Physician Awareness of Drug Cost: A Systematic Review

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ABSTRACT

Background

Pharmaceutical costs are the fastest-growing health-care expense in most developed countries. Higher drug costs have been shown to negatively impact patient outcomes. Studies suggest that doctors have a poor understanding of pharmaceutical costs, but the data are variable and there is no consistent pattern in awareness. We designed this systematic review to investigate doctors' knowledge of the relative and absolute costs of medications and to determine the factors that influence awareness.

Methods and Findings

Our search strategy included The Cochrane Library, EconoLit, EMBASE, and MEDLINE as well as reference lists and contact with authors who had published two or more articles on the topic or who had published within 10 y of the commencement of our review. Studies were included if: either doctors, trainees (interns or residents), or medical students were surveyed; there were more than ten survey respondents; cost of pharmaceuticals was estimated; results were expressed quantitatively; there was a clear description of how authors defined "accurate estimates"; and there was a description of how the true cost was determined. Two authors reviewed each article for eligibility and extracted data independently. Cost accuracy outcomes were summarized, but data were not combined in meta-analysis because of extensive heterogeneity. Qualitative data related to physicians and drug costs were also extracted. The final analysis included 24 articles. Cost accuracy was low; 31% of estimates were within 20% or 25% of the true cost, and fewer than 50% were accurate by any definition of cost accuracy. Methodological weaknesses were common, and studies of low methodological quality showed better cost awareness. The most important factor influencing the pattern and accuracy of estimation was the true cost of therapy. High-cost drugs were estimated more accurately than inexpensive ones (74% versus 31%, Chi-square $p < 0.001$). Doctors consistently overestimated the cost of inexpensive products and underestimated the cost of expensive ones (binomial test, 89/101, $p < 0.001$). When asked, doctors indicated that they want cost information and feel it would improve their prescribing but that it is not accessible.

Conclusions

Doctors' ignorance of costs, combined with their tendency to underestimate the price of expensive drugs and overestimate the price of inexpensive ones, demonstrate a lack of appreciation of the large difference in cost between inexpensive and expensive drugs. This discrepancy in turn could have profound implications for overall drug expenditures. Much more focus is required in the education of physicians about costs and the access to cost information. Future research should focus on the accessibility and reliability of medical cost information and whether the provision of this information is used by doctors and makes a difference to physician prescribing. Additionally, future work should strive for higher methodological standards to avoid the biases we found in the current literature, including attention to the method of assessing accuracy that allows larger absolute estimation ranges for expensive drugs.

The Editors' Summary of this article follows the references.

Exhibit 1100
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Introduction

Financial constraints are a reality in almost all aspects of medicine. Pharmaceutical expenditure ranges from 8.5% to 29.6% of health-care spending within Organisation for Economic Co-operation and Development countries and is increasing faster than other areas of health-care spending in almost all these countries [1]. For example, in Canada pharmaceutical spending increased from 9.5% of total health care costs in 1985 to over 16% in 2004, and its annual growth rate has exceeded that of all health expenditures in every year in that period [2]. Most countries struggle to reduce pharmaceutical spending [3,4] as escalating costs and limited resources threaten other budgetary priorities. While the policy makers in publicly funded systems and insurance agencies struggle to cope, strategies to shift costs, in part or whole, to the consumer are unavoidable. Unfortunately, these initiatives often shift costs to other areas of health care, result in worse patient outcomes, and are not cost-effective overall [5–10]. Initiatives that have targeted doctors to reduce pharmaceutical spending include guidelines, fund-holding, and others [11–13]. One way of helping to control drug costs would be for physicians to autonomously choose the least-costly medication when there are no substantial differences in safety and effectiveness between the least and most expensive. Price variations within drug classes [14,15] or between drug classes are common, and if physicians were to choose therapeutically equivalent but less-expensive drugs, large scale savings could be realized.

