Trends and outlook for clinical diagnostics testing

Results from a global survey of diagnostics laboratories

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Summary

Clinical diagnostic tests have traditionally involved antibody-based recognition of proteins or disease markers, but these immunoassays are prone to both false negative and false positive results, and cannot detect numerous disease markers in one test. In recent years there has been growing interest in using more accurate, efficient and reliable technologies such as mass spectrometry. Despite the important scientific advantages of such technologies, many clinical diagnostics scientists have continued to use traditional immunoassays, due to perceived barriers such as the need for investment and expertise in mass spectrometry (MS) technologies. This report describes the results of a recent independent survey of clinical diagnostics scientists worldwide. The survey explored respondents' current diagnostic assays, instrument and reagent usage; conference attendance; purchasing behaviours and future technology needs. Key findings from the survey showed that the majority of respondents still use immunoassay-based diagnostics and around one third use liquid chromatography with tandem mass spectrometry (LC-MS/MS). There was broad awareness of MS techniques, with a greater proportion intending to purchase MS platforms rather than immunoanalyzers over the next 12 months. However, the majority of respondents said they did not fully understand the concepts or have expert knowledge of MS technologies, despite using these technologies in their labs. Therefore there is an urgent need for improved understanding of MS in clinical labs, so that more scientists can adopt these technologies for more accurate and confident diagnostics.

Introduction

Clinical diagnostics tests are carried out in hospital laboratories, Physician Office Labs and CLIA Labs (or equivalent European labs) worldwide, through analysis of human blood and other tissue samples. These *in vitro* diagnostic (IVD) tests are typically carried out to detect wide-ranging diseases and conditions such as cystic fibrosis, metabolic disorders and vitamin D deficiency, and to monitor levels of drugs in patients, including therapeutic drugs and immunosuppressants, as well as drugs of abuse. For many years, clinical scientists have used immunoassays such as ELISAs (enzyme-linked immunosorbent assays) for diagnostics. More recently, however, there has been growing concern about the accuracy of immunoassays for diagnostics. In particular, immunoassays are susceptible to interference that can lead to both false negative and false positive results, which can have serious impacts on patient care as well as increasing costs and labor burdens for health authorities[1-3]. Immunoassays can also show variation in results, between labs using the same assays as well as between different assays[4]. Furthermore, immunoassays are not always able to detect certain metabolites or can even over-estimate their levels, which can complicate diagnosis of conditions such as vitamin D deficiency that depend on accurate detection of both the vitamin D_2 and D_3 25-OH metabolites[5].

These concerns have driven the development of alternative testing methods based on mass spectrometry techniques, which offer higher accuracy and robustness than immunoassays. Liquid chromatography with tandem mass spectrometry (LC-MS/MS) is particularly powerful for high-resolution separation, identification and quantitation of proteins and peptides, even at very low levels of expression. LC-MS/MS methods are also very versatile and can be developed rapidly for the analyte of interest; moreover numerous proteins can be detected and quantified in a single run, saving considerably on precious samples, as well as time, labor and reagent costs. These benefits for diagnostics are clear, but clinical laboratories have been slow to adopt LC-MS/MS. Part of the reluctance to switch technologies may be attributed to a traditional perception that only mass spectrometry experts could run the instruments and analyse results. Accordingly, instrument providers have made a number of developments to improve the simplicity, ease-of-use and robustness of LC-MS/MS systems in recent years. These include the introduction of *in vitro* diagnostic (IVD) MS analyzers and reagents kits that have been CE marked to the European *in vitro* diagnostics Directive (98/79/EC), and registration of the MS analyzers as general medical devices in other selected countries around the world. These products are developed specifically to be safe and effective for routine clinical diagnostics laboratories, and designed to bring down costs by delivering accurate, rapid and reliable results.

In order to determine the extent to which clinical diagnostics laboratories are using immunoassays or alternative technologies, an independent survey was conducted among clinical scientists worldwide. The survey aimed to find out what assay technologies are currently used, which diagnostic assay types are most commonly carried out, and the immediate and future needs for improved assays and assay technologies. The survey also explored respondents' future plans to invest in new technologies and how and where they keep up to date with scientific developments and new product information.

Method

The survey was carried out through an anonymous web-based questionnaire, conducted independently by Texere Publishing and delivered to clinical diagnostics scientists worldwide.

