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External quality assessment providers' services appear to more impact the immunohaematology performance of laboratories than national regulatory and economic conditions

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Abstract

Objectives: Medical laboratories may, at their own discretion, exceed but not undercut regulatory quality requirements. Available economic resources, however, may drive or hinder eagerness to exceed minimum requirements. Depending on the respective scopes of regulatory and economic framework conditions, differing levels of quality efforts to safeguard laboratory performance can be anticipated. However, this has not yet been investigated.

Methods: Immunohaematology external quality assessment (EQA) results collected by 26 EQA providers from their

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participant laboratories in 73 countries from 2004 to 2019 were evaluated. Error rates were aggregated in groups according to the respective national regulatory and economic framework conditions, to whether or not expert advice was provided in case of incorrect results, and the frequency of EQA samples.

Results: These representative data indicate no association between national regulatory (mandatory participation in EQA, monitoring of performance of individual laboratories by authorities, financial consequences of incorrect results) and economic (level of national income, share of national health expenditure) conditions to the quality performance of medical laboratories in immunohaematology. However, EQA providers' support for laboratories in the event of incorrect results appear to be associated with lower error rates, but a high EQA sample frequency with higher error rates.

Conclusions: Further research into the impact of introducing or changing services of EQA providers is needed to confirm the results found in this first of its kind study.

Keywords: economic conditions; external quality assessment (EQA); laboratory performance; legal background.

Introduction

The performance of medical laboratories is closely linked with patient safety [1]. In the last few decades, several factors have contributed to the improvement of laboratory performance. These include assay automation and standardisation, consistent use of quality controls, the implementation of effective quality assurance systems, qualification procedures for technical equipment and staff competence management. Significant achievements have been made in all these sectors [2]. The extent of these factors may be subject to external influences such as laws and regulations, performance-related financial incentives or disadvantages, national or local economic status and proportionate health expenditure. Third-party supportive services to participants, such as advice and educational feedback of external quality assessment (EQA) providers, and frequency of EQA samples per year may additionally contribute to improvement of their performance. However, the impact of these factors on laboratory performance has not been published so far.

One of the key indicators of laboratory performance is the error rate, which may be defined as the frequency of errors in a series of results [3]. Error rates provide information about the performance of the overall testing procedure in an individual laboratory [4]. The determination of reliable laboratory error rates is not easy since the detection of errors by in-process controls and by their clinical effects is not complete. A certain proportion of analytic errors remains undetected, and therefore error rates based on mistakes detected in medical routine are unreliable and tend to be too low. However, EQA programs – at least for nominal or qualitative analytes – recognise any wrong results reported by the participating laboratories. In such programs, organisers provide the participants with samples to be analysed, compare the reported results with assigned targets, and give feedback about their correctness. In addition to providing individual feedback, EQA programs or rounds are a tool to identify effects on the performance quality of conditions under which participant laboratories work. This has already been demonstrated for the impact of implementing quality systems in laboratories, automating analyses or implementing duplicate tests in immunohaematology [5, 6].

The aim of this study was to investigate the effects of the following factors on error rates in medical laboratories: (1) legal obligation to participate in EQA, (2) monitoring of laboratory performance by authorities and follow-up of corrective and preventive actions in case of incorrect results, (3) potential or actual financial consequences of EQA performance, (4) classification by national income group and (5) national health expenditure rate. In addition

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to national legal and economic influencing factors, the effect of support from EQA providers for laboratories that reported incorrect results (6) and the effect of EQA sample frequency (7) were examined. Immunohaematological tests were selected for this study because the accuracy of their nominal results can be clearly assessed, and the analytical methods used are the same worldwide. Furthermore, commutability has no effect, i.e. the sample material can be used for all test systems and the same results can be achieved [7]. In connection with blood group phenotyping errors, the question arises as to the resulting clinical implications, namely transfusion incidents caused by blood group incompatibility. We have therefore asked the International Haemovigilance Network (IHN) for a contribution on this topic in this manuscript and for country-specific comparisons of EQA error rates and laboratory error-associated transfusion incident rates.

