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OECD

The Supply of Medical Radioisotopes

An Assessment of Long-term Global Demand for Technetium-99m

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NUCLEAR ENERGY AGENCY
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Foreword

At the request of its member countries, the OECD Nuclear Energy Agency (NEA) became involved in global efforts to ensure a reliable supply of Molybdenum-99 (^{99}Mo) and its decay product, Technetium-99m (^{99m}Tc), the most widely used medical radioisotope. The NEA established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) in 2009 to examine the underlying reasons for the shortage and to develop a policy approach to ensure their long-term security of supply. The main objective of the HLG-MR is to strengthen the reliability of ^{99}Mo and ^{99m}Tc supply in the short, medium and long term.

The HLG-MR recognised that understanding the future demand of ^{99}Mo/^{99m}Tc is essential when discussing the need for new ^{99}Mo producing reactors and related infrastructure, especially given the required level of investment. Decision makers need to have information to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile.

However, there are many uncertainties as to what the demand forecast should be now given the shortages of these isotopes seen in 2009-2010 and the associated changes in the use of ^{99m}Tc that occurred during the shortages. In addition, there are other external factors at play that serve to change historical demand, such as changing reimbursement rate policies in key markets or increasing wealth in emerging markets. It is important to understand these factors and their long-term effects on the demand for ^{99m}Tc and ^{99}Mo.

As a result of the uncertainty and the lack of a long-term comprehensive demand overview that includes recent changes in the supply chain, the HLG-MR sought to better understand future demand for ^{99}Mo/^{99m}Tc and related nuclear medicine procedures.

The HLG-MR, working with the Technopolis Group, undertook a study to develop a future demand scenario for ^{99m}Tc, recognising differences in mature and emerging markets and building on available studies. As part of the project, an expert advisory group (EAG) was created and a global survey was conducted. The EAG consisted of nine experts (see Appendix A) with an in-depth understanding of medical imaging and from diverse geographical and experience backgrounds.

This report provides the findings and analysis of the data obtained from a global on-line survey, which sought to understand future demand for ^{99m}Tc and diagnostic imaging out to 2020 and 2030. The analysis of the data enabled the EAG, Technopolis and the NEA to develop the future demand scenario provided in this report.

Acknowledgements

This report would not have been possible without the input from medical professionals from around the world. The basic data for the report came from a global survey. The survey was distributed globally by many medical, radiological, and nuclear medicine associations. Over 700 individuals in the field from 52 countries responded to the survey.

The overall future ^{99m}Tc demand study was supported by an Expert Advisory Group (see Appendix A for a list of members) and by the Technopolis Group. This support included the development and distribution of the survey, and the analysis and evaluation of the data obtained from the survey.

The NEA appreciates the participation and efforts of all these individuals and organisations.

This report was developed by Jon van Til, Ingeborg Meijer, and Marijn Kieft of the Technopolis Group and Chad Westmacott of the NEA Nuclear Development Division. Detailed review and comments were provided by the Expert Advisory Group (EAG) and the NEA High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR).

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Executive Summary

Understanding future demand

Understanding the future demand of Molybdenum-99 (^{99}Mo)/Technetium-99m (^{99m}Tc) is essential when discussing the need for new ^{99}Mo-producing reactors and related infrastructure, especially given the required level of investment. Decision makers need to have information to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile.

However, there are many uncertainties as to what the demand forecast should be now given the shortages of these isotopes seen in 2009-2010 and the associated changes in the use of ^{99m}Tc that occurred during the shortages. In addition, there are other external factors at play that serve to change historical demand, such as changing reimbursement rate policies in key markets or increasing wealth in emerging markets. It is important to understand these factors and their long-term effects on the demand for ^{99m}Tc and ^{99}Mo. As a result, the OECD Nuclear Energy Agency's High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) sought to better understand future demand for ^{99}Mo/^{99m}Tc and related nuclear medicine procedures.

NEA future ^{99m}Tc demand study

The HLG-MR, working with the Technopolis group, undertook a study to develop a future demand scenario for ^{99m}Tc, recognising differences in mature and emerging markets and building on available studies. As part of the project, an expert advisory group (EAG) was created and a global survey was conducted (713 responses from 52 different countries). The EAG analysed the data from the survey and, with Technopolis and the NEA, developed a future demand scenario for 2020 and 2030. The HLG-MR verified the findings and the developed demand scenario.

Even though projecting out to 2030 seems long, and therefore reliability less certain, the time horizon forces respondents to think beyond the life span of existing research reactors for radioisotopes. The study is meant to provide an indication of direction and degree of changes in demand in a timeframe that would be meaningful for new ^{99}Mo-producing infrastructure (e.g. research reactors and processing facilities). Given the uncertainty that exists when looking out so far into the future, the results should be taken as indicative of long-term trends and not as absolute figures.

Expectations on the future of diagnostic imaging

The majority of respondents expect a growth in the total number of imaging procedures (all types). Overall, the respondents expect the total number of imaging procedures to increase by about 35% by 2020 and to 50% by 2030, when compared to the current use. This assumes an average annual growth rate of between 1.1% and 3.0%[1].

Deviations from the average expectations on the future use of diagnostic imaging are to be observed between emerging and mature markets. On average, respondents from the emerging markets expect a much larger growth – 50% by 2020 and 70% by 2030 compared to 35% and 50% in mature

[1] Average annual growth rates: 2020: 3.0% followed by annual growth of 1.1% between 2020 and 2030; when assuming linear growth up from 2010 to 2020 and 2020 to 2030.

markets. However, the results from the emerging markets show more extreme variations (both positive and negative) – the standard deviation is higher.

Expectations on the future demand of ^{99m}Tc

Based on responses from the survey, the expected growth of ^{99m}Tc-based procedures (see Table E1) is lower than the expected growth of diagnostic imaging procedures in general. The results showed no observed bias based on the speciality of the respondent. The Expert Advisory Group endorsed the results presented in the Table.

Table E1: Expected ^{99m}Tc demand growth*

	Mid-term average	Long-term average	Annual growth** 2010-2020	Annual growth 2020-2030
Mature markets	~ +20%	~ +25%	~ +1.8%	~ +0.4%
Emerging markets	~ +40%	~ +50%	~ +3.4%	~ +0.6%
Global market	~ +23%	~ +28%	~ +2.1%	~ +0.5%

* Mature markets consist of Europe, North America, Japan, the Republic of Korea and Oceania; emerging ^{99m}Tc markets consist of South America, Africa and Asia (without Japan and the Republic of Korea). Emerging markets currently represent about 15% of the global market.

** It should be noted that the survey questions focused on the time points 2020 and 2030, therefore the actual growth path to those dates is uncertain. It is possible (and likely) that growth is not linear.

Expectations with regard to substitution of ^{99m}Tc modalities

One factor potentially affecting the growth of ^{99m}Tc/^{99}Mo is the development and growth of alternative imaging modalities, such as PET and combined modalities such as PET/CT or PET/MRI. Substitution of ^{99m}Tc is expected to grow over time: by 2020 11% of the respondents expect that greater than 25% of ^{99m}Tc-based procedures will be substituted by other modalities; by 2030 27% of the respondents expect a substitution of greater than 25% of procedures. However, this substitution will likely come in the form of growth of alternative modalities replacing some growth of ^{99m}Tc-based SPECT imaging.

In terms of modalities that are expected to replace ^{99m}Tc-based imaging, respondents expect that PET/CT will probably grow the most and PET/MRI and MRI will experience a relative growth in the longer term. Respondents did not expect that SPECT using an alternative isotope would replace the use of ^{99m}Tc.

Perceptions on stability and coping strategies

Stability of supply

The majority of respondents (~90%) indicated that they have suffered from the recent ^{99m}Tc shortages. These effects were most notable in Asian countries and least experienced in Oceania. However, even with this experience, over 60% of all respondents still expect that the ^{99m}Tc supply will be stable. Interestingly, the expected stability increases over time: for the period 2021-2030 more people expect the supply to be relatively stable. This assumes a growth of the supply capacity of ^{99m}Tc.

Coping strategies

One potential impact of the current shortage on future demand is that many supply chain participants have worked to improve their processes and logistical arrangements to minimise product loss, and have implemented demand management practices to use the available product in the most efficient way possible. In addition, there are a number of advances in cameras and software that promise significant reductions in the use of ^{99m}Tc per dose from current practices.

Survey respondents indicated that efficient patient scheduling and reduction of doses were the most applied strategies for dealing with the shortages, however respondents indicated that most of the changes would not be permanent. Of the changes seen, more efficient elution from generators and more efficient patient scheduling are the more permanent; the latter has turned to routine in 12% of the cases where it was used during the shortage.

These results may be changed in the future if there is pressure from tightening reimbursement rates or increased costs; for example, better use of generators may result in cost savings. However, expectations today are that the majority of changes have or will return to pre-shortage practices.

Determinants of change

Expectations of surveyed experts

Apart from strategies to cope with the shortages in ^{99m}Tc, there are more general drivers that can influence future demand. Respondents felt that the top drivers that increased demand are availability of ^{99m}Tc, improved technology and more efficient use. Both growing wealth and lower costs of ^{99m}Tc-based imaging were also identified as potential demand increasers. The importance of the last two drivers comes partly from the current situation that ^{99m}Tc-based procedures are much cheaper (by as much as ten times) than PET-based imaging.

Changes in cost are also perceived as a relevant driver for decreased demand. If the cost of ^{99m}Tc-based procedures increases in the future, this could drive a shift towards the more expensive PET-based procedures. The first and second drivers for decreased demand are the development of alternative imaging modalities in general and of new radiopharmaceuticals for PET in particular.

In relation to the demand impact of changing costs, the survey asked respondents how they see price influencing their choice. Responses indicate that ^{99m}Tc demand appears to be quite inelastic – meaning that changes in price have smaller changes in the overall demand of the product. However, the results should be treated with care, as a more elaborate study would be required to accurately determine the price elasticity of ^{99m}Tc demand.

Global trends

Drawing from the results of the global survey, the EAG analysed in more detail some key drivers that represent a wider trend, establishing the potential impact of these trends on the future ^{99m}Tc demand and the probability of the impact occurring, in order to validate the survey results.

Trend 1: Growing population, urbanisation and wealth increases

The EAG indicated that growing global population is expected to lead to an increase in diagnostic imaging, assuming that access to medical care will not decrease. This growth could have a significant impact in emerging ^{99m}Tc markets, given that they already represent an important share of the global population.

Growing population coincides with a growing urbanisation and increasing growth of wealth in low and middle-income countries (World Bank, 2006). Urbanisation generally indicates increased development and growing wealth; however, it is expected that mature markets have already seen the greatest impacts of urbanisation and growing wealth while emerging markets will be most affected by this trend. Therefore urbanisation and growing wealth are expected to have a high positive impact on ^{99m}Tc demand in emerging markets, while mature markets would see a low increase.

The EAG did caution that in mature markets this increase in demand for diagnostic tests may also support substitution to new modalities in the long run; however building infrastructure for PET imaging is much more expensive and complicated than ^{99m}Tc-based imaging (see Trend 4).

Trend 2: Ageing population and changing prevalence of medical conditions

This second trend focuses on the medical consequences of demographic change. Coupling the effect of ageing populations in mature markets with effective healthcare systems means that one could expect an increased need for patient care as an ageing population will likely see increased prevalence of cancer or cardiac diseases and a corresponding increase in treatment. The EAG expects a medium positive impact in the mature markets on ^{99m}Tc demand, with a medium to high probability.

In emerging markets, ageing is not such a challenge as yet, leading to the expectations of a low impact at first (with high probability). However, looking at 2030, the emerging markets' younger populations will have aged and therefore it is expected that there will be a large impact in the long run. By 2030, both ageing and wealth will likely have increased significantly in emerging economies. Consequently, more imaging procedures can be expected, driving an increase in demand for ^{99m}Tc.

Trend 3: Availability of cameras

Use of ^{99m}Tc depends on cameras for imaging. In general, one could assume that sales of cameras serves as a proxy for demand for radiopharmaceuticals – the more cameras available, the more sales will be seen in the related radiopharmaceuticals.

The view of the EAG is that SPECT cameras are not being replaced by PET cameras but rather by a new SPECT or SPECT/CT. In some key emerging markets, the sales of PET cameras are declining because the market seems to be saturated – at least until replacements after the first life cycle. At the same time, there currently is growth in SPECT/CT cameras, which is mainly the replacement of older SPECT cameras.

Key considerations related to the expectation of ongoing availability and demand for SPECT cameras are:

- The costs for PET cameras are substantially higher than for SPECT cameras and second hand SPECT cameras are also available, and even cheaper. It is expected that cardiac PET cameras will remain expensive for some time.

- PET cameras typically operate with tracers with a very short half-life and to be economically viable, a cyclotron needs to be serving four to five PET scanners. This can be a barrier in more remote and rural areas.

- It takes time to increase the availability of cameras, provide training and develop the necessary medical infrastructure.

As a result, the EAG expects that the availability of SPECT cameras will result in a high increase in demand for ^{99m}Tc in emerging markets. The cost impact will be important as SPECT is still the cheapest option and emerging markets (as well as mature markets) are trying to manage the costs of health care. Given uncertainties about the long-term changes, the expected high increase remains for 2030, but with less certainty about the expectation.

For mature markets, the EAG expects an ongoing medium growth impact on the use of ^{99m}Tc, but with certainty of this expectation at only a medium level. One key point that leads to additional uncertainty on the impact is that as new SPECT cameras are installed, they will likely be more efficient and thus lead to reduced demand for ^{99m}Tc for the same number of procedures.