In addition to budget concerns, doctors must consider drug costs to their patients. Increasing pharmaceutical costs negatively impacts patients in two ways. First, high direct expenses for those of limited resources may mean a choice between medicines and necessities such as food or clothing [16,17]. Alternatively, patients who do not take their medicine as directed or go without the potentially beneficial therapies entirely [16,17] often suffer negative health consequences [5–8,10]. Unfortunately, patients may be too embarrassed to tell their physicians when they cannot afford their medicines [18,19].

Background: Drug Costs and Patient Expenses

In the global market, the cost of drugs is highly variable and therefore obtaining accurate and relevant costs is often very complex. The situation in the United States (US) is likely the most complex, and multiple authors have attempted to distil the confusing and convoluted story of drug costs [20,21]. The often-quoted average wholesale price (the distributors' price to pharmacies) can vary due to multiple factors such as demand, recent negotiations with pharmaceutical manufacturers, and changes in coverage from large insurers. At the pharmacy, mark-up of the average wholesale price can be dramatic depending on the type of product (acute medicines have a larger mark-up) or the method of payment (cash customers often pay more). Alternatively, some high-use drugs may be marked down to draw customers in to the store. The amount the patient pays is based on his or her insurance, through private organizations such as managed care organizations and health maintenance organizations, government support (for example, Medicaid), or a combination of the above (families may have two or more providers). Insurers use a wide variety of strategies to control costs including

copayment, tiered copay (the amount of shared payment varies with different drugs), and reference pricing for drugs, to name a few. Each insurer (private or government) covers different drugs and have different copay systems (flat fees, percent copay, or a mixture of the two).

Elsewhere, the system is slightly less complex. In Canada, drug prices are believed to more closely parallel the wholesale price but are still subject to some of the variations and price competition found in the US. There is provincially based drug coverage for seniors and low-income individuals, but many provinces have some form of copay or reference -based pricing. The rest of the population pays for drugs out of pocket or has some form of insurance (which frequently has a copay component). In Europe, there are dramatic (>400%) differences in drug costs between neighboring countries [22,23]. Many countries have some elements of price competition (e.g., United Kingdom [UK] and Germany), but in some countries companies negotiated costs with regional (e.g., Spain) or federal (e.g., Italy) governments [24]. Many countries, including UK, France, Germany, Italy, The Netherlands, Spain, Finland, Denmark, and Austria, have some form of copay [3,23]. The copay systems are often added to a mix of complementary insurance (e.g., France), reference-based pricing (e.g., The Netherlands), drug budgets for physicians (e.g., UK), price control (e.g., Italy) and combinations of them all with regional variation in some countries [3]. The systems are at times irrational. For example, fixed copayments in some countries can result in patients paying more for a prescription than the actual list price of the drug [23]. Although many North Americans believe that drugs are free to patients in Europe, copayments have been shown to be a barrier for patients even in the UK [19]. Many other countries (e.g., Australia and Japan) also use a variety of copayment or cost-sharing schemes for prescriptions [24,25].

Therefore, with global budgets a concern and the welfare of patients at risk, physicians need to consider drug cost when prescribing. If physicians are going to take costs into consideration they need to be cognizant of both the absolute drug cost and the relative differences between prices of products. However, in most places cost information is not easily available for doctors and even where it is, the large difference between inexpensive and expensive equivalents is not emphasized. To determine if it is necessary to enhance both physicians' education about prices and the availability of that information, we undertook a systematic review to determine physicians' level of awareness of the cost of prescription drug products.

Methods

Templates for systematic review of survey studies are not well established, but QUOROM [26] (normally reserved for systematic reviews of randomized controlled trials) is a good guide for most systematic reviews and was used here wherever possible (Table S1).