Materials and methods

This study was performed by the specially established Immunohaematology Task and Finish Group of the European Organisation for External Quality Assurance Providers in Laboratory Medicine (EQALM) [8]. Of all national and international EQA providers known to EQALM or could be identified by the authors, a total of 26 accepted the invitation to participate in this study and contributed data including laboratories in 73 countries.

EQA programs and rounds

All red cell immunohaematology EQA programs included in this study followed the general description of EQA rounds shown in Figure 1. EQA providers distributed samples with known but undisclosed results to the participating laboratories. Depending on analytes included in distinct programs, the samples consisted of suspensions of human erythrocytes in or accompanied by human serum. Assigned targets for samples were set either by expert laboratories or by consensus of the reported results, depending on the EQA provider. Participants were instructed to carry out the examinations of EQA samples in the same manner as for routine samples. Results, and where appropriate the analytical method used for the determination, had to be reported to the EQA provider either electronically via a web portal or email, or by fax or paper. The EQA provider compared each individual result with the target assigned to the specific sample or combination of samples and adjudicated that the result was either correct or incorrect. Finally, the results of all participants were summarised in a general report for the respective round. The evaluated results and the assessment of the performance of each participant were provided in individual reports.

Data request

Regardless of the immunohaematology program portfolio of the EQA provider, the results and targets of individual rounds of ABO phenotyping and RhD phenotyping were requested. The results of individual laboratories were pseudonymised. Thus, the participating laboratories could not be identified, but all results from different rounds could be attributed to the original participant. The information requested to be provided by participant EQA provider organisations is shown in Supplementary Material 1. Classification of countries into high-, middle- and low-income countries was used as defined by World Bank [9] and national health expenditure rates were obtained from the Organisation for Economic Co-operation and Development (OECD) website [10]. It was not explored whether laboratories participated in the programs of several EQA providers.

Data management

Participating EQA provider organisations entered the results of their EQA programs in spreadsheets that were made according to a predefined proposed structure and sent to a central depository, from which they were put into an SQL database. Two possible reporting formats were employed. The first format consisted of individual results of the different parameters reported by the participant laboratories for each sample that was included in the study. The second format contained aggregated data, for which for each sample, the number of correct and incorrect results was given per parameter. Parameters included ABO phenotyping and RhD phenotyping. Data from different EQA providers were combined according to country, parameter and year of reported EQA result. Target values for each parameter for each sample were reported by the EQA providers. The data of the first, more detailed format were aggregated in order to fit them with the data of the second format. This compiled data set was stored in one table containing the number of correct and incorrect results for every included parameter and sample that was part of the database, specifying the country of origin of the laboratories, the EQA provider and the parameter. A first data filtering was performed to identify

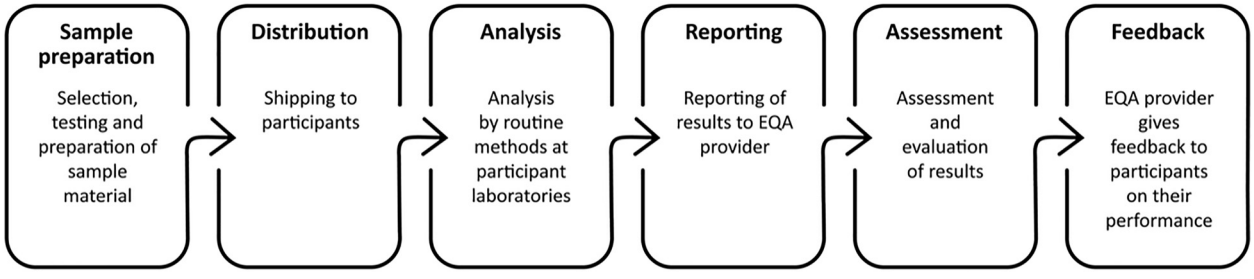

Figure 1: Schematic description of an external quality assessment (EQA) round.