Trend 4: SPECT/PET shift

One of the major issues in the discussions on future demand of ^{99m}Tc is whether PET will substitute for ^{99m}Tc-based procedures. More than 75% of the survey respondents expect that PET and combined PET modalities will eventually be more dominant and will replace SPECT procedures.

The EAG believes that PET modalities will substitute for some SPECT procedures between now and 2020/2030, although the level of substitution is expected to be low. Although this expectation is slightly contrary to the survey results, the EAG recognised that a key uncertainty is related to the timing and pace of substitution; therefore substitution may occur, but may be at a slower pace than predicted by the survey respondents. In addition, they felt that there are a number of factors that would prohibit or hinder the substitution of SPECT procedures by other modalities in the next decade or so, especially in emerging markets:

- SPECT infrastructure and procedures are generally much cheaper than PET infrastructure and procedures.

- PET based infrastructure requires a larger team at the hospital or clinic compared to SPECT infrastructure.

- A large SPECT installed base and much experience compared to the smaller PET installed base means less experience with the technology and the need for more education and training to move to PET.

- There are only a few PET radiopharmaceuticals approved for use, and the EAG indicated that the development and approval process of new radiopharmaceuticals is difficult and expensive.

- Not all the current SPECT procedures can be replaced by currently available PET radiopharmaceuticals.

- SPECT provides high quality scans, so there is not an obvious incentive for a quick replacement with other PET procedures.

The EAG did recognise that the medical community is looking towards PET and other modalities for the future. However, it is expected that these alternative modalities will more likely supplement current SPECT procedures by moving into different areas, but not directly replacing SPECT. In addition, the EAG recognised that some of the PET growth will capture the expected growth in overall diagnostic imaging, meaning that SPECT will have a smaller share of the overall market, but will not see an overall decline in absolute terms.

However, the EAG indicates significant uncertainty around this prediction as there are a number of factors that could impact the substitutability of modalities. All it takes is one paradigm shift and the system could completely change. For example, an ongoing unstable supply of ^{99m}Tc could increase the pace toward technology substitution. If new PET-based radiopharmaceuticals come onto the market or if there is a breakthrough in the costs of PET infrastructure, there could be a significant substitution of SPECT.

Taken these issues together, substitution of SPECT by PET would have a negative effect on ^{99m}Tc demand, but the impact is expected to be low; however with great uncertainty.

Trend 5: New radiopharmaceuticals

As indicated by the respondents, the development of new radiopharmaceuticals for PET for studies that are currently done by SPECT cameras could have a significant negative impact on ^{99m}Tc demand. This expectation is partly based on the fact that there has not been any development of new radiopharmaceuticals based on ^{99m}Tc, while there has been a lot of attention given to the development of new PET tracers.

However, the actual uptake of new radiopharmaceuticals could be quite limited as health regulatory approvals take time and are seen to be quite difficult. Taking a radiopharmaceutical to the market reportedly takes up to EUR 15 million in investment and not many players are willing to take such a risk. In addition, in some jurisdictions it is difficult to get new radiopharmaceuticals approved for reimbursement through health care systems, supporting the ongoing use of ^{99m}Tc-based radiopharmaceuticals that have already been approved.

The EAG expects a negative impact of new (PET) radiopharmaceuticals on ^{99m}Tc demand, having a medium probability up to 2020, which is related mainly to a cardiac PET tracer that could come to market. In the long run, the development of new PET-based radiopharmaceuticals would significantly reduce demand for ^{99m}Tc in mature markets; however, there is still significant uncertainty on whether new radiopharmaceuticals will actually be developed and approved. In emerging markets, the effect of new radiopharmaceuticals is expected to have less of a negative impact on ^{99m}Tc demand between now and 2030 as mature markets are expected to lead the development of new radiopharmaceuticals, with emerging markets picking up the product later.

Demand scenario

Key results

The results from the survey and the views of the Expert Advisory Group have allowed for an educated analysis of the long-term future demand for ^{99m}Tc. The EAG analysis of the key drivers of change has validated the survey results, recognising the significant uncertainty when discussing future demand almost 20 years out.

The key findings are that:

- The pace of change away from ^{99m}Tc is expected to be slow and before 2030 there will not be substitution at such a level to actually reduce ^{99m}Tc demand.

- Other external factors potentially affecting ^{99m}Tc demand will slow historical growth rates, but will not remove its overall demand.

- The majority of the actions taken during the 2009-2010 shortages will not be permanent. There are some cases where more efficient elution from the generator and more efficient patient scheduling may remain.

- The EAG endorsed the results of the survey, and found it probable that ^{99m}Tc demand will grow as shown in Table E1.

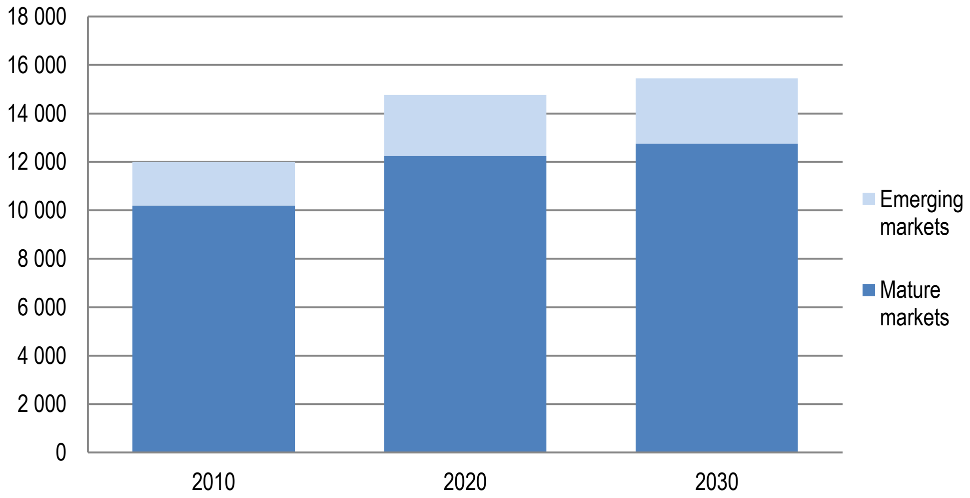
- Unexpected changes of any kind could have a large effect on demand, especially if changes take place in jurisdictions where demand is currently large (i.e. Europe and North-America). For example, the EAG recognised the importance of costs of ^{99m}Tc and emphasised that reimbursement rates for ^{99m}Tc-based procedures and competing imaging modalities could play a crucial role.

Scenario of ^{99}Mo demand

The original purpose of the overall project was to understand the impacts of future demand on the need for new ^{99}Mo-producing infrastructure. From the results, it is clear that there will be ongoing demand for ^{99m}Tc at least until 2030, with continued, albeit slow, growth.

Given that global ^{99m}Tc supply comes from ^{99}Mo produced in research reactors, we can derive a reasonable idea of the expected future need for ^{99}Mo from our results. Based on a global demand for ^{99}Mo for ^{99m}Tc production of approximately 12 000 6-day curies per week (levels demanded prior to the 2009-2010 shortages), the following table shows the forecasted demand of ^{99}Mo for 2020 and 2030.

Figure E1: Forecasted ^{99}Mo Demand per week



Conclusions

The results from the survey and the EAG analysis has provided a better understanding of the possible long-term effects of changes in the demand and use of ^{99m}Tc, resulting in an expected steady growth of ^{99m}Tc demand, albeit at a slow pace. Demand is expected to grow faster in emerging markets, but from a smaller base. The results show that substitution of ^{99m}Tc-based procedures by alternative modalities or isotopes will likely have an impact on the overall share of ^{99m}Tc in diagnostic procedures, but will not reduce the absolute amount of ^{99m}Tc being demanded.

This forecast for ^{99m}Tc growth translates reasonably well to a similar situation for ^{99}Mo demand. If the changes seen during the 2009-2010 shortage related to efficient use of ^{99m}Tc were predicted to continue, there would have been a greater impact on ^{99}Mo demanded. However, survey results indicate that most of the pre-shortage practices were returned to after the shortages ended. Based on these results, it is reasonable to predict that ^{99}Mo demand will continue to grow at levels equal to approximately two percent annually until 2020 and then levelling off to a growth rate of less than one percent annually until 2030.

1. Introduction

1.1 Background to the study

The OECD Nuclear Energy Agency (NEA) with the assistance of the Technopolis Group has carried out a forecasting exercise to assess the future demand of technetium-99m (^{99m}Tc), which is used in approximately 80% of all nuclear medicine diagnostic procedures globally, and its parent isotope molybdenum-99 (^{99}Mo). Molybdenum-99 is produced predominately from irradiation of uranium targets in nuclear research reactors.

Understanding the future demand of $^{99}Mo/^{99m}Tc$ is essential when discussing the need for new ^{99}Mo-producing reactors and related infrastructure, especially given the required level of investment. Decision makers need to have information on future $^{99}Mo/^{99m}Tc$ demand to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile. Forward-looking studies can retrieve strategic knowledge that provides insight that can be used to anticipate and respond in a timely manner to developments that have yet to take place. This is particularly important for problems that may have far-reaching consequences and a large time span before solutions may be realised.

Any study of the future is plagued by uncertainty; most forward-looking studies therefore start with one of the many famous quotes on how hard it is to predict the future. We need to make a similar claim: while looking into the future is easy – we do so all the time – making robust predictions of the future is hard. Often unexpected minor events can have large effects on the course of history. Moreover, the further ahead you look, the greater the level of uncertainty. In this study, which looks out to 2030, this is shown by the divergence in the expectations of experts when the timespan of their predictions increases.

There are different ways to study the future; up until now, many studies at a global level took past growth and extrapolated this growth to the future. In the past, this type of forecast has proven to be quite adequate, but recent shortages in the supply of $^{99}Mo/^{99m}Tc$ has shown that small events – such as corrosion in a reactor – may have large impacts on the use of ^{99m}Tc. Extrapolations may overlook trends that may impact the demand for ^{99m}Tc dramatically.

There are many trends that may change the demand for ^{99m}Tc; some are to be expected, such as the development of alternative imaging modalities and isotopes that could potentially replace or reduce the demand for ^{99m}Tc. At the same time, there are some trends such as aging populations and the potential for increased use in emerging economies that could serve to drive the demand upward. The overall impacts of these trends on ^{99m}Tc demand are yet unknown and uncertain, especially in the long-term. In addition, many important changes may occur in key determinants of demand for ^{99m}Tc such as changes in reimbursement rates in key markets.

There is currently a significant degree of uncertainty in the industry about the future of $^{99}Mo/^{99m}Tc$ with some supply chain participants expecting continued or increasing growth, while others predict demand rising to a saturation point then levelling off, and others predicting a decrease in demand. As a result of the uncertainty and the lack of a long-term comprehensive global demand overview that includes recent changes in the supply chain, the NEA and its High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) sought to better understand future demand for $^{99}Mo/^{99m}Tc$ and related nuclear medicine procedures.

The main aim of this report is thus to gain insight on the expectations on the future use of $^{99}Mo/^{99m}Tc$ by its current users. We looked at the determinants of change in the use of $^{99}Mo/^{99m}Tc$ and the assessments of the current users of their future use. This facilitated the development of a scenario of the future demand for $^{99}Mo/^{99m}Tc$ that can be used for strategic decision making on the supply and infrastructure needs for $^{99}Mo/^{99m}Tc$.

1.2 Approach

This study is part of an action plan defined by the HLG-MR, aimed at developing future demand scenarios for ^{99m}Tc, recognising differences in mature and emerging markets and building on available studies. The process consisted of three phases:

- Phase 1: Creation of an expert advisory group (EAG, see Appendix A) consisting of nine experts with an in-depth understanding of medical imaging, and from diverse geographical and experience backgrounds.

- Phase 2: Development and implementation of a global on-line survey to obtain data to increase understanding of future demand for medical imaging, various imaging modalities[2] and ^{99m}Tc. The EAG helped to ensure the usefulness and completeness of the questions and provided contact data to spread the survey globally to as many medical-imaging and user communities as possible. Data was collected from the survey in the period January-March 2011.

- Phase 3: Assessment, verification, and communication of collected data, including a workshop with the EAG on 5 April 2011, in Paris.

- Phase 4: Drafting of a survey report, which is validated by the EAG.

This background report provides a comprehensive overview of the results of the survey. An executive report is included in the HLG-MR final report (NEA, 2011) as a chapter, presenting the concise results of the study.

1.3 Justification

Forward-looking exercises often consist of a range of methods, including iterative consultation rounds, interviews, surveys, etc. Two components are at the core of this study: a forecast, based on expert-consultation through interviews and survey; and a review of the results by the HLG-MR. The importance of forecasting is that it retrieves knowledge that can be used to anticipate and respond in a timely manner to developments that have yet to take place, but have a reasonable probability of occurring. This is particularly important for problems that may have far-reaching consequences and a large timespan before solutions may be realised. In the case of the medical radioisotope ^{99m}Tc, shortages could cause great difficulties that would take years to remedy. The main difficulty is the reduction of diagnostic procedures in clinics, for instance for cardiovascular diagnostics, oncology, bone scans, etc.

In this forecast study the future timespan of 2020 and 2030 has been chosen. Even though projecting out to 2030 seems long, and therefore the reliability is less certain, the 2030 time horizon forces respondents to think beyond the life span of existing research reactors for radioisotopes. The study is meant to provide an indication of the direction and the degree of changes in demand in a timeframe that would be meaningful for new ^{99}Mo-producing infrastructure (e.g., research reactors

[2] i.e. types of imaging techniques and technologies from both nuclear imaging as radiology, thus including X-ray, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and single-photon emission computed tomography (SPECT).

and processing facilities). Given the uncertainty that exists when looking out so far into the future, the results should be taken as indicative of long-term trends and not as absolute figures.