The survey was fielded for three weeks (3-24 March 2015) and collected 266 qualified surveys that served as the basis for this report. The margin of error for the full set of data is ±6.0% at the 95% confidence level.

Results

Demographics

Of the 266 qualified respondents, 71% were located in Europe and 21% in North America; the remaining 8% were located in India (2%) and other regions including Australia, New Zealand, Singapore and South America.

Respondents' job positions are shown in Table 1. The majority of respondents (73%) stated that they are involved in the purchasing process for their laboratory, with either final approval on purchases, shared approval on purchases, or having influence on purchasing decisions.

Just over half of respondents (57%) were based in hospital labs, and 23% were in university or research laboratories. The remainder were in Government (8%), private testing (7%), and other types including biotech or pharma.

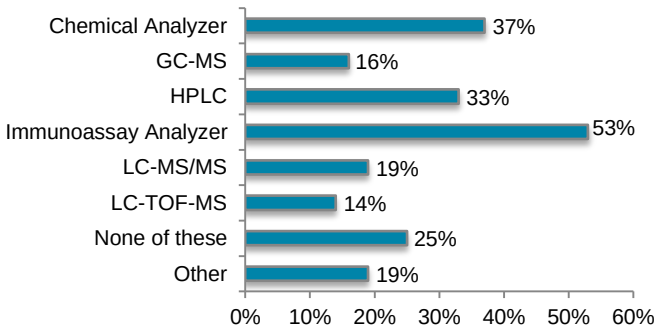
Table 1. Responses to the question, "What is your role?"

Primary job function	Percentage of respondents
Laboratory manager/director	31%
Clinical/biomedical scientist	22%
Medical doctor	19%
Research scientist	16%
Student	4%
Laboratory technician	3%
Administration	1%
Other	4%

Clinical diagnostics technologies

When asked what analytical instruments are currently used in their laboratory (see Fig 1), more than half of the respondents (53%) selected immunoassay analyzers. Chemical analyzers and HPLC systems were checked by 37% and 33% of respondents, respectively. Mass spectrometry-based technologies were used less often, with LC-MS/MS used by 19%, GC-MS by 16% and LC-TOF-MS by 14% of respondents. One quarter of respondents said they did not use any of these analytical instruments. Almost one fifth (19%) of respondents selected 'other' and supplied fill-in responses that included DNA sequencers, flow cytometers, haematology analyzers and MALDI-TOF systems.

Figure 1. Current use of analytical instruments in diagnostics laboratories.

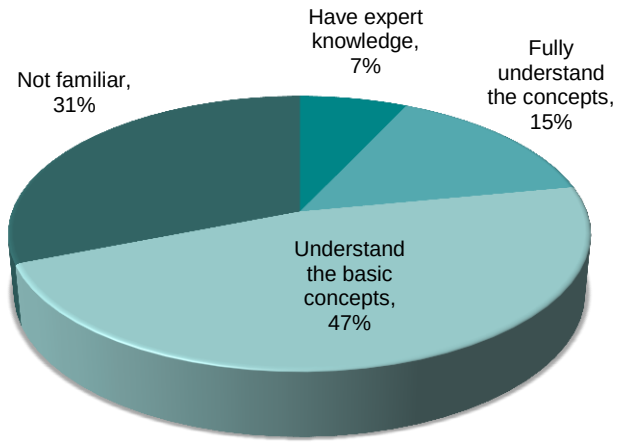


Bar chart showing the frequency of responses to the question, "What analytical instruments are currently used in your laboratory? Please check all that apply".

However, when respondents were asked about their plans to purchase instruments over the next 12 to 18 months, MS systems were selected on a much higher frequency than chemical analyzers and immunoassay analyzers.

This would indicate a growing interest in and use of mass spectrometry-based technologies, particularly LC-MS/MS; 35% of respondents said their laboratories currently have LC-MS/MS technologies. Despite this, respondents showed a lack of confidence in their understanding of clinical mass spectrometry (Fig 2). Just under half (47%) said that they understood the basic concepts of mass spectrometry and 31% said they were not familiar with the technique. Only 15% claimed to fully understand the concepts and 7% said they have expert knowledge of clinical mass spectrometry.

Figure 2. Familiarity with mass spectrometry.



Pie chart showing respondents' agreement with the question, "How familiar are you with clinical mass spectrometry?".