"challenging" samples, which had an unexpectedly high number of incorrect results. They were excluded from further analysis. For every EQA provider and parameter, a 95% one-sided Bayesian confidence interval using a noninformative prior for the mean percentage of mistakes was calculated. Results related to samples that had a percentage of mistakes above 95% were excluded from further analysis. A second data filtering was performed by excluding data that could not be assigned to countries, e.g. reported by the respective EQA provider in a group of "other countries" or "foreign". For each parameter, only data from countries with at least 10 laboratories reporting at least 100 results were considered. A third data filtering was applied by excluding data from countries with too few data from the analysis. Data management and evaluation programs are shown in Figure 2.

The EQA-results were matched with the policy towards laboratory quality of the country where the participating laboratory was situated and practises of the EQA provider. For policy towards laboratory quality, investigated variables were legal obligation to participate in EQA, presence of binding guidelines, obligation of third-party review or financial consequences in case of bad performance. From these variables a new variable was created: mandatory EQA participation, together with third-party review and financial consequences were considered as "complete policy". If one of these criteria was not met, the policy was considered as "incomplete". In addition, the country's income level group and health expenditure rate were considered. For practises of EQA providers, it was investigated whether individual support is given to participating laboratories.

Statistical analysis

The statistical analysis was performed by matching the information of the EQA-results with country policy regarding EQA participation, country economic background and practises of the respective EQA provider. These data were extended by the rate of incorrect results found in the database of aggregated data.

In a first analysis, the country characteristics were evaluated. For income level (high vs. middle and low), presence or absence of legal obligation to participate in EQA, obligation of third-party reviews and financial consequences of bad performance, the data were each time divided into two groups and the EQA error rates were compared between the two groups. In a second instance, EQA practises were evaluated in the same way, based on the type of sample material (native or stabilised) and the presence or absence of individual support from EQA providers.

The comparison between the different groups was assessed by means of a weighted generalised linear mixed model for binary responses using a logit link with country as random variable [11]. The rates that were considered for each group were weighed, in such a sense that the results of every included country had the same influence on the percentages, regardless of the number of data that were obtained for each country. The expected error rates as predicted by the weighted generalised linear model were calculated and the p-value of the comparison between each set of two rates as well.

Since this study is an observational study, data were not present for all combinations of investigated variables. For this reason, differences were assessed in a univariate way and the error rates and differences between the groups were assessed for two different selections of the data. First, an assessment was made for all the countries with sufficient volume of data provided. These total data include data from countries with full participation of all laboratories as well as data from countries that include only an unknown proportion of the laboratories. The overall data were compared with the subset from countries with full laboratory representation.

Results

A total of 26 EQA providers participated in this study and provided data from 73 countries. Of these, 18 contributed individual results of all their pseudonymised participants, and eight provided aggregated summaries of individual rounds. For reasons of data privacy, no country-specific error rates are disclosed in this report. Participant EQA provider organisations, their characteristics and the data volume provided are shown in Supplementary Material 2. The volume of data available for each country is shown in Supplementary Material 3.

After data cleansing, a total of 756,369 results from analyses of laboratories in 36 countries remained for evaluation. Characteristics of these countries are shown in Supplementary Material 4. They included 387,527 results of ABO phenotyping and 368,842 of RhD phenotyping. In order to investigate whether there were different error rates between countries where all or only some of the laboratories were represented, the data from 15 countries in which all resident laboratories are represented were also evaluated as a subset. These included 120,940 results of ABO phenotyping and 116,316 of RhD phenotyping.

Obligation to participate in EQA

When all results from eligible countries are considered, more errors were found for ABO and RhD phenotyping in countries where there is a legal obligation for participation in EQA (1.4% vs. 0.32%, p=0.4428 for ABO phenotyping; 0.49% vs. 0.46%, p<0.0001 for RhD phenotyping). When looking only at data from countries that included all resident laboratories, significantly less ABO and RhD phenotyping mistakes were recorded in countries with a legal obligation to participate in EQA (0.34% vs. 0.52%, p<0.0001 for ABO phenotyping; 0.38% vs. 0.58%, p<0.0001 for RhD phenotyping). For details see Table 1.