The forecast study has a global focus. This has implications for the way in which the survey was spread and for the response rates from the different countries. Results from one jurisdiction cannot simply be extrapolated to other jurisdictions as the access to and availability of the various imaging technologies may differ between countries in different parts of the world. As a result, survey questions were focused on the respondent's national situation, reflecting the assumption that respondents may not be able to accurately comment on demand and use in other jurisdictions.

The survey was developed for response by imaging specialists, nuclear medicine experts, as well as referring physicians. Even though there were many different types of specialists who answered the survey, respondents were predominantly nuclear medicine experts, as they had the most relevant knowledge on expected future use.

1.4 Structure of this report

The report starts with a presentation of the survey results. Section 2.1 provides basic information on the sample of the survey. Section 2.2 subsequently presents the expectations of these respondents on the future of diagnostic imaging in general, the future demand for ^{99m}Tc and on substitution by other modalities. Section 2.3 focuses on the issue of recent issues with supply and strategies to cope with a hampered ^{99m}Tc-supply. In Section 2.4 we explore the possible determinants that could lead to an increasing or decreasing use of ^{99m}Tc. Based on previous sections, Chapter 3 presents a scenario of future demand for ^{99m}Tc and ^{99}Mo. Finally, Chapter 4 presents the conclusions of our study.

All sections that presents survey data (Section 2.2.1-2.4.2) end with a summary of the results presented.

2. Survey Results

2.1 Information on response sample

The survey consisted of 15 questions in an online questionnaire (see Appendix B). It was distributed globally through official medical professional organisations and professional contacts of the EAG and the HLG-MR. The survey obtained 713 responses from 52 different countries (see Appendix C). From these, almost 50% came from North America (United States and Canada); more than one-third from Europe and the remaining responses (96) from the rest of the world (see Figure 1). Even though the response was not high in the rest of the world, it does reflect the actual use of ^{99m}Tc, which is highest in North America and Europe.

Figure 1: Geographical spread of respondents – 49 responses were undefined

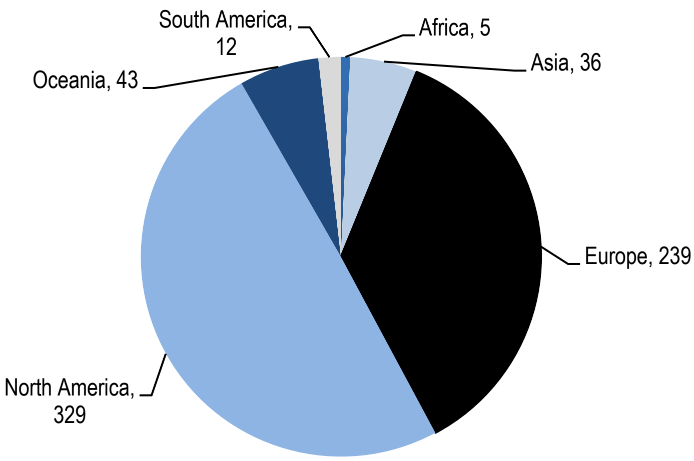
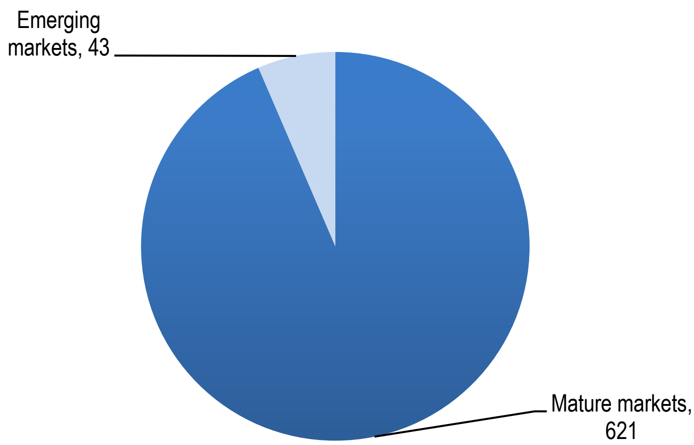


Figure 2: Distribution of respondents in the categories *mature* versus *emerging markets – 49 responses were undefined**



* Mature markets include: Japan, the Republic of Korea, Turkey, Europe, Oceania and North America; emerging markets include: Africa, Asia (except Japan and the Republic of Korea) and South America.

With regard to future demand of $^{99}Mo/^{99m}Tc$ it is important to make a distinction between emerging and mature markets for ^{99m}Tc. The Expert panel stressed that the mature markets are not likely to show important growth-rate shifts, whereas emerging markets are much less predictable. In emerging markets spectacular growth is possible and even expected. We thus identified two different samples based on geographical spread and the maturity of ^{99m}Tc markets, i.e. *mature* versus *emerging markets*. The mature markets consist of Europe, North America, Japan, Korea and Oceania. The responses in South America, Africa and Asia (without Japan and Korea) are considered as emerging markets. In the following sections, the emerging markets opinions are derived from 6% of the respondents (Figure 2).

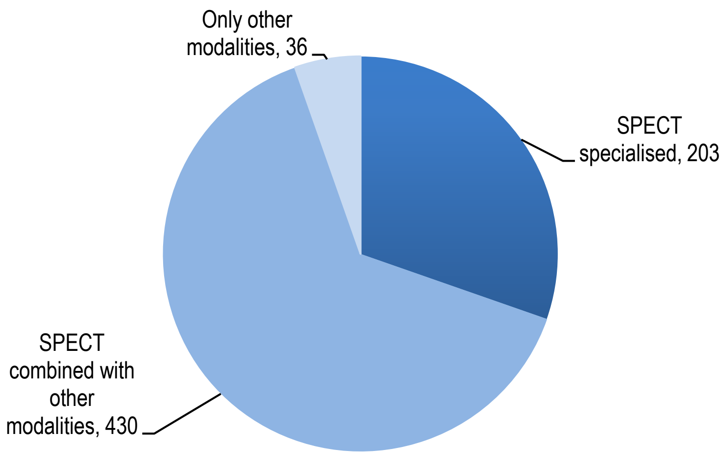
The professional background of the respondents is dominated (40%) by medical doctors that are imaging specialists using nuclear medicine, which rises to 60% if we add the nuclear medicine technologists to the 'nuclear medicine' group (see Appendix D). The remaining 40% have a diverse professional background, including radiologists, cardiologists, oncologists, internists, pharmacists, medical physicists and others.

The descriptor "nuclear medicine background" does not discriminate between ^{99m}Tc-based modalities (conventional planar and SPECT modalities) and PET modalities. Therefore we also asked respondents to identify their specific expertise (^{99m}Tc-based, PET-based, or other expertise). To deal with a potential bias within the sample, we have discriminated between expertise. It can be argued that experts relying on ^{99m}Tc-based modalities in their daily practice may be more positive about the future demand for ^{99m}Tc. Therefore, we made a distinction between backgrounds of the experts. We have asked respondents for their expertise, making distinctions between expertise:

- in ^{99m}Tc-based modalities only – the SPECT-only category;
- in a range of diagnostic imaging modalities – the SPECT-combined category;
- in other modalities or imaging in general, with no specific expertise of ^{99m}Tc-base modalities – the 'Other' category.

Almost 90% of respondents have expertise with ^{99m}Tc based imaging modalities. Of these, one-third has expertise in ^{99m}Tc-based modalities only, while almost two thirds has combined expertise. A group of 36 respondents (5%) has no SPECT or PET expertise: they only work with other modalities (see Appendix D for more detail).

Figure 3: Distribution of expertises in the sample



This section showed the distribution of the different respondent groups divided on basis of geography (continents), maturity of markets, professional background and expertise. In the analysis of expectations of the experts in the survey, we additionally analysed responses on basis of the following respondent groups:

- continents (Asia, Europe, North America, South America, Oceania);
- ^{99m}Tc market maturity (mature and emerging markets);
- or expertise (SPECT-only, SPECT-combined and Other);

when appropriate.

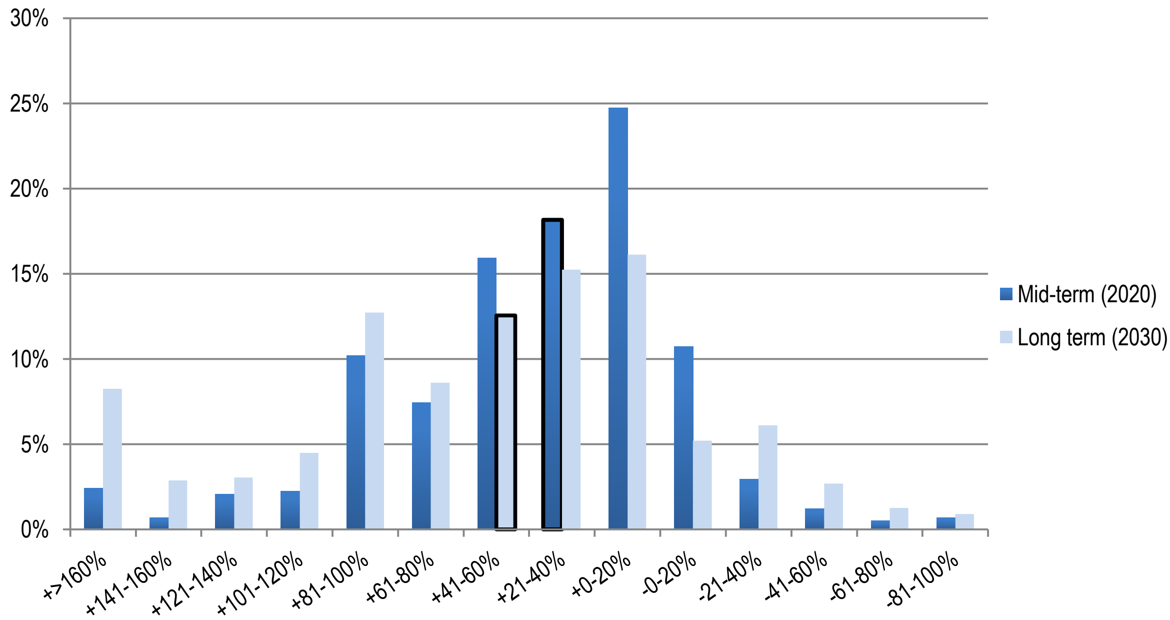
2.2 Expectations on future demands of ^{99}Mo/^{99m}Tc

The core of the survey consisted of questions aimed at understanding and determining the future demand for ^{99m}Tc. In a previous study on the future demand of ^{99m}Tc in the Netherlands, experts pointed towards a trend of increased use of diagnostic imaging in general (Technopolis, 2008). We therefore distinguish the expectations with regard to the use of diagnostic imaging in general (including CT, MRI, PET, SPECT, etc.) and that of only ^{99m}Tc-based modalities (SPECT).

2.2.1 Expectations on the future of diagnostic imaging

Respondents were asked to estimate how many diagnostic imaging procedures will be performed in the years 2020 and 2030, compared to the level at the end of 2010. The majority of the respondents expect that the total number of procedures will increase (see Figure 4). For the mid term (2020), the average increase is estimated to be about 35%. For the longer term, the respondents expect the growth to slow down; but continuous growth will lead to an average increase of about 50% by the end of 2030.

Figure 4: Increase in diagnostic imaging; compared to 2010 – median boxed*



* Please note that the median is a range, as the survey provided answer categories.

Interesting deviations from the average expectation on the future use of diagnostic imaging are observed between emerging and mature markets. On average, respondents from emerging markets expect a much larger growth: 50% by 2020 and 70% by 2030, compared to 35% and 50% in mature markets; the median for the longer term is even higher for emerging markets (see Table 1). Emerging markets expect a growth in imaging procedures of up to 100% by 2030, which can be explained by the increasing wealth in these countries and consequently better access to healthcare. Respondents from emerging markets have more diverse expectations (both positive and negative) – the standard deviation of the average is thus much higher in emerging markets[3].

Table 1: Expectations on the total number of diagnostic scans by 2020 and 2030*

	Mid-term average	Long-term average	Mid-term median	Long-term median
Mature markets	~ +35%	~ +50%	+21-40%	+41-60%
Emerging markets	~ +50%	~ +70%	+41-60%	+81-100%

* Please note that the median is a range, as the survey provided answer categories.

Overall, the respondents expect the total number of imaging procedures to increase by about 35% by 2020 and 50% by 2030 compared to current use. This assumes an average annual growth rate of between 1.1%-3.0%[4].

2.2.2 Expectations on the future demand for ^{99m}Tc

Experts were asked for their expectations of the future use of ^{99m}Tc in their country by 2020 and 2030, when compared to the situation in 2010. The expected growth of ^{99m}Tc-based procedures is lower than the expected growth of diagnostic imaging procedures in general, as demonstrated in Figure 5 (compared to Table 1). Most experts expect the demand for ^{99m}Tc to increase in their country. On average, experts expect an increase of about 20% by 2020 from 2010 levels, while they foresee an increase of about 25% by 2030[5]. Average expectations thus imply that growth will level off over the longer term.

When comparing the expectations of growth for 2020 and 2030, it appears that the experts have more diverse opinions over time, both negative and positive. Standard deviations from the average increase, and experts' opinions become less consistent over time. The expected growth of ^{99m}Tc-based procedures is lower than the expected growth of diagnostic imaging procedures in general. This estimation is also backed by the opinions of the Expert Advisory Group. They foresee stronger growth for modalities that are not relying on ^{99m}Tc, as will be further discussed in more detail in section 2.2.3.