Mass spectrometry sample preparation and reagents

Almost one half (45%) of the respondents indicated that their laboratories develop their own "homebrew" tests (or laboratory-developed tests, LDTs) for clinical mass spectrometry. However, 39% agreed that fully validated and appropriately registered or CE-marked IVD reagent kits are valuable for mass spectrometry and only 3% said such kits are not at all valuable.

*Types of assays performed**

Respondents were presented with a list of six commonly used diagnostic assay types and asked to indicate which they currently use in their labs (Table 2). The most widely used was 25-OH Vitamin D, followed by therapeutic drug monitoring. Approximately one third of respondents used assays for detecting drugs of abuse and immunosuppressant drugs. Steroid profiles and newborn screening assays were less widely used. 'Other' was selected by 31% of respondents and fill-in responses included hormone assays, antibody-based assays and genetic tests.

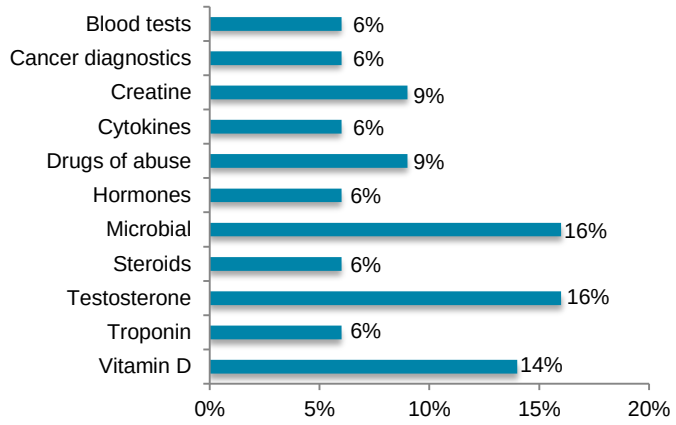
Table 2. Commonly used diagnostic assays

Types of assays used by respondents
Vitamin D
Therapeutic drug monitoring
Immunosuppressant drugs
Drugs of abuse
Steroids
Newborn screening assays
Hormone assays
Genetic tests

Needs for improvements in diagnostic assays

Respondents were asked to state which current diagnostic assays need to be improved. The most common types of assays that were mentioned were microbial (16%), testosterone (16%) and vitamin D (14%) assays (Fig 3).

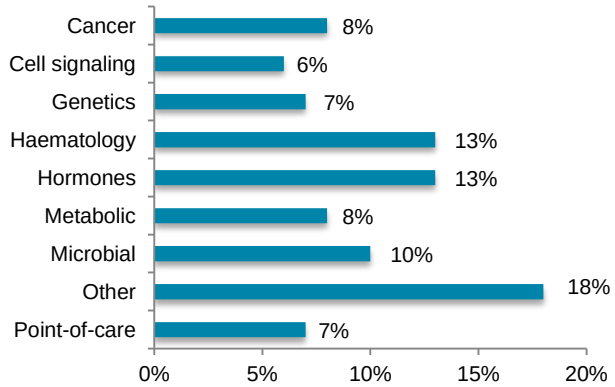
Figure 3. Current diagnostic assays that need to be improved.



Bar chart showing the categories of topics that were mentioned in response to the open-answer question, "What current diagnostic assays or immunoassays need to be improved?".

When asked about the need for new diagnostic assays over the next five years (Fig 4), respondents most commonly mentioned the need for application development (17%), such as integrated assays and MALDI-TOF. The needs for new haematology assays and hormone assays were each mentioned by 13% of respondents.

Figure 4. New diagnostic assays that are needed.



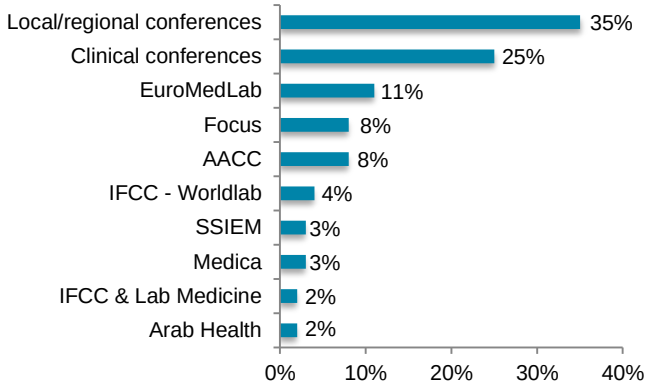
Bar chart showing the categories or topics that were mentioned in response to the open-answer question, "What new diagnostic assays are most needed in the next five years?"