Authorities monitoring the performance or notified of poor performance

In countries with a third-party monitoring of laboratory performance by authorities, ABO and RhD phenotyping

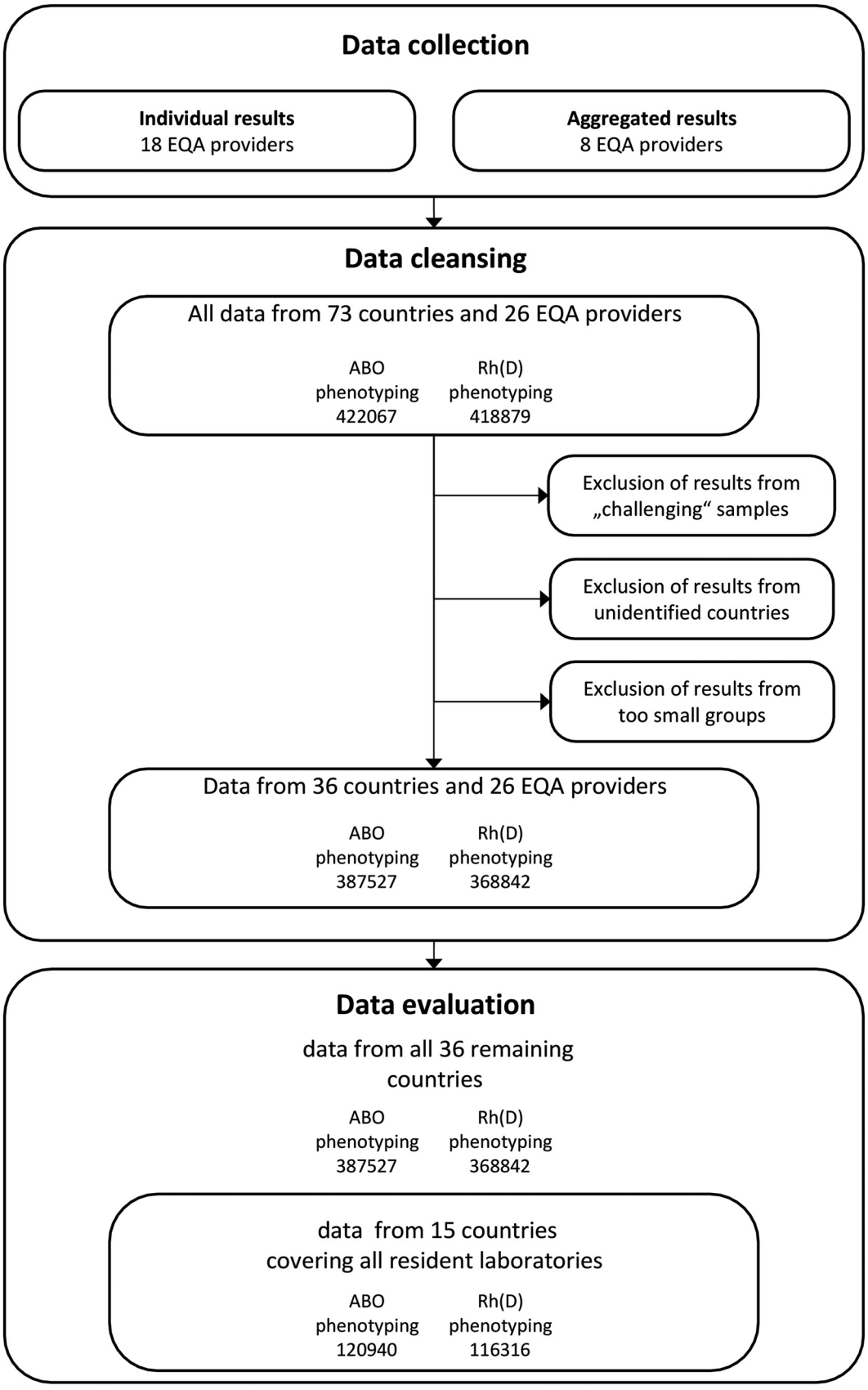

Figure 2: Data management and evaluation scheme of external quality assessment (EQA) rounds.

Table 1: National regulatory conditions concerning EQA participation and their relation to error rates in immunohaematology EQA.