Search

We searched the Cochrane Library (from 1966), EconLit (from 1969), EMBASE (from 1974), and MEDLINE (from 1950) up to 31 May 2005 using the search terms "physician", "doctor", "medical student", "house staff", "intern" or "resident"; "medicine", "medications", "drug", "therapeu-

tic", "test", "investigation" or "diagnostic test"; "cost" or "price"; and "knowledge", "awareness" or "understanding". The original search attempted to capture all cost awareness studies including those in which doctors estimated the costs of investigations (knowledge of the cost of investigations will be presented in another publication). The titles and abstracts, where available, were independently screened by GMA and JL and if either investigator thought that the article would be potentially eligible, a complete copy was obtained. To identify additional studies, the reference list of any potentially eligible article was searched and authors with two or more publications in the area or who had published in the 10 y preceding the start of our review were contacted.

Eligibility

Articles were included if: either doctors, trainees (interns or residents), or medical students were surveyed; there were more than ten survey respondents; costs of pharmaceuticals were estimated; results were expressed quantitatively; there was a clear description of how authors defined "accurate estimates"; and there was a clear description of how the true cost was determined. Because costs are variable and complex, we felt it was only reasonable for doctors to have knowledge of the total costs of the prescription, whether that cost was borne partially or completely by the patient and/or the insurer (private or government), in their local practice environment. Therefore, "true cost" was operationally defined as the actual cost the study authors verified from one or more locally relevant reliable sources for each drug in their study. This source would vary by location, but in the UK drug prices are more uniform so the British National Formulary would be a reasonable source, while in US quotes from local pharmacies (averaged from a broad sample) is most appropriate [21]. The definition of "accurate estimates" was taken from the authors and typically fell within a defined "accuracy range" (e.g., ±25%) around the true cost. Articles were excluded if they were not published in English or if participants were asked to estimate costs within ranges or cost increments only (for example "please estimate which $20 cost category/range is most appropriate for drug A"). GMA and JL independently assessed each potential article for eligibility. Differences in decisions about inclusion and exclusion were resolved through consensus.

Data Extraction

From each eligible article GMA and JL independently extracted the following information: publication year; study country; response rate and number of participants, sample selection method (random, entire specified population, convenience); mode of survey administration (postal, hospital mail, meeting, face-to-face); participant level of training (medical student, intern, resident, qualified doctor); specialty; number of different drugs estimated; method of ascertainment of true cost (from formulary, acquisition cost, amount billed to patient, survey of retail pharmacies, wholesale price); method of assessing accuracy of cost estimate (within a specified percent or dollar range of true cost); and estimation accuracy (percent of respondents with accurate estimate, percent above and below true cost, median percent error of estimations). Primary quality measures were method of sample selection, mode of survey administration, and response rate, as well as errors or unclear description of

calculations (e.g., incorrect method of calculating estimation error). This selection was based on our understanding of the places where the greatest biases can occur in survey studies. Where data were not reported in a way that allowed extraction in one of our categories, we attempted to calculate the information from available data (e.g., number of respondents calculated from the number of surveys distributed multiplied by the response rate). Comparisons within studies, such as differences between medical student and resident accuracy, were extracted when available. Qualitative information, such as surveys of physicians' opinions, was also extracted when available. Authors were contacted for further data where necessary. After each investigator independently extracted the above information, the results were compared and differences resolved by consensus.

Data Analysis

The studies were too diverse to pool meta-analytically (e.g., different therapies, different cost estimation procedures, different groups of physicians), but we did examine accuracies by grouping studies with nonparametric summaries. Mean accuracy (expressed as the percent of physicians who correctly estimated drug costs) for each study was calculated by averaging the accuracy from each participant group or drug estimated with weighting for the number of estimation attempts. For example, if accuracy was 30% for drug A ($n = 100$) and 50% for drug B ($n = 80$), the average accuracy would be 39% ($[(0.30 \times 100) + (0.5 \times 80)] \div 180$). We calculated nonparametric summaries (median and ranges [minimum – maximum]) for the following outcomes: average cost accuracy (within defined percent margins of error), average percent of estimates over and under true cost, average percent of estimates over and under the margins of error (as defined by the original authors) around the true costs, and average percent error (|estimate – true cost|/true cost).