Keeping up-to-date with scientific developments and new products

The majority of survey respondents (81%) had attended one or more scientific conferences in the past two years; local or regional conferences were attended most often (35%), and 25% of respondents had attended clinical conferences in the past two years (Fig 5).

When asked about their preferred sources for new product information, just over half of respondents selected articles in scientific publications (52%) and 51% checked scientific conferences. Information from other people was commonly cited, with information from co-workers and colleagues selected by 45%, and information from sales representatives by 30% (see Table 3).

Figure 5. Top 10 conferences attended in the past two years



Bar chart showing responses to the question, "Which of the following conferences have you attended in the past two years? Please check all that apply".

Table 3. Responses to the question, "Which of the following do you most rely on for new product information? Please check up to three".

Information source	Percentage of respondents
Articles in scientific publications (print or online)	52%
Scientific conferences	51%
Information from co-workers & colleagues	45%
Sales representatives	30%
Product reviews	20%
Product demonstrations in your lab	20%
Supplier websites	19%
e-Newsletters	15%
Catalogs mailed to your lab	11%
Print advertisements in journals	11%
Webinars	10%
Direct mail	7%
Buyers' guides (print or online)	5%
Print newsletters	5%
Social media sites/online forums	5%
Blogs	3%
Online videos	3%
White papers	3%

Discussion and conclusions

Patients around the world depend on clinical laboratories to provide accurate data to assist doctors in the diagnosis of their conditions and manage their treatment regimes with accuracy and confidence. The ever-expanding global population, evolving diseases and modern-day demands for instant access to information are placing increasing burdens on clinical diagnostics laboratories. For over a decade, evidence has accumulated to show that traditional diagnostic immunoassays are prone to inaccurate results, giving misleading patient test results and increasing the labor and cost burden for healthcare providers[3].

Rapid advances in technologies such as LC-MS/MS have brought accurate, robust and cost-efficient alternatives for clinical diagnostics. Our recent survey of 266 clinical diagnostics laboratories worldwide found that over one third of clinical diagnostics laboratories currently have LC-MS/MS technologies, but only one fifth of respondents use LC-MS/MS for clinical diagnostics assays, compared with more than half that are using immunoassay analyzers. This suggests that clinical scientists are still reluctant to adopt LC-MS/MS for clinical diagnostics, despite the proven benefits of this more accurate approach for laboratories, healthcare and, most importantly, for patients. Reasons for this reluctance to switch could be due to habit and fear of change, but respondents appear to welcome new developments; they cited a number of assay types that they feel need to be improved or newly developed in the near future. The majority of respondents also keep up-to-date with scientific and new product developments within the industry. Results from this survey suggest that perceived lack of confidence or training in mass spectrometry technologies is a significant hurdle for clinical scientists. Approximately one third of respondents said they were not familiar with clinical mass spectrometry technologies. Just under one half said they understood the basic concepts but only 7% of respondents felt they were experts.

However, a high number of respondents said that their laboratories planned to invest in new mass spec technologies for clinical diagnostics during the next 12 months. In contrast, under 7% plan to purchase an immunoassay analyzer during the next 12 months. This indicates growing interest and intention to switch towards clinical mass spectrometry methods, but the scientists' apparent lack of confidence in their own understanding of mass spectrometry clearly needs to be addressed.

Instrumentation vendors have taken significant steps to improve matters, for example with the introduction of specially developed, LC-MS/MS analyzers which are CE-marked for in vitro diagnostic use for the European market (or appropriately registered medical devices for other regions) that are designed to be simple for non-mass spec experts to use. Other developments have included availability of reagent kits which are CE-marked for in vitro diagnostic use for the European market (or appropriately registered medical devices for other regions) that are designed for use in conjunction with analyzers; nearly 40% of survey respondents agreed these are valuable for clinical diagnostics. There remains an urgent need for improved understanding and adoption of clinical mass spectrometry among clinical diagnostics laboratories, so that laboratories can perform diagnostic tests with confidence, delivering accurate results to patients, faster and more cost-effectively.

*SCIEX does not claim to offer IVD products for all applications referenced in this report. For a full listing of our IVD products and their availability, please refer to our website: www.sciexdiagnostics.com. Not available in all countries.

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