Inappropriate Requests for Glycated Hemoglobin (HbA1c) Are Widespread: Assessment of Prevalence, Impact of National Guidance, and Practice-to-Practice Variability

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BACKGROUND: Estimates suggest that approximately 25% of requests for pathology tests are unnecessary. Even in diabetes, where international guidance provides recommended testing frequency, considerable variability in requesting practice exists. Using the diabetes marker, HbA1c, we examined (a) the prevalence of under- and overrequesting, (b) the impact of international guidance on prevalence, and (c) practice-to-practice variability.

METHODS: We examined HbA1c requests (519 664 requests from 115 730 patients; January 2001 to March 2011) processed by the Clinical Biochemistry Department, University Hospital of North Staffordshire, and calculated prevalence of requesting outside guidance from intervals between requests. Requests were classified as “appropriate,” “too soon,” or “too late.” We also assessed the effect of demographic factors and publication of guidance, along with between-practice variability, on prevalence.

RESULTS: Only 49% of requests conformed to guidance; 21% were too soon and 30% were too late. Underrequesting was more common in primary care, in female patients, in younger patients, and in patients with generally poorer control (all P < 0.001); the reverse generally was true for overrequesting. Publication of guidance (e.g., American Diabetes Association, UK National Institute for Health and Clinical Excellence) had no significant impact on under- or overrequesting rates. Prevalence of inappropriate requests varied approximately 6-fold between general practices.

CONCLUSIONS: Although overrequesting was common, underrequesting was more prevalent, potentially affecting longer-term health outcomes. National guidance appears to be an ineffective approach to changing request behavior, supporting the need for a multisystem approach to reducing variability.

Health care budgets worldwide are facing increasing pressure to reduce costs while maintaining quality. Laboratory test utilization has not escaped this pressure, particularly since pathology investigations are involved in 70%–80% of all healthcare decisions affecting diagnosis or treatment and cost the UK National Health Service (NHS),6 for example, £2.5 billion ($4 billion US) per year (representing almost 4% of total NHS expenditure) (1). Furthermore, many laboratories face an average annual increase in workload of 8%–10%.

One area of increasing importance is the management of inappropriate test requests. Many reports estimated that approximately 25% of pathology tests are unnecessary (1, 2)—and there have been higher estimates in some studies (2, 3)—representing a huge waste of resources. The Carter Review, a UK Department of Health–commissioned review of pathology services in England, acknowledges that there is “probably a similar amount of underrequesting” (1). There is little published evidence on this, possibly reflecting the difficulty in capturing such data.

The large variability in rates of test requests between general practitioners (4–7) and hospitals (8) also supports the view that inappropriate requesting is...
widespread. This is observed even in diseases such as diabetes mellitus (DM), where the American Diabetes Association (ADA) (9), the UK National Institute for Health and Clinical Excellence (NICE) (10, 11), and the Canadian Diabetes Association (12), among others, provide guidance on testing frequency. Unlocking the key to this variation and identifying the prevalence and impact of inappropriate requests, both under- and overrequesting, would have major implications for reducing patient inconvenience and allow targeting of finite health service resources to areas of known patient benefit (13).

To identify the magnitude of inappropriate requesting, we determined the prevalence of requesting outside guidance with glycohemoglobin (HbA1c) in patients with DM as a model. We also examined the impact of publication of UK and US guidance on this prevalence, with data on 519,664 HbA1c requests in 115,730 patients over a 10-year period. Using requests from primary care, we then elucidated the variability in prevalence between general practitioners.

Materials and Methods

Patients
We extracted data on all HbA1c test requests (n = 520,273) between January 2001 and March 2011 from the LabCentre Laboratory Information Management System database (Clinisys Ltd.) at the Department of Clinical Biochemistry, University Hospital of North Staffordshire NHS Trust, UK. During this period, there was little evidence (from clinical details supplied with requests) that HbA1c was being used as a diagnostic tool locally.

The data collected comprised request date, HbA1c result, anonymized patient identifier, age, sex, and requester. Data were processed in Excel 2007 (Microsoft) to remove external quality assurance–associated tests and assign requests to each unique patient ID, thereby allowing longitudinal assessment of intervals between results within individual patients. This left a core set of 519,664 requests from 115,730 patients. As expected, during the study period, new patients joined while others left the main cohort. Hence, the 115,730 comprised the patients who were included during the study period.