Percent error is the statistic used to demonstrate the degree of estimation error. To be reliable, each estimate error (the amount above or below the true cost) must be converted to an absolute value. If it is not, high estimates will be positive numbers and low estimates will be negative numbers, and when summed will partially cancel each other giving a lower value and a false impression of accuracy. For example, if the true cost of a drug is $100 a month and two doctors estimate $50 and $150 respectively, the correct percent error would be 50%. However, if absolute values were not used, the percent error of the high estimation error would be 50% and the low would be −50%. This would make the combined percent error 0%, indicating no error in estimation and yielding a false representation of perfect accuracy.

Additionally, a priori-defined subgroups, such as year of publication (divided by median year of publication of studies), location of study, training level of participants, and specialty were examined to determine if these variables influenced the accuracy of the cost estimation. We also examined the influence of study quality on estimation accuracy by separating studies with a similar accuracy range into those of high, mid, and low quality. For this analysis, we used weaknesses of response rate (≤50% or unclear), sampling method (convenience or unclear), and survey distribution (unclear) as markers of quality. While there is no defined adequate response rate, low response rates can
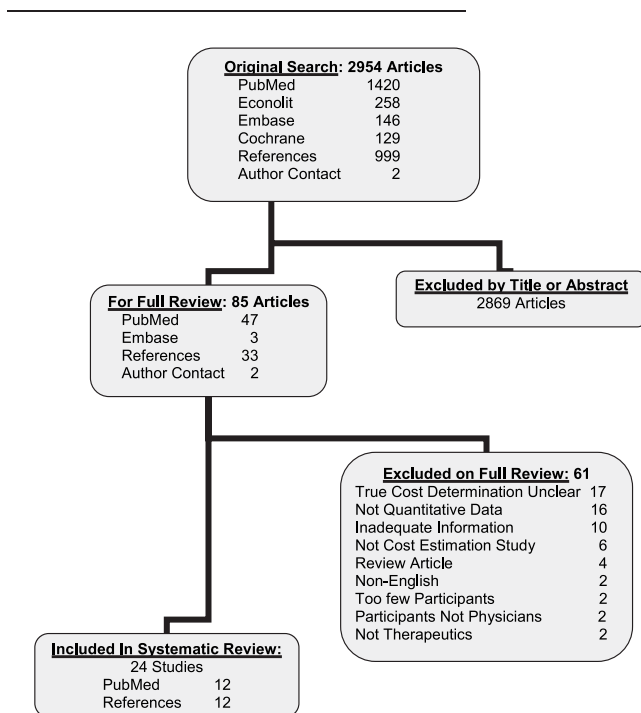
Figure 1. Study Identification and Selection Process
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bias surveys [27,28] and we felt 50% was generous. Non-probability sampling, such as convenience sampling, can bias studies because the sample is not representative of the population. Different modes of questionnaire administration have different inherent biases, and while there is no clearly superior method [29], we felt the information was important in reviewing surveys. High-quality studies had none of these weaknesses, mid-quality studies had a single weakness, and low-quality had two or more weaknesses. In post hoc analyses, where studies reported potential within-study factors influencing the accuracy of cost estimation (e.g., cost of drug), we used the binomial test to combine "votes" across studies.

We also performed two sensitivity analyses. To minimize the heterogeneity inherent to comparing studies with multiple different drugs, we compared the average cost accuracies for specific drugs common among three or more studies. When data cannot be combined and nonparametric statistics such as medians and ranges must be used, there is a concern that larger studies are weighted equally with smaller ones. To determine the potential influence of "weighting," we performed sensitivity analyses where the median nonparametric statistic was selected based on the number of therapies in each study, the number of physicians in each study, or the total number of estimates in each study.

Ethics approval was not required as the research involved publicly available material.

Results

Literature Search and Study Selection

A study flow diagram is provided in Figure 1. Eleven authors were contact to identify possible studies and six responded, to yield two previously unidentified studies. From a total of 2,954 studies, 24 were included in the systematic review (Table S2 provides the list of articles excluded after full review and the reason for exclusion). Disagreement between reviewers was rare (2% in eligibility and 6% in data extraction).