Again, respondents from countries with emerging markets for ^{99m}Tc expect larger growth rates; they expect a 40% increase by 2020 when compared to 2010, and 50% by 2030[6], while expectations from mature markets are about half as large (see Table 2). The differences in the average expectations of the mature and emerging market are significant using a 95% confidence interval (respectively 3.7% and 1.4%). The relatively small participation of respondents from emerging markets may cause an underestimation of the future use of ^{99m}Tc; only 6% of the respondents come from an emerging market. We further discuss this in a scenario that deals with the rapid growth in emerging markets.

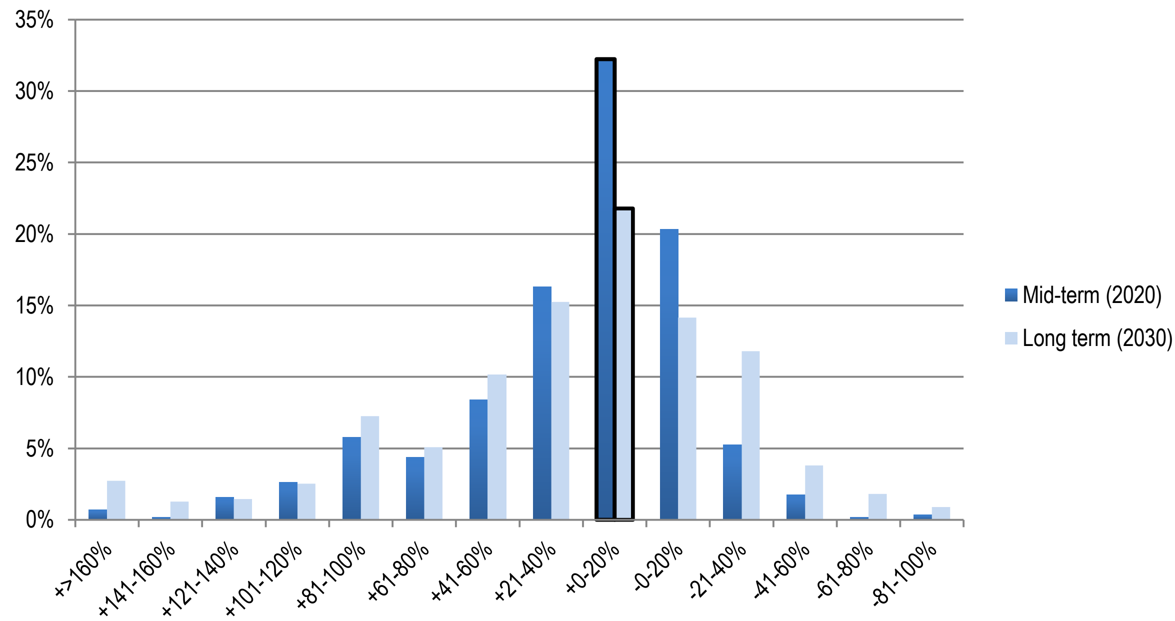
[3] However, the difference between these populations is not statistically significant using a 95% confidence interval (significance at 20% for 2020 and 18% for 2030).

[4] Annual growth rates: 35% by 2020: 3.0% followed by annual growth of 1.1% between 2020 and 2030; assuming linear growth from 2010 to 2020 and 2020 to 2030.

[5] Representing an annual growth rate of 1.8% between 2010 and 2020 followed by an annual growth of 0.41% between 2020 and 2030; assuming linear growth.

[6] Representing an average annual growth of 3.4% until 2020 followed by annual growth of 0.7% from 2020 until 2030, assuming linear growth from 2010 to 2020 and 2020 to 2030.

Figure 5: Expected future demand for ^{99m}Tc by 2020 and 2030, compared to 2010 – median boxed*



* Please note that the median is a range, as the survey provided answer categories.

Table 2: Break-down of expectations on ^{99m}Tc-based imaging in 2020 and 2030: maturity of markets*

	Mid-term average	Long-term average	Mid-term median	Long-term median
Mature markets	~ +20%	~ +25%	+0-20%	+0-20%
Emerging markets	~ +40%	~ +50%	+21-40%	+41-60%

* Please note that the median is a range, as the survey provided answer categories.

Differences between sub-groups in the surveyed population, based on expertise (SPECT-only, SPECT-combined, non-SPECT; see section 2.1) are shown to be not important. The imaging expertise of the respondents did not play a large role in their expectations. The sample with expertise on SPECT-only does predict the highest increase; but this difference is only 1-2% by 2020 and 1% by 2030. Part of this difference might be explained by the location of the respondents (mature versus emerging markets).[7]

Table 3: Break-down of expectations on ^{99m}Tc-based imaging in 2020 and 2030: expertise background*

	Mid-term average	Long-term average	Mid-term median	Long-term median
SPECT specialised	~ +23%	~ +24%	+0-20%	+0-20%
SPECT combined with other modalities	~ +21%	~ +23%	+0-20%	+0-20%
Only other modalities	~ +22%	~ +23%	+0-20%	+0-20%

* Please note that the median is a range, as the survey provided answer categories.

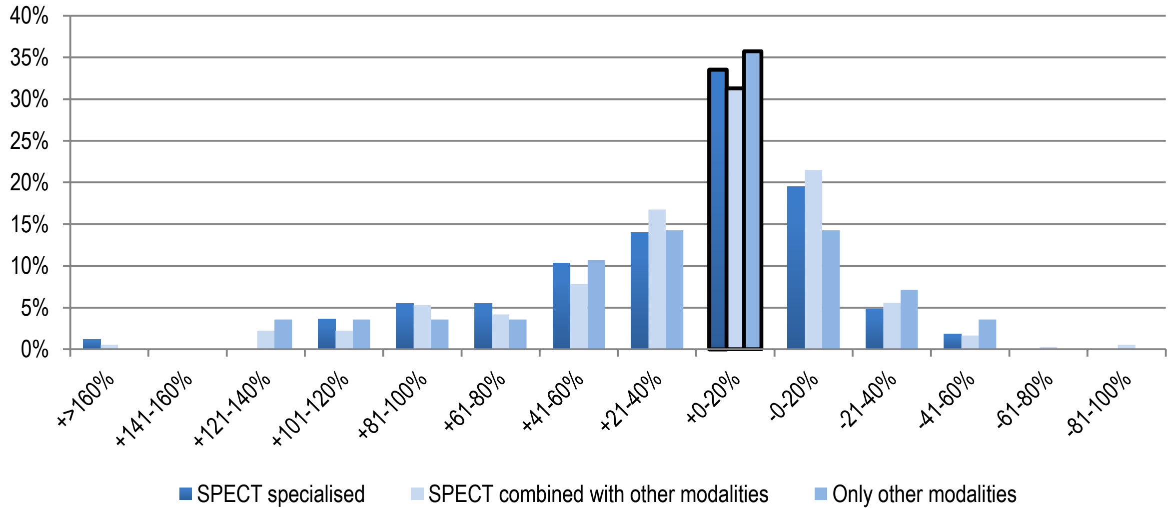
Similarly, we also analysed whether the expertise background was a significant determinant for the expectations for future use of ^{99m}Tc (see Figure 6 for a breakdown). This was not the case;

[7] The sample size did not allow for reasonable cross-analysis.

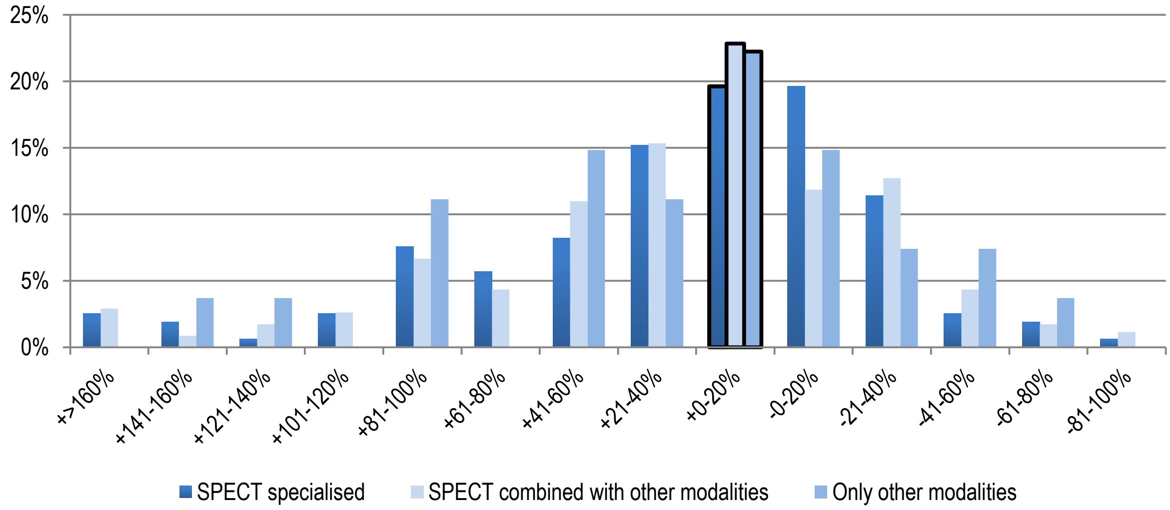
however, the small sample of the group of respondents with non-SPECT imaging experise might play a role in this conclusion[8].

Figure 6: Future demand for ^{99m}Tc in 2020 and 2030; broken down by expertise background – medians boxed*

Mid-term (2020)



Long term (2030)



* Please note that the median is a range, as the survey provided answer categories.

In conclusion, respondents anticipate an average growth of ^{99m}Tc use of 20% by 2020 and 25% by 2030, when compared to their use in 2010. Respondents from emerging markets expect a larger growth on average (2020: 40% and 2030: 50%). Respondents from mature markets expect a growth of 20% and 25% respectively. Moreover, expectations of respondents from emerging markets are less consistent and show more spread. The sample of emerging markets shows a higher standard deviation (i.e. the respondents expect higher increases and decreases). Respondents with expertise on ^{99m}Tc-based scanning have only slightly higher expectations of the growth of demand for ^{99m}Tc (on average

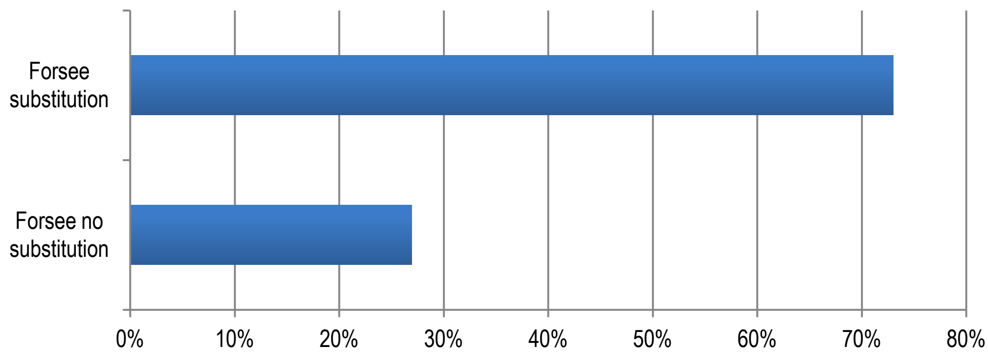
[8] Significance between SPECT-specialised and other groups: 44% with SPECT-combined and 34% with non-SPECT; for the division of respondents over the group, see Figure 3.

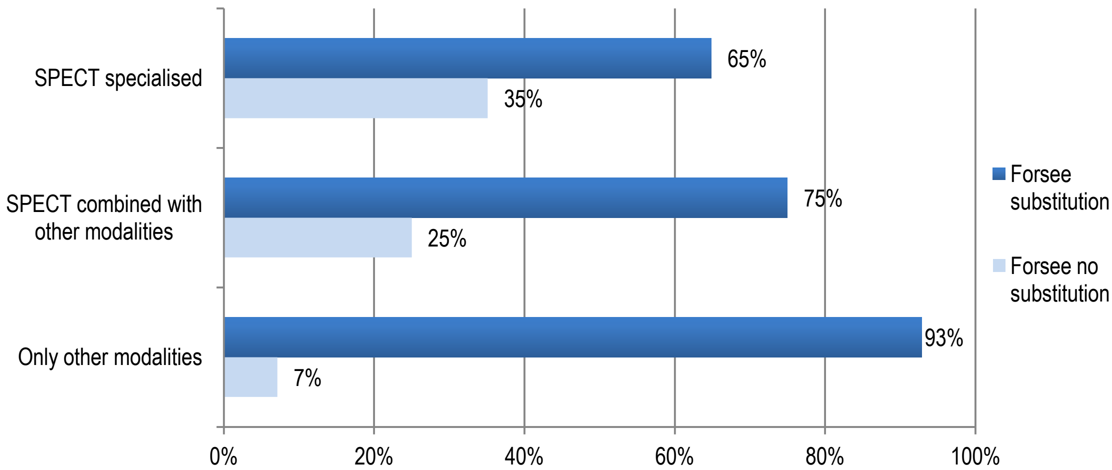
1-2% higher by 2020 and 1% by 2030 when compared to SPECT-combined); but this difference is not significant using a 95% confidence interval.