Definitions of Under- and OverRequesting
UK NICE guidance documents for type I and type II DM recommend HbA1c testing at 2- to 6-month intervals in patients with unstable diabetes, with a measurement made at an interval of <3 months being used as an indicator of direction of change rather than of a new steady state (10, 11). In those with stable diabetes onunchanging therapy, intervals of 6–12 months are recommended. This is reinforced in the NHS Clinical Knowledge Summaries (14). Similarly, the ADA recommends testing at least twice per year in patients who are meeting treatment goals (and who have stable glycemic control) and quarterly in patients whose therapy has changed or who are not meeting glycemic goals (9).

Further details on the guidance from these bodies is provided in Supplemental Table 1, which accompanies the online version of this article at http://www.clinchem.org/content/vol58/issue5. With an HbA1c cutoff of <7.0% (<53 mmol/mol) to define stable diabetic control, as suggested by NICE and ADA, we used the following guidance intervals to define requests as either “too soon” (overrequesting) or “too late” (underrequesting); tests requested too soon comprised those with an interval between requests of <6 months in patients with an initial HbA1c value of <7.0% and <2 months in patients with an initial HbA1c of ≥7.0%; tests requested too late comprised those requested >12 months after the previous test in patients with an initial HbA1c value of <7.0% and >6 months later in patients with an initial HbA1c of ≥7.0%. The previous HbA1c value was used to define the appropriate testing frequency for the next request. Hence, the optimum interval for each patient may have altered as their glycemic control changed over time.

Data Analysis
We analyzed data with 2 approaches. First, we calculated the most accurate estimate of the prevalence of tests requested too soon and too late from those tests requested during 2010 (the 2010 data set) by use of data from the whole study period (i.e., a 9-year run-in period). Examination of the data showed that prevalence of tests requested too late increased with increasing length of data collection (online Supplemental Fig. 1). This was expected, as some patients with larger gaps between requests are included in the too-late prevalence figure as the data collection period went on. As this estimate of prevalence reached a plateau by 9 years, it is unlikely that further extension of the data collection period would result in a significantly improved estimate. In contrast, the prevalence of tests requested too soon remained relatively stable irrespective of the length of the baseline data collection period. This again is expected, as the definition of too soon is <3 or 6 months, thereby requiring relatively short data collection periods. We also used these 2010 data to assess general practice (GP) practice-to-practice variability in prevalence of tests requested too soon and too late.

To determine whether inappropriate requesting varied at the patient level, rather than at the request level, we first used multilevel modeling using MLwiN software (version 2.22, Centre for Multi-Level Modeling, University of Bristol). This method is also available.
with Stata statistical software, version 8.0, by use of “gllam” and “xtmixed” with the “xt” commands. Models were fitted with 2 levels: requests nested within patients. Within the models, the intercept and slope were both allowed to vary at the patient level (implying a reasonable assumption of correlation between the results of laboratory tests within patients). However, no significant patient level variation was observed in any of the models fitted. Therefore, we used logistic regression models (Stata “logistic” command) at the test level; these analyses are presented in “Results.” We therefore examined the relationship between prevalence of requests too soon or too late and age, sex, requester, and degree of glycemic control by fitting logistic regression models with the Stata statistical software to obtain odds ratios and significance values.

Second, we assessed changes in prevalence over time and the impact of national guidance on a month-by-month basis from January 2003 to March 2011 with the previous 2 years as a rolling run-in period. For example, January 2003 prevalence estimates were obtained from tests requested during that month. They were identified as too soon or too late with prior data from January 2001 to December 2002 as run-in period. Although this shorter run-in period appears to consistently underestimate (by approximately 6% compared with the plateau at 9 years) overall prevalence of tests requested too late (online Supplemental Fig. 1), it does allow month-by-month assessment.