		Results from all 36 eligible countries		Subset of results from 15 countries including all resident laboratories	
		ABO phenotyping	RhD phenotyping	ABO phenotyping	RhD phenotyping
Obligation to participate in EQA	Yes	1.4 (129,717; 18)	0.49 (139,262; 18)	0.34 (42,054; 7)	0.38 (48,886; 7)
	No	0.32 (245,188; 11)	0.46 (230,189; 11)	0.52 (68,831; 7)	0.58 (68,897; 7)
	p-value	0.4428	<0.0001	<0.0001	<0.0001
Verification of participation by authoritative third-party or reporting of incorrect results	Yes	2.02 (177,732; 10)	0.58 (171,223; 10)	0.41 (33,475; 4)	0.48 (40,270; 4)
	No	0.36 (197,173; 19)	0.43 (198,228; 19)	0.44 (77,410; 10)	0.48 (77,513; 10)
	p-value	<0.0001	0.0299	0.5067	0.8746
(Potential) Financial consequences of incorrect results	Yes	2.34 (93,859; 8)	0.63 (102,900; 8)	0.48 (14,394; 3)	0.68 (21,660; 3)
	No	0.36 (283,534; 22)	0.42 (266,551; 21)	0.42 (96,491; 11)	0.43 (96,123; 11)
	p-value	<0.0001	0.0219	0.2311	<0.0001
Policy (complete = all three above, incomplete = less than three above)	Complete	2.59 (91,371; 7)	0.66 (100,412; 7)	0.13 (11,919; 2)	0.60 (19,186; 2)
	Incomplete	0.36 (283,534; 22)	0.42 (269,039; 22)	0.48 (98,966; 12)	0.46 (98,597; 12)
	p-value	0.2067	0.8985	<0.0001	0.0166

Data represent results from all participant countries (left) and from those countries that include all resident laboratories (right). Numbers before brackets are percentages of incorrect results, numbers between brackets are the number of results and the number of countries from which percentages were calculated. The total of 36 or 15 countries will not be reached if the respective information was not available for all countries. EQA, external quality assessment.

showed worse performance in data from all eligible countries (2.02% vs. 0.36%, p<0.0001 for ABO phenotyping; 0.58% vs. 0.43%, p=0.0299). When looking at data from countries including all resident laboratories, no significant difference was found for any of the parameters (0.41% vs. 0.44% for ABO phenotyping, p=0.5067; 0.48% vs. 0.48% for RhD phenotyping, p=0.8746). For details see Table 1.

Financial consequences of incorrect results

When the data from all eligible countries are considered, there were more ABO (2.34% vs. 0.36%, p<0.0001) and RhD phenotyping (0.63% vs. 0.42%, p=0.0219) mistakes observed in the countries with financial consequences of incorrect results in EQA. In data from countries including all resident laboratories, countries with financial consequences had slightly more mistakes in ABO and significantly more mistakes in RhD phenotyping (for ABO phenotyping 0.48% vs. 0.42%, p=0.2311, for RhD phenotyping 0.68% vs. 0.43%, p<0.0001). For details see Table 1.

Combination “complete policy”

The combination “complete policy” includes obligation to participate in EQA, verification of participation or notification of authorities about incorrect results and (at least potential) financial consequences of poor EQA performance. When the data from all eligible countries are considered, no significant differences were found (2.59% vs. 0.36%, p=0.2067 for ABO phenotyping, 0.66% vs. 0.42% for RhD phenotyping, p=0.8985). When only data from countries including all resident laboratories are considered, fewer mistakes were observed for ABO phenotyping in countries with complete policy (0.13% vs. 0.48%, p<0.0001), while in contrast, for RhD phenotyping, more mistakes were observed (0.60% vs. 0.46%, p=0.0166). For details see Table 1.