2.2.3 Expectations with regard to the share of ^{99m}Tc modalities

External factors could impact the future growth of ^{99m}Tc/^{99}Mo. One of these factors is the development and growth of alternative imaging modalities both in the domain of nuclear imaging and radiology, such as PET and combined modalities such as PET/CT or PET/MRI. Respondents were asked whether they expect a trend in which other modalities will substitute for ^{99m}Tc-based imaging in the total share of imaging modalities by 2020-2030. According to 73% of the respondents, ^{99m}Tc-based imaging procedures will be substituted, at least partially, while 27% do not foresee any substitution effects until 2030. This implies that the respondents expect that the *relative share* of ^{99m}Tc-based imaging (including combined modalities such as SPECT/CT) will decrease. This does however not mean that the absolute demand for ^{99m}Tc will decrease; as total diagnostic imaging is expected to continue to grow, even with a falling share, the absolute demand for ^{99m}Tc is expected to increase.

Figure 7: Overview of substitution of ^{99m}Tc-based diagnostic imaging by different groups of respondents



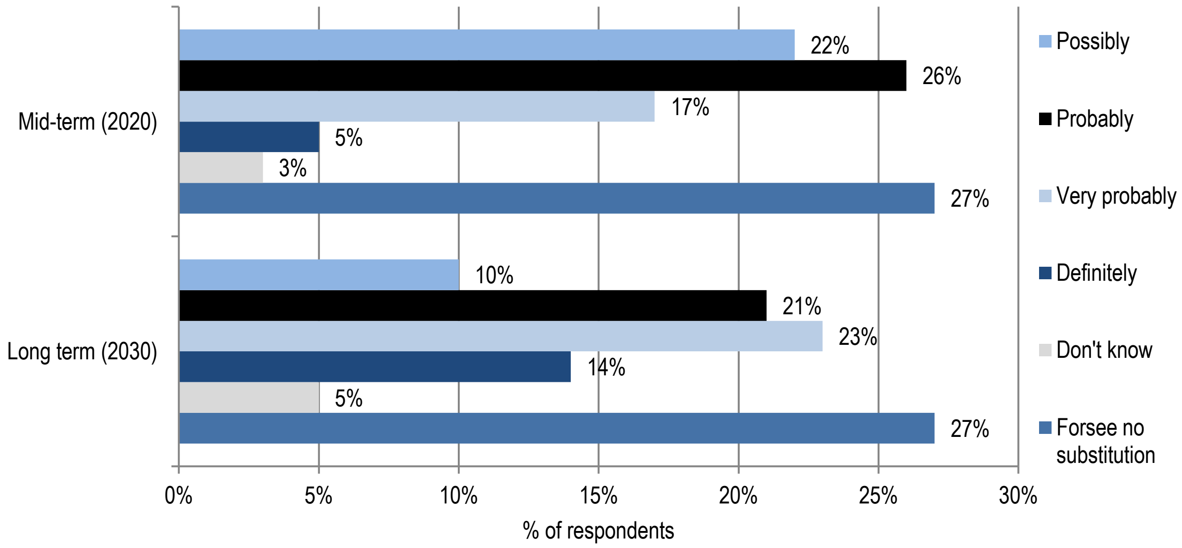


Large differences are observed for the different expertises of respondents. More respondents (75%) with broad (nuclear) imaging expertise expect substitution to take place compared to those with expertise of ^{99m}Tc-based scanning only (65%). Moreover, most respondents with expertise of other modalities or miscellaneous expertise expect substitution (93%).

Those respondents that indicated that they expect a substitution of ^{99m}Tc-based imaging were also asked to assess the likelihood of substitution. Figure 8 displays the results of this question; we have also added the group of respondents that indicated in an earlier question that they did not foresee any substitution. The most selected answer for 2020 was that substitution occuring was “probable”, whereas for 2030 substitution is “very probable”. Clearly, the average respondent believes that substitution of ^{99m}Tc-based imaging becomes more likely over time, resulting in 14% of the respondents indicating that by 2025 ^{99m}Tc-based diagnostic imaging will be “definitely” substituted.

Several members of the HLG-MR commented on the issue of substitution, emphasising that previous innovations in the imaging domain enhanced the use of diagnostic imaging. Innovations primarily led to imaging of other medical indications, rather than replacement of older technologies for the same purpose. New technology thus served as an add-on to the existing set of modalities. As an example it was noted that X-ray is still used, while many new technologies have been introduced since the introduction of X-ray.

Figure 8: Likelihood of substitution of ^{99m}Tc-based diagnostic imaging, including those respondents that foresee no substitution at all (see Figure 7)



Moreover, the respondents were asked to quantify the substitution of ^{99m}Tc-based imaging in the total mix of modalities for diagnostic imaging. Substitution of ^{99m}Tc is expected to grow over time: by 2020, 11% of the respondents expect that greater than 25% of ^{99m}Tc-based procedures will be substituted by other modalities; by 2030, 28% of the respondents expect a substitution of greater than 25% of procedures (see Figure 9). When taking an weighted average, including the respondents that foresee no substitution, the effect is estimated to be 12% by 2020 and 18% by 2030.

In emerging markets the largest part of respondents expect no substitution at all. However, for those that expect substitution, the effect is expected to be stronger: 25% of respondents expect substitution for over 25% of procedures by 2020 and 31% by 2030; in mature markets, respondents on average estimate this to be 10% and 27%.

In conclusion, substitution of ^{99m}Tc-based imaging becomes more likely over time: 74% of the respondents expect substitution effects by alternatives; 90% of this group find it “probable” to happen by 2030. On average, the substitution effect is estimated to be 12% by 2020 and 18% in 2030. The results of the survey showed that the substitution effect is expected to be stronger in emerging markets.

Figure 9: Expectations on degree of substitution of ^{99m}Tc by other modalities

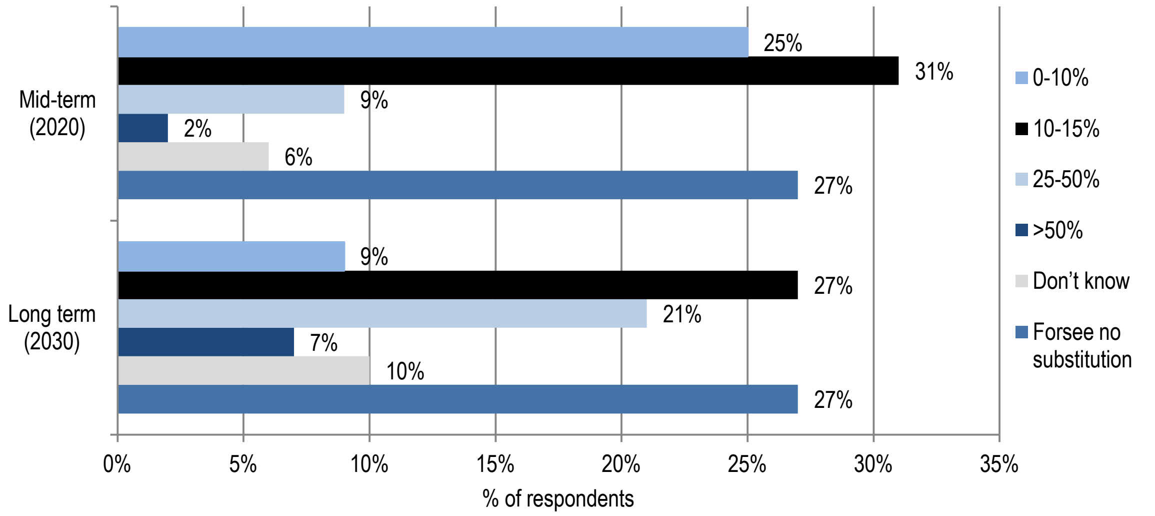
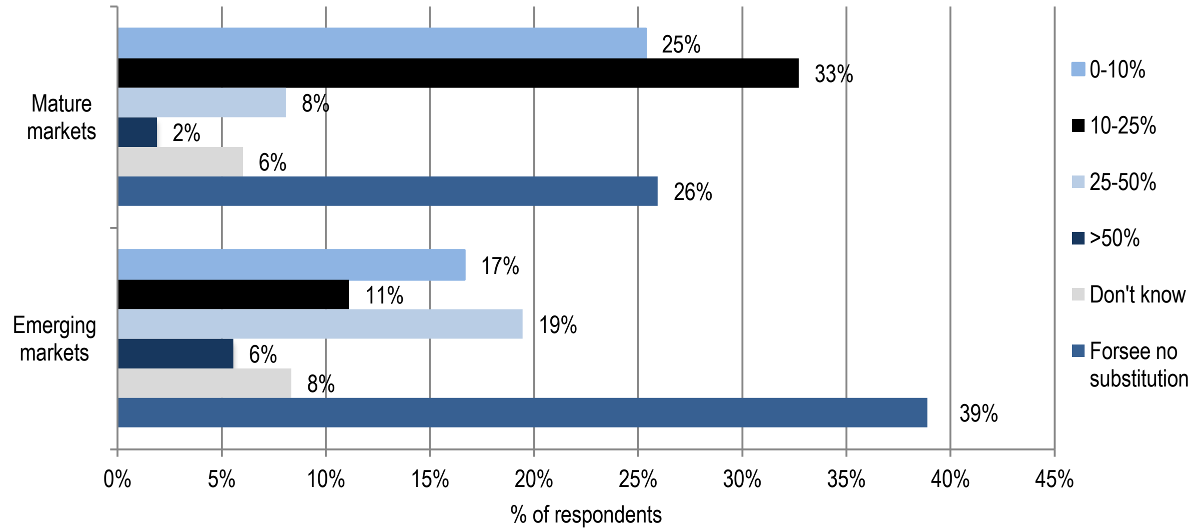
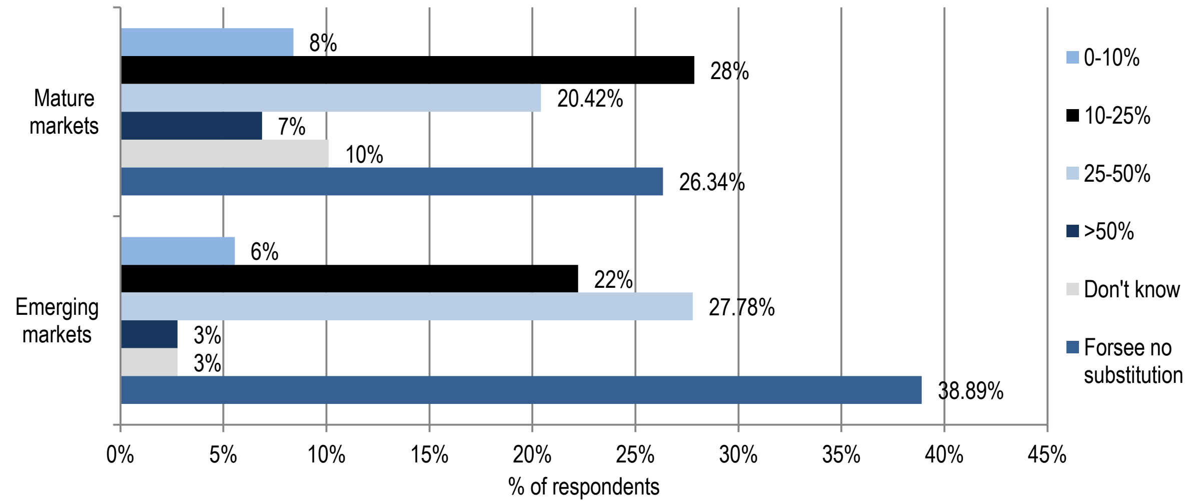


Figure 10: Expectations on degree of substitution of ^{99m}Tc-based imaging in mature & emerging markets on mid and long term

Mid-term (2020)



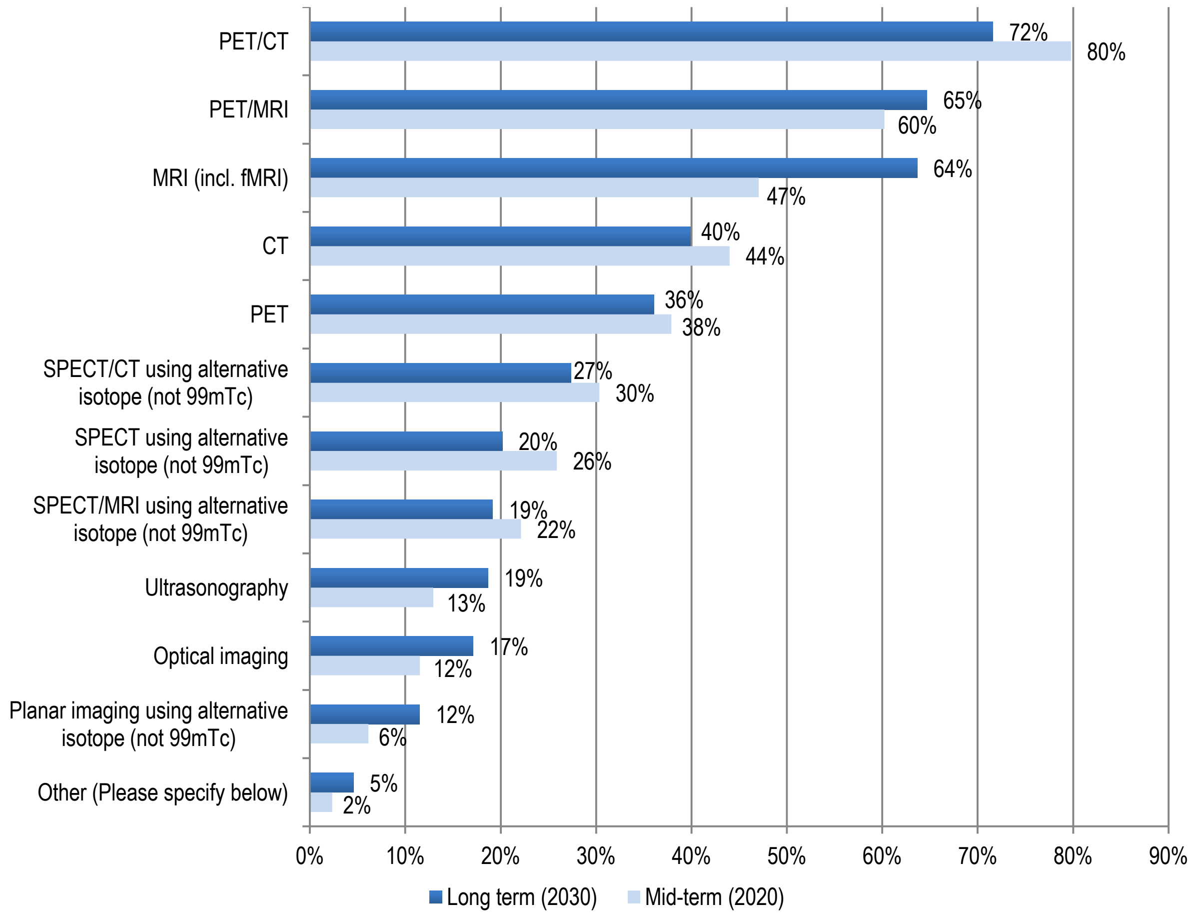
Long term (2030)