**Table 1. Prevalence of inappropriate repeat requesting for HbA1c.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total, n</th>
<th>Too late, n (%)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>Too soon, n (%)</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>54 537</td>
<td>16 291 (29.9)</td>
<td></td>
<td></td>
<td>11 614 (21.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary care</td>
<td>47 698</td>
<td>14 489 (30.4)</td>
<td>&lt;0.001</td>
<td>0.82 (0.77–0.87)</td>
<td>2330 (34.4)</td>
<td>&lt;0.001</td>
<td>2.17 (2.05–2.29)</td>
</tr>
<tr>
<td>Secondary care</td>
<td>6783</td>
<td>1783 (26.3)</td>
<td></td>
<td></td>
<td>2330 (34.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>25 706</td>
<td>7995 (31.1)</td>
<td></td>
<td></td>
<td>2330 (34.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;40 years</td>
<td>3766</td>
<td>1860 (49.4)</td>
<td>&lt;0.001</td>
<td>1.12 (1.08–1.16)</td>
<td>6003 (20.8)</td>
<td>0.005</td>
<td>1.06 (1.02–1.10)</td>
</tr>
<tr>
<td>Age ≥40 years</td>
<td>50 771</td>
<td>14 431 (28.4)</td>
<td>&lt;0.001</td>
<td>0.41 (0.38–0.44)</td>
<td>10 839 (21.4)</td>
<td>0.266</td>
<td>1.05 (0.97–1.14)</td>
</tr>
<tr>
<td>Well controlled</td>
<td>29 521</td>
<td>8099 (27.4)</td>
<td></td>
<td></td>
<td>8043 (27.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poorly controlled</td>
<td>25 016</td>
<td>8192 (32.8)</td>
<td>&lt;0.001</td>
<td>1.29 (1.24–1.34)</td>
<td>3571 (14.3)</td>
<td>&lt;0.001</td>
<td>0.44 (0.43–0.46)</td>
</tr>
</tbody>
</table>

*Significance (P), odds ratios (ORs), and 95% CIs were calculated using logistic regression.

**Results**

**PREVALENCE OF TESTS REQUESTED OUTSIDE GUIDANCE**

Examining the 2010 dataset of 65 610 requests, 11 614 (17.7%) were requested too soon (overrequests) relative to guidance and 16 291 (24.8%) were requested too late (underrequests). For the purpose of comparison with previous data (e.g., Lyon et al. (16)), we then excluded the first request in each patient (assumed to be appropriate by default), leaving a total of 54 537 repeat requests. Hence, all patients for whom only 1 test was requested were excluded from subsequent analyses. This further reduces any potential impact of diagnostic rather than monitoring requests.

Of the repeat requests, 21.3% were too soon (overrequests) relative to guidance (Table 1) which, on the basis of a HbA1c test cost of £3 ($4.80 US), would equate to £34 842 ($55 747 US) in laboratory costs alone. However, the proportion of repeat requests considered too late (underrequests) was 29.9%, equating to £46 242 ($73 987) in laboratory costs.

Table 1 also shows the effect of patient and requester factors, individually, on prevalence of inappropriate requesting. Compared with secondary care (hospital requesters), primary care (general practitioners) requested more tests too late and fewer tests too soon (both \(P < 0.001\)). However, as primary care requests constituted 87.5% of the total number of repeat requests, this group was the largest absolute contributor to tests requested outside guidance (Table 1). Tests requested too soon were more common in patients with stable diabetic control than those with poorer control (\(P < 0.001\)) (Table 1), whereas the reverse was true for tests requested too late. To illustrate the distribution of retest intervals, we then plotted the relative frequency of requesting at weekly intervals for the 2003–2011 da-
taset. These data showed prominent peaks at 3, 6, and 12 months for requests in both well- and poorly-controlled patients from general practitioners, but a less clear (and generally earlier) pattern for hospital requests (Fig. 1A, 1B).

Proportions of tests requested too soon and too late were significantly more common in female than male patients, though the absolute differences were small (reflected in relative frequency plots) (Fig. 1C, 1D). In terms of age, the data were first examined in 5-year bands, and this demonstrated a skewed distribution toward older age, as expected from the expected proportion of type I and type II DM patients (data not shown), although the actual number of type I and II patients in each age group was not known. On the basis of this examination and the shape of the distribution, we chose to dichotomize patients into groups of <40 vs ≥40 years of age. Tests requested too soon were similar in the 2 age groups; relative frequency plots, however, showed marked changes in pattern of repeat requesting with the younger age group and no discrete peaks with the over-40 age group (Fig. 1E, 1F). The older age group had significantly fewer tests requested too late ($P < 0.001$).

