriptions' following recommendations with 95% confidence intervals (CIs) and p-values for a log-linear trend. RAAS, drugs acting on the renin-angiotensin-aldosteron system; ACE, angiotensin converting enzyme.

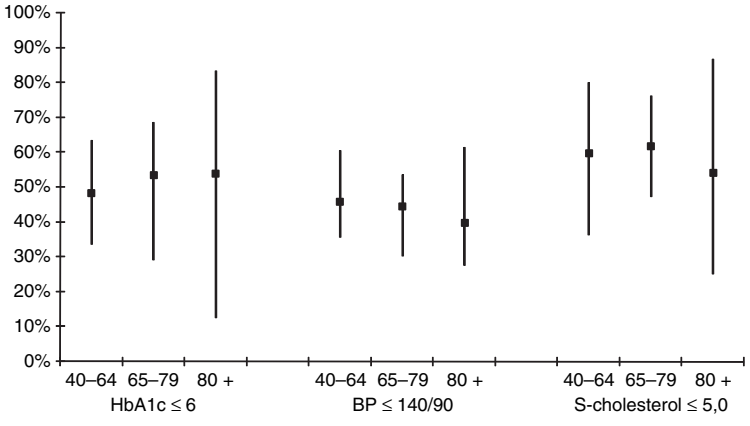

Figure 1 Proportions of patients with diabetes, hypertension and ischaemic heart disease reaching targets for HbA1C, blood pressure (BP) and s-cholesterol broken down by age group. Mean and range depicted between practices (n = 24)

Discussion

We found a wide variation between different primary care practices in quality of prescribing, both measured as attaining targets for cost-effective drug treatment of diabetes, hypertension and hyperlipidaemia and outcomes measured by surrogate markers BP, HbA1C and s-cholesterol. This is in agreement with several studies showing a wide variation in practice performance, only to some extent explained by

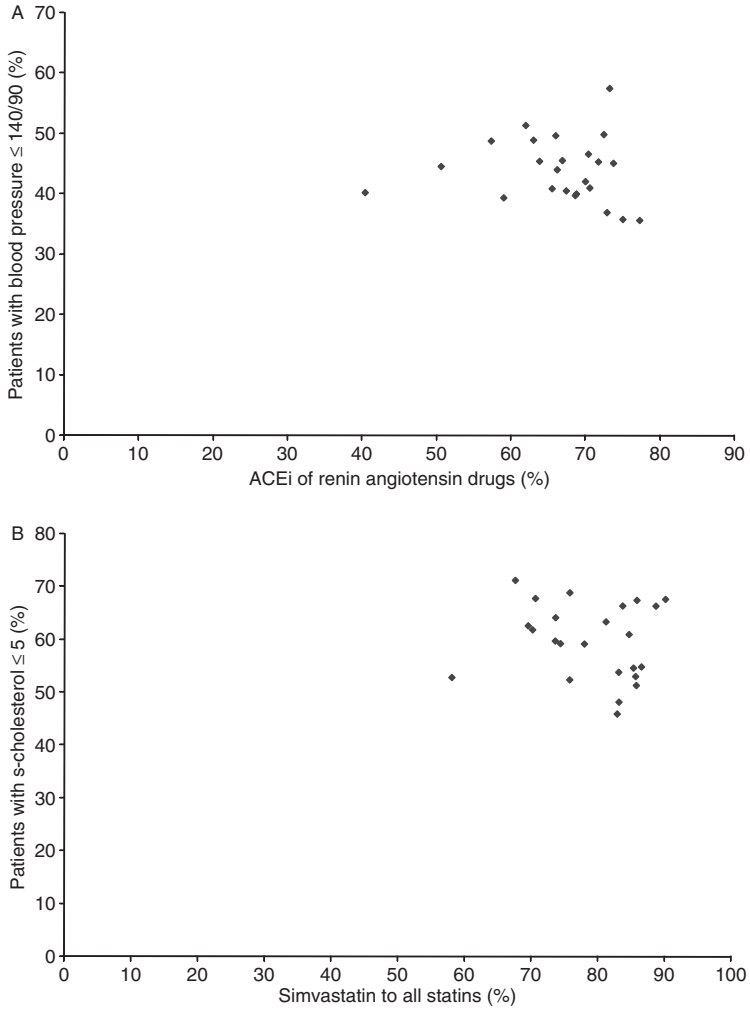

Figure 2 (A) Ratio of ACEi to all renin–angiotensin drugs compared with % patients with hypertension reaching targets for blood pressure (BP) (n = 24 practices). (B) Ratio of simvastatin to all statins compared with % patients with ischaemic heart disease reaching targets for s-cholesterol (n = 24 practices)

differences in patient or prescriber characteristics (5,26,31–35).