2.2.4 Alternatives for substitution

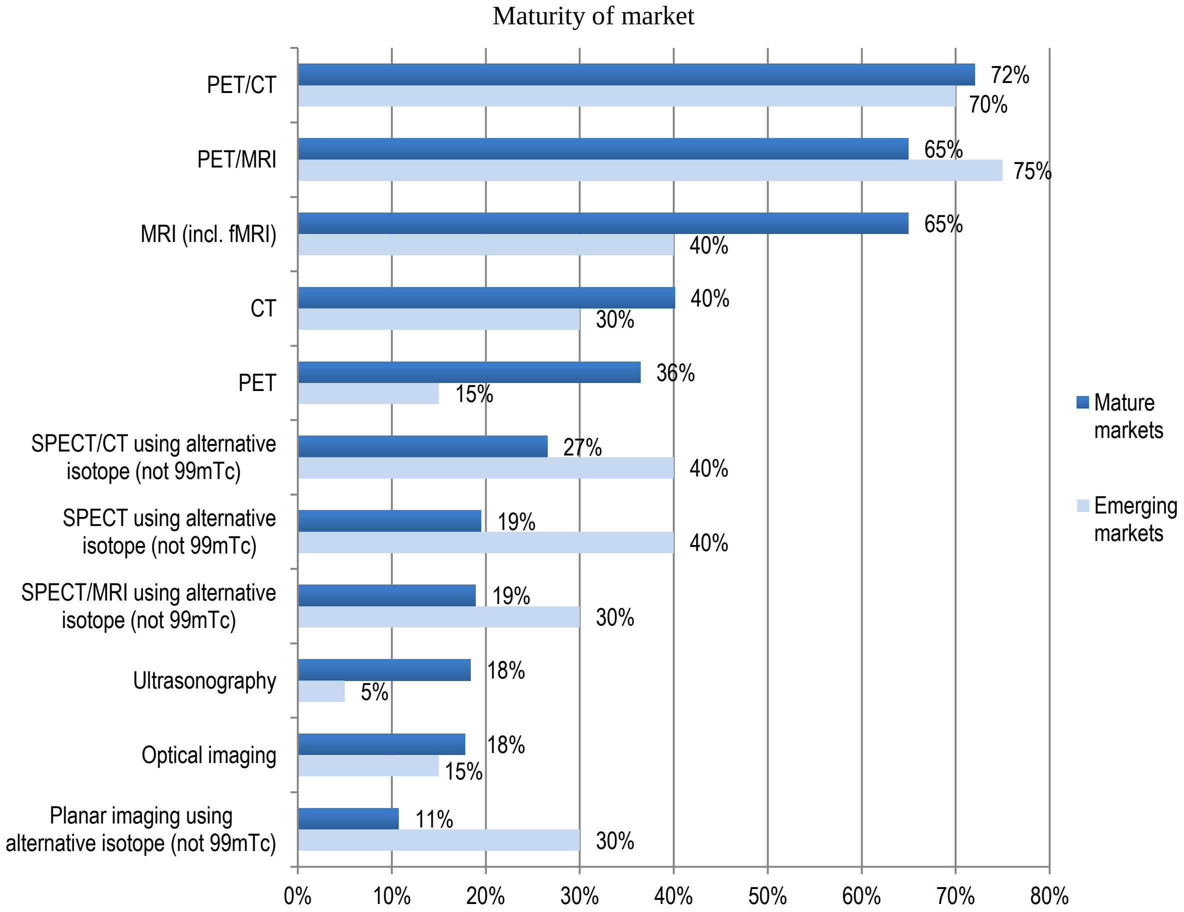
Given the expected substitution of ^{99m}Tc-based imaging, the question arises as to what will be the substitutes. The survey presented a list of possible alternatives and the respondents were asked to indicate whether they expected the modality to substitute for ^{99m}Tc-based modalities. Figure 11 shows which modalities were most frequently mentioned as substitutes for ^{99m}Tc-based imaging. PET/CT is the modality most expected to replace modalities based on ^{99m}Tc. In the longer term, PET/MRI and MRI will experience relatively greater growth. Members of the EAG also indicated that alternative isotopes to ^{99m}Tc could be used, replacing only the radiopharmaceutical and not the camera and its infrastructure. In recent shortages of ^{99m}Tc, alternative radiopharmaceuticals were used, especially in North America. The respondents however do not (yet) expect the replacement of ^{99m}Tc by an alternative radiopharmaceutical using the same infrastructure.

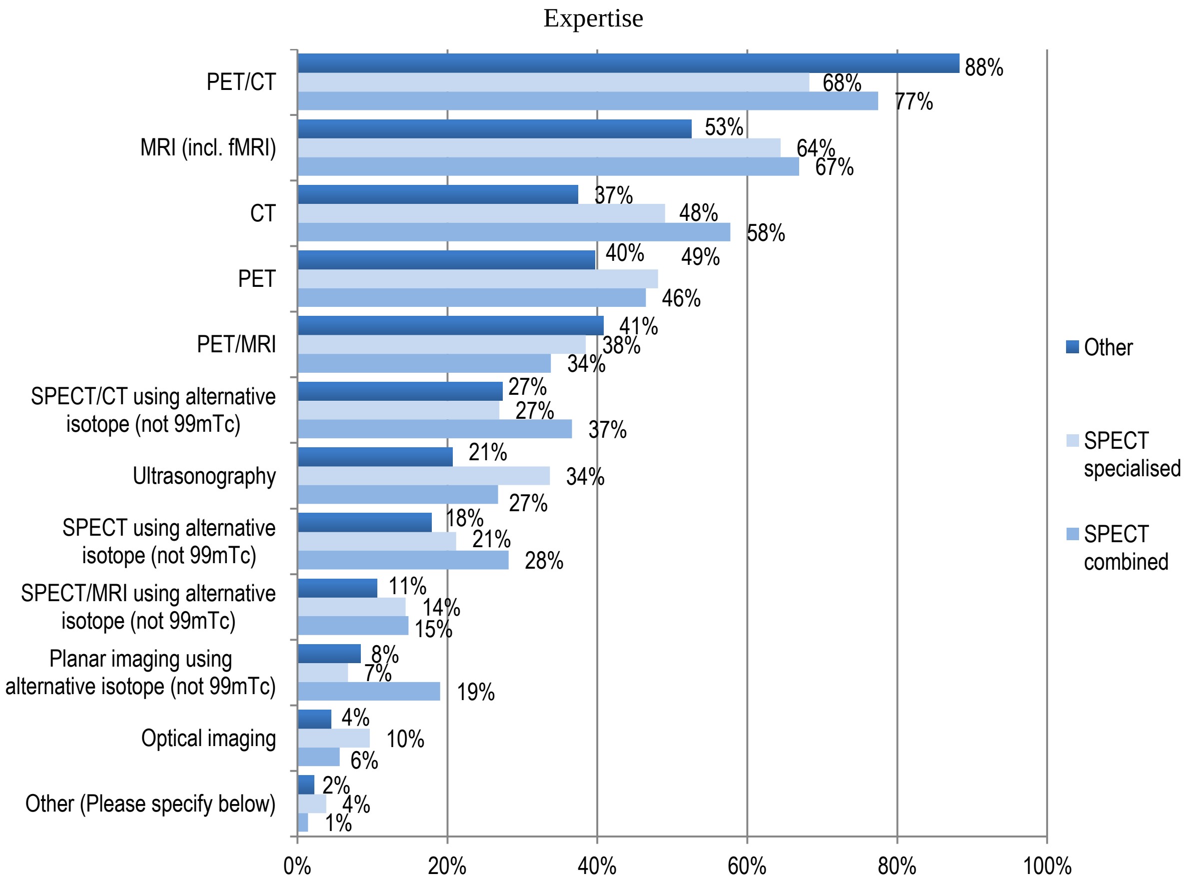
Figure 11: Alternative modalities expected to replace ^{99m}Tc



Both in mature and emerging markets the most frequently mentioned substitutes are combined modalities. In mature markets, most frequently mentioned alternative technology is PET/CT, whereas respondents from emerging markets mention PET/MRI most often (see Figure 12). The EAG raised doubts about this last expectation, as PET/MRI is not yet market ready and still requires development. In mature markets, MRI, including functional MRI, are also important; in emerging markets respondents mention alternative isotopes much more often. Using alternative isotopes is not seen as a substitute by SPECT specialised respondents; they see PET/CT and then traditional modalities as more plausible substitutes (i.e. CT, MRI, PET, and even ultrasonography) (see Figure 12).

Figure 12: Alternative modalities for mature & emerging markets (a) and expertise (b)





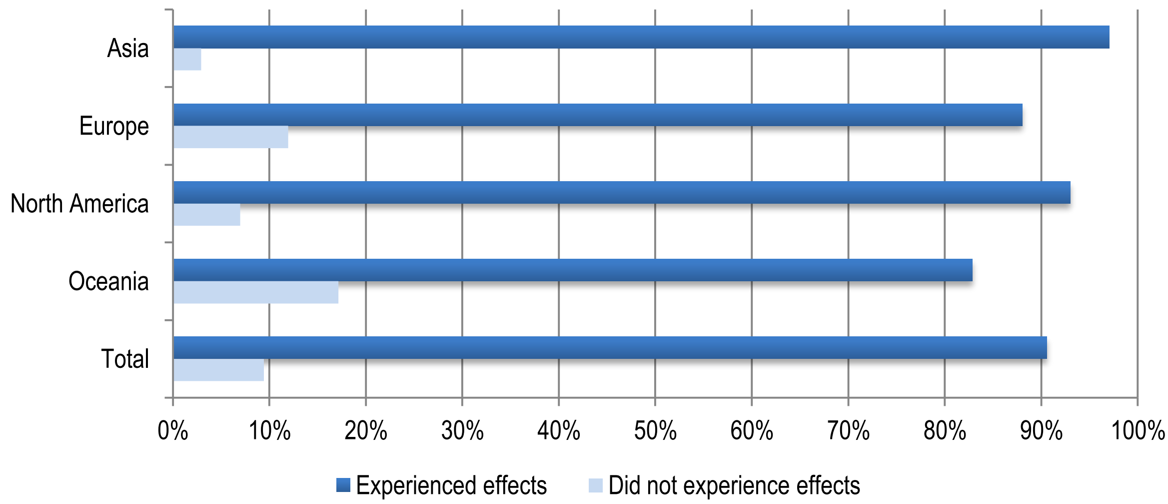
In summary, PET/CT is most often seen as the main substituting technology for modalities based on ^{99m}Tc. In the longer term, PET/MRI and MRI are also often mentioned. Most often-mentioned substitutes are combined modalities, notably PET/CT; emerging markets mention PET/MRI as most important. MRI including functional MRI are also often-mentioned alternatives, especially in mature markets. In emerging markets, respondents mention alteratative isotopes often. Respondents that are specialised in SPECT-only do not expected alterative isotopes to be a significant substitute.

2.3 Perceptions on stability of supply & coping strategies

2.3.1 Stability of supply

On average, 90% of the respondents experienced effects of reduced supply in the last four years. The effects were most notable in Asia and North America and to a smaller extent in Oceania and Europe. Nevertheless, in all regions more than 80% of the respondents had to cope with shortages (see Figure 13).

Figure 13: Experienced effects of shortages of ^{99m}Tc in the last 4 years



Given the recent shortages of ^{99m}Tc in the world market, respondents were asked about their expectations on the stability of the future supply. These expectations could indicate an interest to move to alternative modalities or isotopes, if stability is seen to be important but not expected to occur. However, in the shorter term (until 2020), about 60% of the respondents think the supply will be more or less stable, whereas 40% believe it to be unstable to a certain degree. In the longer term, the respondents expect increased stability of supply; about 65% expect the supply to be at least moderately stable. As indicated by the EAG, this implies that new production sources (e.g., new research reactors) for molybdenum-99 are expected to be installed and used by that time. It has to be noted that generally, the respondents found it difficult to make an estimate of long term stability; for the mid-term, 4% of the respondents did not have an opinion, which increased to 20% of the respondents for 2030. This underlines the difficulty of making predictions for the longer term.