Income Group by World Bank List of Economies

When all data from all eligible countries are considered, significant differences were found for ABO and RhD phenotyping. For ABO testing, low- and middle-income countries showed significantly fewer mistakes (1.04% vs. 0.51%, p<0.0001), in contrast to their higher RhD phenotyping error rates (0.45% vs. 0.76%, p<0.0001). In data from countries including all resident laboratories, higher rates of incorrect ABO and RhD phenotyping results were observed for low- and middle-income countries (0.3% vs. 1.06%, p<0.0001 for ABO phenotyping; 0.43% vs. 0.56%, p=0.022 for RhD phenotyping). For details see Table 2.

National health expenditure

Countries with the highest health expenditure recorded fewer mistakes in EQA testing for ABO phenotyping, which

Table 2: National economic conditions and their relation to error rates in immunohaematology EQA.

		Results from all 36 eligible countries		Subset of results from 15 countries including all resident laboratories	
		ABO phenotyping	RhD phenotyping	ABO phenotyping	RhD phenotyping
Income Group by World Bank List of Economies	High	1.04 (190,456; 26)	0.45 (202,801; 26)	0.3 (104,153; 13)	0.43 (113,708; 13)
	Low-middle	0.51 (189,669; 9)	0.76 (173,602; 9)	1.06 (9,357; 2)	0.56 (8,542; 2)
	p-value	<0.0001	<0.0001	<0.0001	0.022
National health expenditure (% of GDP)	≥10	0.22 (126,727; 10)	0.67 (134,759; 10)	0.24 (48,075; 5)	0.56 (54,375; 5)
	<10	1.31 (185,174; 19)	0.57 (188,523; 19)	0.46 (62,750; 8)	0.39 (65,209; 8)
	p-value	<0.0001	0.0473	<0.0001	<0.0001

Data represent results from all participant countries (left) and from those countries that include all resident laboratories (right). Numbers before brackets are percentages of incorrect, numbers between brackets are the number of results and the number of countries that were taken into account for the calculation. The total of 36 or 15 countries will not be reached if the respective information was not available for all countries. EQA, external quality assessment.

held true irrespective of the mode of analysis (all eligible countries 0.22% vs. 1.31%, p<0.0001; countries including data from all resident laboratories 0.24% vs. 0.46%, p<0.0001). In contrast, for RhD phenotyping, significantly more mistakes were observed for the countries with the highest health expenditure, irrespective of the mode of analysis (0.67% vs. 0.57%, p=0.0473 for all eligible countries; 0.56% vs. 0.39%, p<0.0001 for countries including data from all resident laboratories; Table 2).

Individual support for incorrect results

When all data are considered, individual EQA provider's support was associated with significantly fewer mistakes in ABO (0.59% vs. 0.94%, p=0.0016) and fewer mistakes in RhD phenotyping (0.39% vs. 0.57%, p=0.2042). For data representing all laboratories in the respective countries, fewer ABO and RhD phenotyping errors were seen when individual support for incorrect results was given (0.03% vs. 0.5%, p<0.0001 for ABO phenotyping; 0.4% vs. 0.46%, p=0.1512 for RhD phenotyping). For details see Table 3.

Frequency of samples

When all data are considered, a frequency of more than eight samples per year was associated with more mistakes in ABO (1.29% vs. 0.48%, p=0.0266) and less mistakes in RhD phenotyping (0.54% vs. 0.55%, p<0.0001). For data representing all laboratories in the respective countries, more ABO and RhD phenotyping errors were seen when

Table 3: EQA provider's services and their relation to error rates in immunohaematology EQA.

		Results from all 36 eligible countries		Subset of results from 15 countries including all resident laboratories	
		ABO phenotyping	RhD phenotyping	ABO phenotyping	RhD phenotyping
Individual support	Yes	0.59 (84,154; 9)	0.39 (74,156; 8)	0.03 (13,310; 3)	0.4 (19,682; 3)
	No	0.94 (295,971; 34)	0.57 (302,247; 34)	0.5 (100,200; 12)	0.46 (102,568; 12)
	p-value	0.0016	0.2042	<0.0001	0.1512
Frequency (samples per year)	>8 (high)	1.29 (213,334; 25)	0.54 (216,896; 25)	0.61 (29,635; 3)	0.54 (30,319; 3)
	≤8 (low)	0.48 (166,791; 26)	0.55 (159,507; 26)	0.35 (83,875; 12)	0.43 (91,931; 12)
	p-value	0.0266	<0.0001	<0.0001	0.0183