No correlation was found by between adherence to the recommendations on drug choice and patient outcome. A limitation with the study was the ecological study design with no record linkage at the patient level between exposure and outcome. There are several reasons why the overall prescribing of these drugs does not completely represent the same population as the patients studied with data from the electronic records. Some reasons include the time lag between consultations and (repeat) dispensing as well as the time lag between initiation of therapy and expected outcome. Furthermore, the dispensing data consisted of all prescriptions dispensed regardless of the diagnoses registered in the medical records. There is also room for improvement in the accuracy and validity of data derived from medical records (36–38). In our study, laboratory analyses on HbA1C and s-cholesterol were performed in a few central laboratories for all participating practices. Routines for measuring BP may vary between practices. However, there were common rules for registration and record keeping among the practices and it is not likely that this will have introduced any systematic error. It is also important to emphasise that outcomes are influenced by a many other factors ranging from compliance to life style factors and concomitant diseases. Consequently, there is probably no association between which specific drugs are prescribed and patient outcomes assuming the drugs prescribed have been shown in clinical trials to improve outcomes.

Our study indicates that a substantial amount of money can be saved in primary care without compromising the quality of care. The estimated savings

were 9 million SEK (0.94 million €), in the same magnitude as the total annual expenditure for all drugs prescribed at one PHC. The substantial savings in reality are likely to be higher than this as the prices for generic drugs in Sweden have been decreasing since the study was undertaken (3). There is also empirical evidence from other settings to support switching statins to save considerable resources. In a recent UK study carried out in a primary care practice, no significant change was observed in mean total cholesterol levels 2 years after the switch from atorvastatin to simvastatin (39). No adverse events attributable to the switch were reported, and substantial savings were achieved (4,39). The resources saved by more cost-effective drug selection could for instance be re-directed to interventions to improve patient compliance as this has been shown to be a significant problem for these disease areas (40).

It has been suggested that proposed process quality indicators must be linked to at least one outcome subcomponent (e.g. morbidity, mortality or quality of life) to be called a quality indicator (41). Quality indicators that lack this evidence should only be called 'putative' or 'aesthetic' (41). However, factors including the data availability and time delay between process and outcome make it very difficult to demonstrate the existence of such a link. Consequently, the way forward is to only recommend drugs in DTC guidelines that have been shown to improve outcomes in the long-term and monitor their utilisation by means of surrogate markers. For instance, there is evidence that lowering HbA1C by using metformin, sulphonylurea or insulin correlates to better clinical outcomes (42,43). Alongside this, drugs should not be recommended which improve surrogate markers, but as yet either have shown no beneficial impact on outcomes or have a detrimental impact on outcomes in reality. For example, the thiazolidinediones lower HbA1C but appear to worsen clinical outcomes (44) Similar findings were shown in the Illuminate study in which torcetrapib was added to atorvastatin for patients at high risk for coronary events (45). The number of adverse cardiovascular events increased significantly despite a 25% decrease in LDL and a 72% increase in HDL, for the patients additionally treated with torcetrapib.

The growing interest in cost-effective use of drugs has increased the need for observational studies. It is well known that patient compliance may be as low as 50% in clinical practice and patient recruitment in randomised clinical trials is regularly skewed (46,47). Consequently, there is an urgent need for the pharmaceutical industry, regulatory agencies and healthcare providers to assess which drugs are prescribed to which patients and what are the effects in real life on morbidity, mortality and quality of life. The ecological study design used in our study has several shortcomings, but may be useful to generate hypothesis to be analysed more in depth using record linkage between exposure and outcome. In Sweden, these studies have been facilitated with the establishment of a nationwide patient identity register on dispensed prescriptions (48), and further studies are now being planned.

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