There are geographical differences in the expectations on the stability of future supply of ^{99}Mo/^{99m}Tc (see figure 15). When focusing on the long term, almost three-quarters of the Oceanian and European respondents believe the supply of ^{99}Mo/^{99m}Tc to be at least moderately stable. These differences are in line with the effects felt by the respondents during the last supply shortages: North America and Asia were generally affected greater than other regions. In addition, European respondents may have a higher trust in future supply given their larger network of ^{99}Mo/^{99m}Tc production capacity.

Figure 14: Expected stability of ^{99m}Tc supply, excluding no-opinion responses

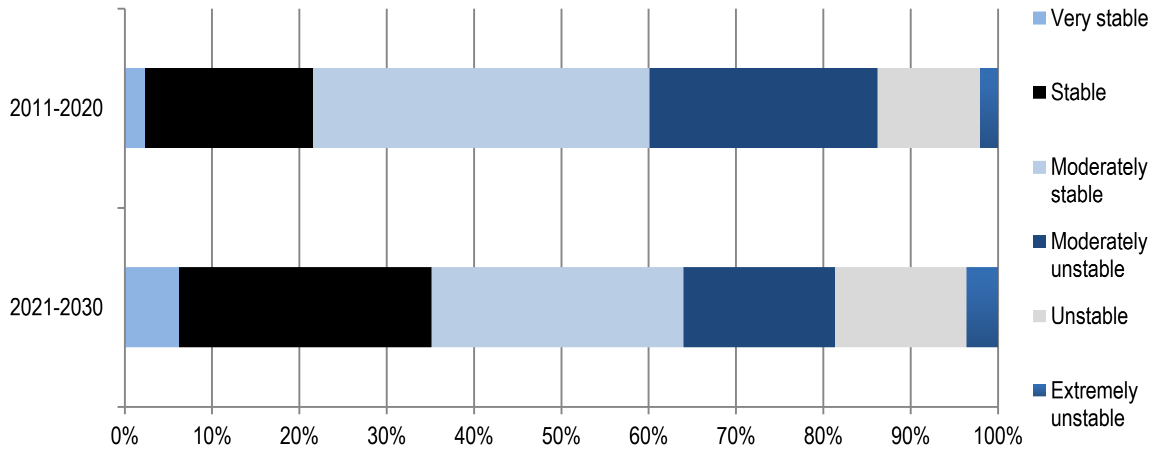
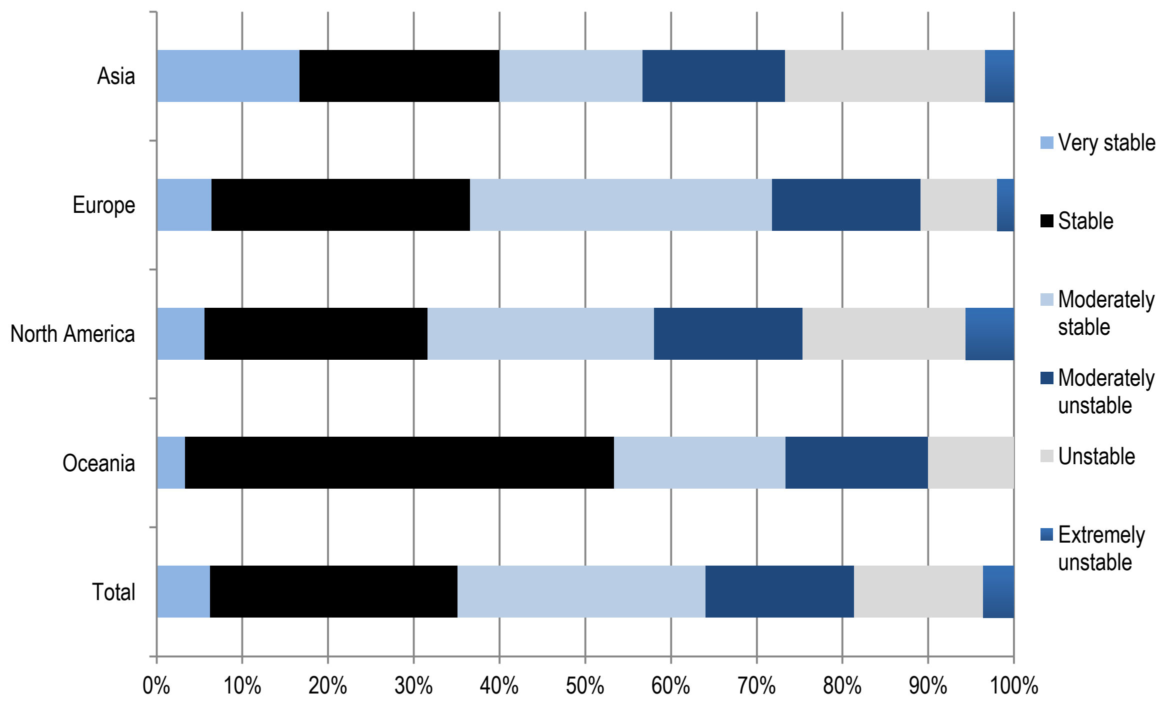


Figure 15: Geographical expectations on stability of supply of ^{99}Mo/^{99m}Tc, excluding no-opinion responses

Long term (2030)



Over 90% of the respondents experienced the shortage in their day-to-day activities. Although margins are small, Oceania and Europe have a larger share of people that did not experience the shortage (up to 17% in Oceania). The recent shortage seems to influence the expectations of the respondents for the future; Oceanian and European respondents are more confident on future supply.

2.3.2 Coping strategies during ^{99m}Tc shortage

With regard to the shortages of ^{99m}Tc, respondents were asked what type of coping strategies they used and how effective these were in terms of limiting the use of ^{99m}Tc. Even the least used strategy (sharing of generators) was attributed at least a minor saving in over 50% of the cases. This makes it plausible that those who had to implement strategies to deal with shortages made use of a mix of coping strategies. In this mix, more efficient patient scheduling and reduction of per unit doses were the most effectively applied strategies. Next were loss of procedures, use of alternative modalities and use of alternative radiopharmaceuticals using the same infrastructure – this type of strategy was most often used in the Americas and in Asia.

Figure 16: Impact of coping strategies

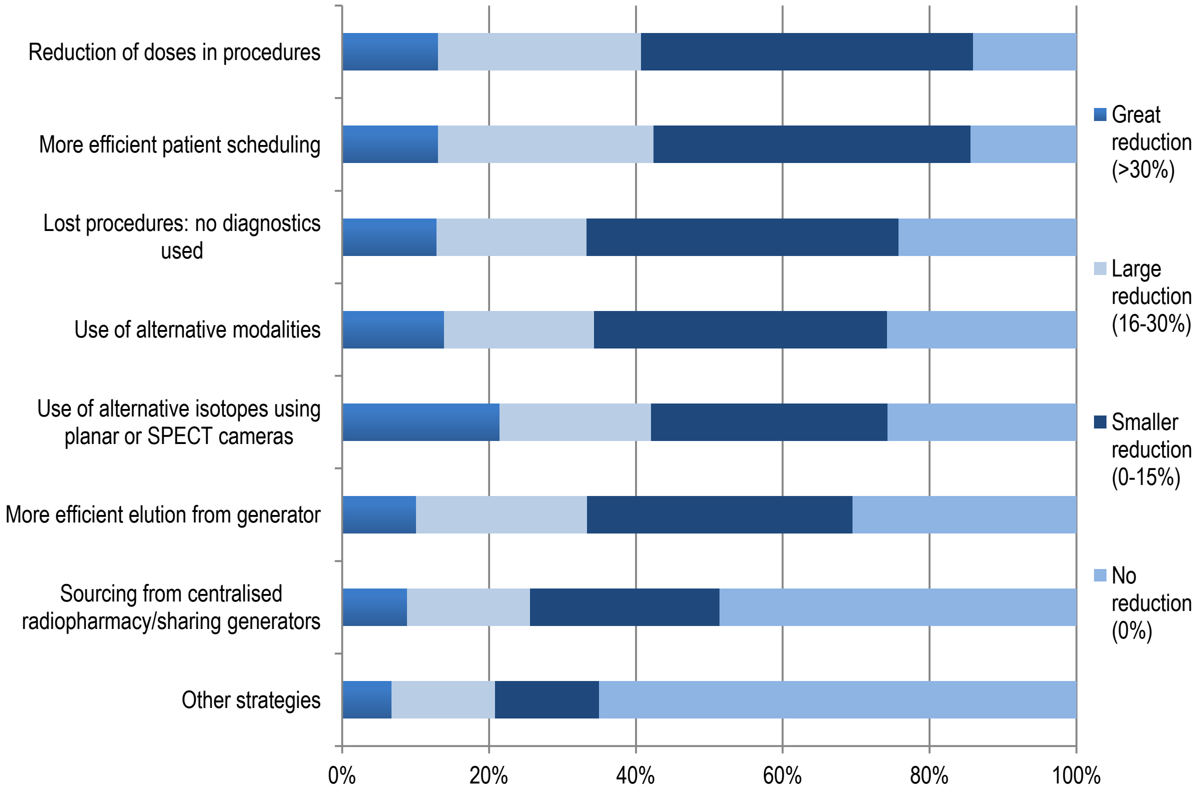
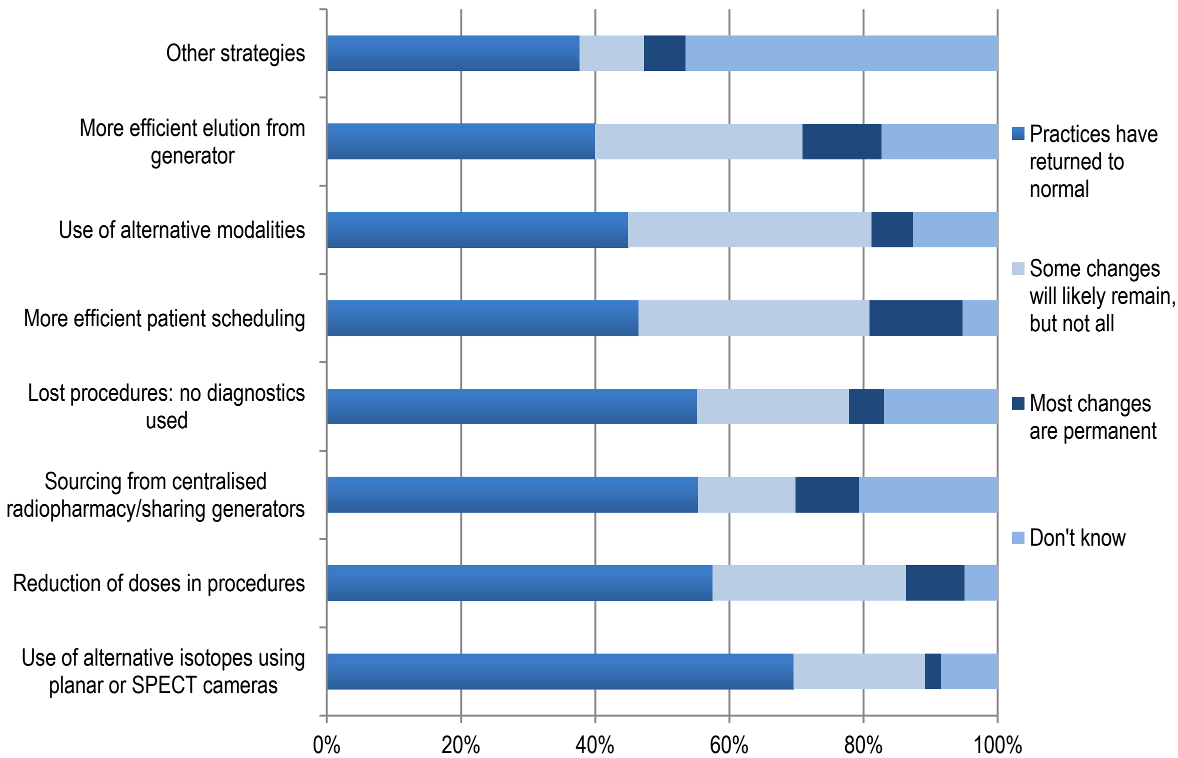


Figure 17: The longer term effects of the coping strategies, post-shortages



After the ^{99m}Tc supply shortage several coping strategies have turned into routine practice, however only in small percentages of the total market. The shortage has thus in hindsight caused a small increase in efficiency. More efficent elution of ^{99m}Tc from generators and scheduling of patients, as well as the use of alternative modalities became, to some extent, daily practice in more than half of the cases.

In conclusion, in reaction to recent shortages respondents used a mix of strategies to cope with shortages of ^{99m}Tc. Survey respondents indicated that the most important coping strategies for dealing with the shortages were more efficient patient planning and reduction of doses used. In most of the cases the coping strategies were not permanent and day-to-day "pre-shortage" routines have returned. However, several strategies are still being used to a certain extent. More efficient elution from the generator as well as more efficient patient scheduling are the strategies most still used today.

2.4 Determinants of change

Apart from changes resulting from the shortages in ^{99m}Tc, there are more general drivers that can influence future demand. In collaboration with the Expert Advisory Group an extensive list of drivers was put together. These include categories such as: cost of ^{99m}Tc and alternatives, supply availability and reliability, alternative modalities, medical demand, policy and technology.

Respondents were asked which drivers they thought would increase or decrease demand. They were able to choose the five strongest drivers that would increase demand as well as those that would decrease demand.