Study Characteristics

The main characteristics and methodological aspects of each study are provided in Table 1. Studies were conducted from 1978 to 2004 in six countries, with the US (nine studies), UK (eight), and Canada (four) predominating. Eleven studies included licensed physicians only, two involved house staff only, and 11 included a mixture of participants. Eight studies involved general practitioners (GPs) alone, seven specific specialists groups, six a mix, and three were unclear as to the specialty of the doctors.

Hospital-based studies in Canada, Denmark, Italy, India, and the UK defined true costs with formulary lists from the hospital [30], government formularies [31,32], wholesale costs paid by the hospital [33,34], or total cost to the hospital [35–37]. The only US study of in-hospital physicians used hospital charges as true costs [38]. Most US outpatient studies [39–45] used the averaged prices from surveys of local pharmacies to determine true costs, but one [46] used the average wholesale price. Most of the remaining outpatient studies from Canada and the UK, where price varies little from the single-payer agreed reimbursement, determined true cost from single sources such as the wholesale costs [47,48] or the British National Formulary [49–52]. One Canadian study used a pharmacy survey for outpatient prescribing and cost to the hospital for inpatient prescribing [53].

The majority of studies (79%) selected drugs based on the common drugs for that specialty. The others picked agents based on specific representative mixes of generic/branded medications [41,50–52] or based on cost impact by frequency and expense [35]. Only two studies specifically identified the percent of generics (30% [46] and 39% [52]), but it appears the proportion in studies overall was approximately 50%.

Study Quality

Quality and methodological reporting were poor in most of the studies. The method of survey distribution was unclear in seven studies, and sampling was convenience or unclear in 12 studies. The response rates were ≤ 50% or unknown in seven studies. Only seven (29%) of 24 studies [30,39,45,47,50–52] did not have any of these three weaknesses. In addition, of 12 studies attempting to quantify the degree of estimation error (for example percent error), nine used average estimations without regard for signage (that is, averaging overestimates with underestimates) or inadequately described the calculation. In total, 19 (79%) of the 24 studies had one or more of these four weaknesses, and only five trials [30,39,47,50,51] were without substantial weaknesses. There was also a large variation in study design; five methods were used to determine true costs, and reasonable accuracy was defined nine different ways.

Estimation Accuracy

Table 2 summarizes cost estimation accuracy outcomes. In general, average estimation accuracy was less than 50%, decreasing with tighter definitions of accuracy. Overestimation tended to be more frequent than underestimation, and