Data represent results from all participant EQA providers (left), and from those EQA providers that include all resident laboratories (right). Numbers before brackets are percentages of incorrect results, numbers between brackets are the number of results and the number of countries that were taken into account for the percentages. If they are served by more than one EQA provider, countries can appear in both the "yes" and "no" or the ">6" and "≤6" groups, and therefore the counts of countries exceed the total of 36 eligible countries. EQA, external quality assessment.

sample frequency was >8 per year (0.61% vs. 0.35%, p<0.0001 for ABO phenotyping; 0.54% vs. 0.43%, p=0.0183 for RhD phenotyping). For details see Table 3.

Immunohaematology EQA error rates and transfusion incident prevalence

Data collected by the IHN in the International Surveillance of Transfusion-Associated Reactions (ISTARE) database includes the total number of reported ABO-incompatible transfusions [12]. This data shows that most ABO-incompatible transfusions are caused by non-laboratory errors, like misidentification of the recipient, and that laboratory phenotyping errors cause less than 1% of all reported adverse transfusion incidents. The absolute numbers of those events are in the single-digit range and therefore a statistical evaluation and a comparison with error rates in immunohaematology EQA are not possible. See Supplementary Material 5.

Discussion

The aim of this study was to identify factors that can contribute to a reduction of the error rates in medical laboratories and thus to an improvement of laboratory quality performance. In summary, the error rates in ABO and RhD phenotyping examined in this study are low and the differences between the groups of countries analysed are small, even though some differences are statistically significant.

None of the national regulatory conditions examined (legally required participation in EQA, monitoring of laboratories' EQA performance by authorities, and potential financial consequences of poor performance) was associated with lower error rates. The combination of all three factors showed no clear, but even contradictory results for error rates in ABO and RhD phenotyping. Although there is no data from before and after a change in the legal framework in a country, we nonetheless conclude that the influence of the national legal framework on the laboratory performance shown in error rates in immunohaematology EQA seems to be lower than expected. The macroeconomic framework and national health expenditure also seem to have no influence on the error rates. The only factors that appear to be consistently associated with slightly lower error rates are the EQA provider's advisory services for those laboratories that reported incorrect results, and a frequency of EQA samples of eight or less per year. To validate these assumptions, comparisons of data before and after implementation of supportive counselling for participants who reported incorrect results and change in sample frequency would be needed.

EQA data are an excellent tool for objectively assessing factors that affect quality performance of medical laboratories. Their weakness, however, is that verification of proper conduct of analyses corresponding to routine examinations is impossible. It cannot be excluded that in order to achieve correct results, laboratories deviate from routine procedures when analysing EQA samples. This can include repetition of analyses, the use of other test systems than in routine, analysis by particularly experienced technicians, but also cross-checking of results with other laboratories prior to result submission. Furthermore, unavoidable deviations from routine procedures for EQA sample handling and analysis can be additional sources of errors. These include inadvertently swapping EQA samples and transcription or transmission errors of EQA-results, as in laboratory routine, samples often are processed automatically, and results are transmitted electronically without human intervention where possible. Therefore, EQA error rates may not exactly reproduce the actual error rate of a single laboratory or a group of laboratories, but they are still useful for inter-laboratory comparison and, consequently, for assessing external factors to which laboratories are exposed. A limitation of this study is that we cannot directly demonstrate the impact of external factors examined here on the performance quality of laboratories, as no data is available before and after a change in regulatory or economic conditions. Another limitation is that it has not yet been clarified whether the effects on results in immunohaematology EQA also apply to other analytical methods.

We presented the results of a first retrospective investigation into associations between national legal and economic conditions and the performance of medical laboratories in immunohaematology EQA. Further prospective and controlled investigations are required to validate the findings that the advisory services of the EQA provider in the event of incorrect results have positive effects on the error rates and in contrast, a higher EQA sample frequency has a negative effect, and whether the findings shown for immunohaematology also apply to other laboratory analyses.

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