Overall, the group with the highest proportion of tests requested too soon comprised men age ≥40 years with well-controlled diabetes requested from secondary care (41.6%). The group with the highest proportion of tests requested too late comprised women age <40 years with poorly-controlled diabetes requested from secondary care (54.9%).

**Impact of National Guidance**

We assessed impact of guidance with the 2003–2011 data and the 2-year run-in period. Overall, the introduction of UK Diabetes National Service Frameworks, NICE guidance, the UK general practice Quality Outcomes Frameworks, and ADA guidance had no effect on requesting pattern. Furthermore, the requesting pattern from secondary care, and in younger patients, appears to be more ad hoc (with no clear pattern), highlighting these areas as requiring particular attention. Interestingly, we also observed the weekly spikes in requesting intervals described by Lyon et al. (16), confirming the tendency for phlebotomy to be performed on the same day each week within general practices (online Supplemental Fig. 2). The relative frequency plots also suggest that some patients attend for tests 1–2 weeks on either side of the guidance limits. When we reanalyzed the data to include a 2-week “grace period,” the proportions of tests requested too soon and too late were reduced slightly from 21.3% to 18.2% and from 29.9% to 27.0%, respectively. These data suggest that requesters, at least in general practice,
Fig. 1. Relative frequency plots showing the distribution of repeat request intervals in well-controlled (initial \( \text{HbA1c} < 7\% \)) and poorly controlled (initial \( \text{HbA1c} \geq 7.0\% \)) patients: primary care (A), secondary care (B), males (C), females (D), 40 years and older (E), <40 years old (F).
Fig. 1. Continued.
prefer a guide target retest interval, rather than a recommended range for repeat testing.

Our findings on overrequesting are consistent with those of Salvagno et al. (17), who showed that repeat testing within 3 months was higher in inpatients (particularly with HbA1c values of <7%) than outpatients (particularly with values of >7%), although it should be stressed that interpretation of the inpatient data with definitive cutoffs (Table 1) should be treated with caution, as illustrated by the relative frequency plots. Similarly, Akan et al. (19) showed that overrequesting was more common in inpatients than outpatients and, in the latter group, in those with HbA1c <7%. Neither study examined underrequesting or the effect of age. It also appears that this inpatient effect is not restricted to HbA1c (18). The excess in secondary care does not appear to reflect a higher prevalence of difficult-to-control patients (who may require more frequent testing) than in primary care, as the proportion of patients with HbA1c ≥7% (≥53 mmol/mol) was similar in the 2 groups (approximately 44%). The lower-than-average prevalence of tests requested too soon in younger patients mirrored the high prevalence of tests requested too late in this group. Indeed, our data showed that, in younger patients who were poorly controlled (HbA1c ≥7%), 42.2% of tests (786/1862) were too late. The reasons for this may, in part, reflect limitations in the dataset, as students who move away to further their education may have follow-up tests performed elsewhere. However, factors such as access to services for younger people and an increased proportion of type 1 patients in this group, who may be more difficult to engage with management of their condition, may also be important, as supported by the relative frequency plots. Rankin et al. (20) suggested that reasons for poor knowledge and understanding of the condition in people with type 1 diabetes included diagnosis at a young age, assumption of decision-making responsibility by parents, lack of engagement when feeling well, transitions in care, inconsistency in information provision, and lack of awareness of poor or incomplete knowledge. These factors would present health care professions with challenges in providing optimum testing in this group.

The finding that individual general practices or larger regions display large variations in number of
Fig. 3. Variability in proportion of repeat tests requested too soon (A) and too late (B) between the 87 GP practices in North Staffordshire, with the 2010 data set.
tests requested, even in well-recognized scenarios, has been suggested (4–8). Indeed, O’Kane et al. (7) have recently identified this in the context of HbA1c. However, the variability in request appropriateness has not been assessed previously. Although a range of factors including training or specialist knowledge in some practices, variation in basic medical training, patient demographics, attitudes to risk and litigation, length of local knowledge, etc., may account for some of the variability, the standardization of best practice across the healthcare community should remain a goal. Approaches to reducing this variability have been discussed elsewhere (2, 3, 13, 21) and are beyond the scope of this article. Availability of data on previous test date and result has been suggested as a tool to limit overrequesting (3, 13). In our local health economy, secondary care has had access to general practitioners’ results throughout the study period, but the converse was not always the case. In October 2009, the rollout of electronic requesting systems for general practitioners to allow their access to secondary care results began, albeit slowly. When we examined the effect of this rollout on proportion of inappropriate tests (by comparing early vs late implementers), we found surprisingly little impact (data not shown). Indeed, we are now examining ways to enhance the educational content of the electronic requesting system with a view to reducing overrequesting.