Table 1. Study Characteristics

Author	Publication Year	Country	Participants' Training Level	Specialty	Number of Therapies	Number Responding (Response Rate as %)	Sample Selection	Mode of Survey Administration	True Cost Determined from
Allan 1 [47]	2002	Canada	HS	GP	20	82 (85)	Entire	Meeting/mail	Wholesale
Allan 2 [48]	2004	Canada	Lic	GP	20	283 (47.2)	Random	Mail	Wholesale
Bailey [31]	1993	UK	Lic, HS	Anesthesia	15	40 (100)	Convenience	Face to face	Formulary
Beringer [39]	1984	US	Lic, HS	Neurology	39	24 (75)	Entire	Mail	Survey
Conti [30]	1998	Italy	Lic, HS	Mix	15	60 (100)	Random	Face to face	Acquisition
Dresnick [38]	1979	US	Lic, HS, MS	Mix	3	427 (ns)	Unclear	Unclear	Billing
Fairbass [33]	1988	UK	Lic	Anaesthesia	17	20 (100)	Unclear	Unclear	Acquisition/wholesale
Fink [40]	1978	US	Lic	Mix	22	114 (31.2)	Random	Mail	Survey
Glickman [41]	1994	US	Lic	Mix/GP	14	132 (80[a])	Convenience	Meeting	Survey
Innes [35]	2000	Canada	Lic	Emergency	20	75 (100)	Convenience	Face to face	Survey
Mills [34]	1993	UK	Lic	Anaesthesia	17	20 (100)	Convenience	Face to face	Wholesale
Mishra [32]	1998	India	Lic, HS	ns	6	42 (ns)	Unclear	Unclear	Wholesale
Oppenheim [42]	1981	US	Lic, HS	GP	10	152 (68.2)	Mix	Unclear	Survey
Perrine [43]	1982	US	Lic, HS	GP	15	58 (48[b])	Unclear	Unclear	Survey
Ringenberg [44]	1988	US	HS	GP	18	65 (72)	Convenience	Meeting	Survey
Rowe [49]	1986	UK	Lic, HS	Mix/GP	15	50 (100)	Unclear	Unclear	Formulary
Ryan 1 [50]	1990	UK	Lic	GP	21	281 (76.6)	Mix	Mail	Acquisition
Ryan 2 [51]	1992	UK	Lic	GP	21	244 (61)	Random	Mail	Acquisition
Safavi [45]	1992	US	Lic, HS	Mix/GP	5	188 (71)	Entire	Hospital mail	Survey
Schlunzen [36]	1999	Denmark	Lic	Anaesthesia	19	47 (92.2)	Unclear	Hospital mail	Survey
Silcock [52]	1997	UK	Lic	GP	31	627 (62.7)	Random	Mail	Formulary
Walzak [46]	1994	US	Lic, HS	Mix/GP	20	137 (50)	Random	Mail	Wholesale
Weber [53]	1986	Canada	Lic, HS, MS	Pediatrics	6	71 (90)	Unclear	Mail/face to face	Acquisition/survey
Wynick [37]	1985	UK	Lic	ns	2	82 (48)	Entire	Unclear	Acquisition

HS, house staff; Lic, licensed physicians; Mix, mixture of specialized physicians; MS, medical students; ns, not specified.
[a]Exact response rate and number surveyed not given (">80%" stated)
[b]Exact number surveyed unclear ("approximately 120") so response rate approximate.
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percent error was very large (well over 200%). In the sensitivity analyses of the most commonly used margin of error (±20% or ±25%), the number of therapies, the number of physicians, or the number of estimates from each study did not change the median cost accuracy by more 2%. This finding demonstrates that weighting would not have influenced the final result and that the median accuracy is very similar to a weighted mean if the data could have been combined.

Table 3 presents nonparametric summaries for subgroups

using the most commonly used margin of error (±20% or ±25%). Results were similar using the ±50% or 50%–200% margin of error (unpublished data). While dramatic differences were not apparent, the quality of the studies may play a role in reporting the accuracy of cost estimation. By comparison, the highest-quality studies had a median accuracy of 29% (range 16%–33%) while the lowest quality studies had a median accuracy of 38% (range 27%–45%).

There is large estimation variability within studies (percent error), and between studies accuracy varied widely (for

Table 2. Cost Accuracy Summaries

Definition	Number of Studies	Median (Range), %	References
Within ±10% or ±15%	4	15 (9–26)	[32,38,39,43]
Within ±20% or ±25%	12	31 (16–51)	[30,32,35,38,40,43,47,48,50–53]
Within ±50% or 50%–200%	9	44 (32–60)	[31,33,34,36,37,44,47–49]
Overestimation[a]	4	68 (60–86)	[33,34,47,48]
Underestimation[a]	4	32 (14–40)	[33,34,47,48]
Above 120/125%[b]	6	39 (16–49)	[32,40,50–53]
Below 75/80%[c]	6	23 (18–48)	[32,40,50–53]
Percent error[d]	3	243 (218–301)	[35,47,48]

[a]Percent of estimates over or under the true cost.
[b]Percent of estimates above the 20% or 25% acceptable margin of error around the true cost.
[c]Percent of estimates below the 20% or 25% acceptable margin of error around the true cost.
[d]Calculated as |estimate – true cost|/true cost.
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