What our data clearly show is the overall lack of conformity to national guidance and the lack of effectiveness of guidance in influencing requesting behavior. In the UK, NICE guidance for both type 1 and type 2 DM suggest minimum and maximum retest intervals for HbA1c (10, 11) although, like most guidance on this subject, this guidance is often ambiguous and not well evidenced. Local guidance on testing frequency, as expressed in the UK Quality and Outcomes Framework for general practitioners, is extremely limited, focusing only on ensuring that each practice maintains a register of DM patients who have had a HbA1c test within the previous 15 months. This emphasizes the need for local incentives and feedback to underpin robust, evidence-based guidance.

Other possible reasons for underrequesting in some cases can be proposed: lack of access to primary care practices outside working hours, comorbidity in elderly patients affecting mobility, lack of awareness of guidance, etc. Similarly, patients may have tests sooner than guidance because of patient pressure, lack of awareness of the capability of the test itself, etc. (13, 21). Although some of these reasons may be justifiable, they can in no way account for the magnitude of nonconformity. Smellie et al. (22) indicated that, although guidance exists, it is often spread among a range of literature sources and directed at laboratory specialists rather than requesters. Hence, our study supports the view that inappropriate testing should be a major target for health services to reduce costs (direct and indirect) and improve quality. Importantly, as current national guidance appears ineffective, new approaches that encompass the entire local healthcare economy, use a multisystem approach, and involve both patients and requesters are required (3, 13, 21). Furthermore, laboratories need to engage with requesters in defining the minimum time interval between tests needed to identify a significant change/difference.

In addition to the limitations outlined above, our analysis may be affected by factors such as the recently advocated use of HbA1c in diagnosis, bias due to a relatively small number of atypical patients influencing intervals, the limited lead-in period for the 2010 dataset, and the difficulty in differentiating between type I and type II diabetes. To mitigate these factors, we have (a) focused on repeat tests to remove single requests and collected data before publication of the recent guidance on use of HbA1c in diagnosis, (b) performed multilevel modeling to examine whether the observations were influenced by patient-specific factors, (c) provided data on the magnitude of the underestimate of tests requested too late (online Supplemental Fig. 1), and (d) separated patients by age (although we accept this is, at best, a crude surrogate of diabetes type in the absence of more definitive data).

Whereas we recognize that the absolute prevalence of inappropriate testing estimated by our analysis will have its limitations, our data clearly show that testing outside guidance (both under- and overtesting) is a major problem. While there may be legitimate reasons for some of this, our study suggests that there is likely to be wide variation in protocols among general practitioners. Although the Carter Report is being used to focus on reducing costs associated with unnecessary overt-testing, its acknowledgement that there is probably a similar amount of underrequesting (1) is borne out by our findings. The cost implications of this, at least in terms of HbA1c testing, are likely to be substantial. Extrapolating our data to the UK national context would mean ~£5 million ($8 million US) in additional test costs alone for this 1 test. However, these costs may be offset by the potential benefits to patients and overall healthcare budgets arising from better control and reduced complications. Therefore, a more holistic approach to assessing the impact of pathology testing, taking account of the whole patient pathway, may be appropriate. Finally, it should be noted that our data are based on national retest interval guidance. The evidence base used to support these intervals is severely limited, and the potential impact on clinical outcome or patient experience of requesting patterns is currently
poorly understood. Recent data from Fu et al. (23) suggest, as expected, that testing frequency is inversely associated with diabetic control. This study suggested that the optimal testing frequency to achieve HbA1c below a target of 7% (53 mmol/mol) was 4 times per year. Turchin et al. (24) also showed that frequent HbA1c testing in DM patients resulted in shorter time to target HbA1c value, independently of confounders such as initial HbA1c value, treatment-associated factors, frequency of encounters with healthcare professionals, and patient demographics. More such data, to provide a clearer evidence base for the intervals suggested in national guidance, would be welcome.

Author Contributions: All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

References