2.4.1 Drivers of increased demand

Figure 18 displays how often the drivers of increased demand were mentioned, as a share of the total responses. Availability of improved technologies for ^{99m}Tc-based imaging is most often identified as a positive driver for ^{99m}Tc demand (81%); shortly followed by stable supply of ^{99m}Tc (77%). The most important driver for increased demand are thus from a technological or an infrastructural nature. An increase in the efficiency throughout the whole imaging procedure in clinic or radiopharmacies is a third important driver (60%). The next set of mentioned drivers concerns the price and cost of the procedure and the reimbursements offered for the procedure. According to the EAG, the price of ^{99m}Tc-based imaging is relevant as well; this has to do with the current situation where ^{99m}Tc-based procedures are much cheaper (> ten-fold) than PET-based imaging.

Geographical differences in the answers were not very high – the greatest differences were observed for Asia (see Figure 19). The driver "more efficient use by clinic and radiopharmacies" is mentioned relatively often by respondents from Asia. "Growing wealth in the economy" also is a more important factor in Asia, and to a smaller extent the same goes for North America. Cost issues, such as the wealth of patients and the costs of imaging are relatively unimportant; the EAG suggested that this could be explained by the payment for procedures from private and public health care systems. European health care systems might be more inclusive and less privately oriented. In Oceania, technological and infrastructural circumstances are mentioned less as important drivers; instead, more emphasis lies on pricing and costs. The background of the respondents can partially explain this: they typically had no background in health financing, health insurance or hospital administration.

Figure 18: Drivers of increased demand

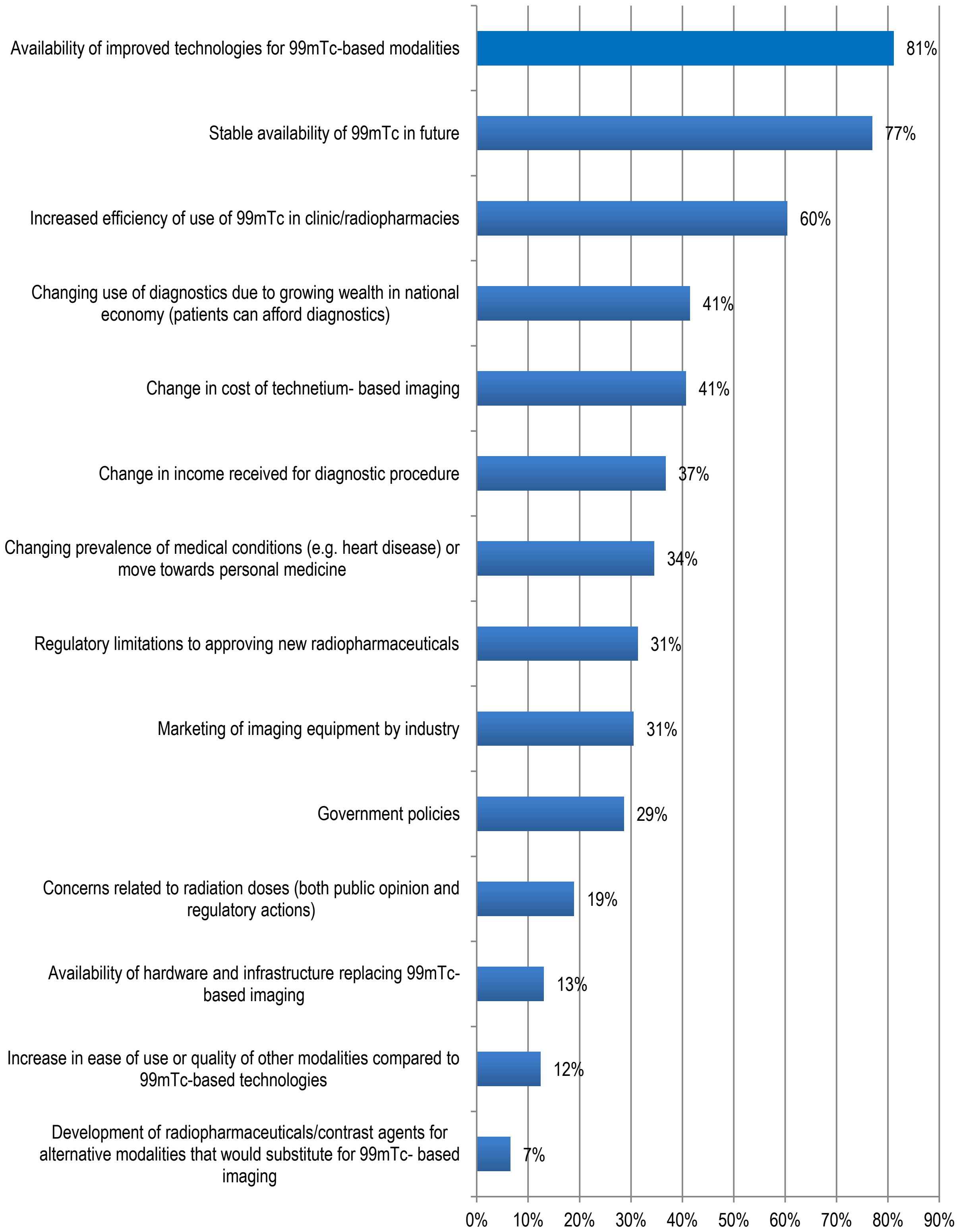
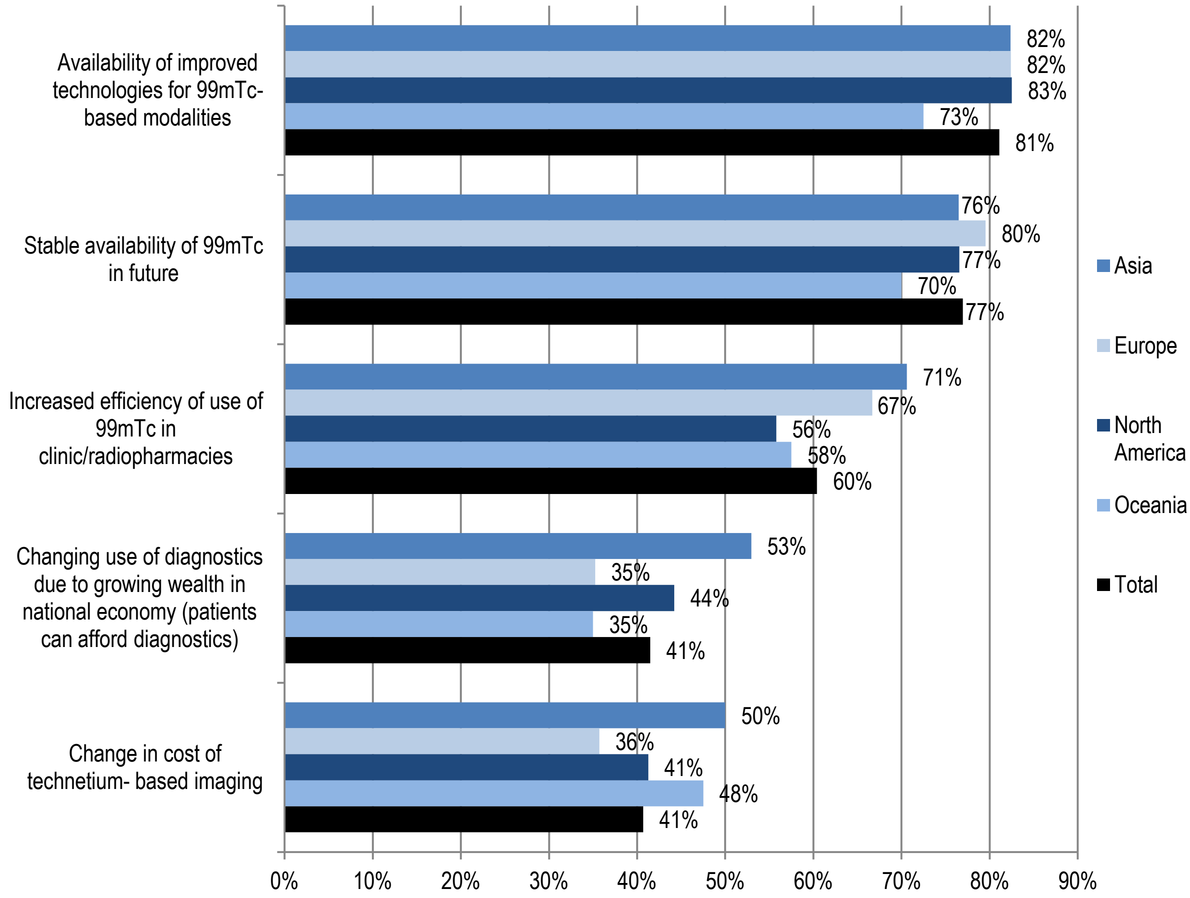


Figure 19: Drivers of increased demand

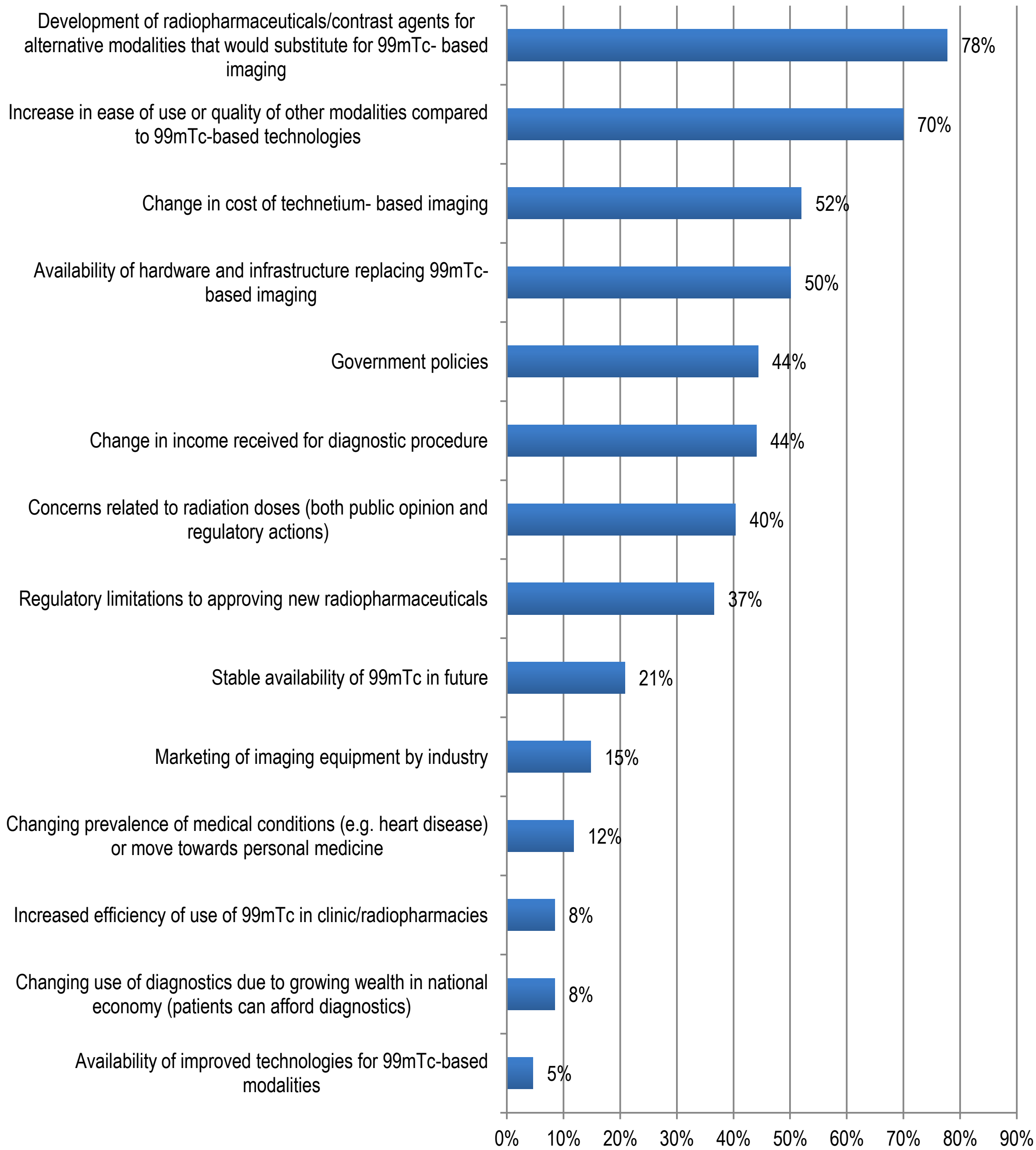


2.4.2 Drivers of decreased demand

Similar to drivers of increasing demand, the most often mentioned drivers for decreasing demand are also of technological nature. For decreased demand, development of competing technologies is seen as the most important group of drivers. Development of radiopharmaceuticals and new contrast agents in association with the expansion of competing technologies is the most mentioned driver with 78%. An increase in the ease of use of competing technologies is the second most mentioned driver. It is notable that respondents have primarily chosen technological drivers, rather than non-technological drivers. However, changes in cost are also perceived as a relevant driver for decreased demand: if the cost of ^{99m}Tc-based procedures increase in the future, this could drive a shift towards the more expensive PET-based procedures. The EAG members emphasised that the cost of infrastructure and cameras is significantly higher and therefore cost increases of ^{99m}Tc may have very little net effect on demand (see also the discussion on price elasticity later in this report). The cost of a PET camera is about 2.5 times higher than that of a SPECT camera.

Geographical differences for drivers of decreased demand are significant, even though in all regions the development of alternative radiopharmaceuticals and contrast agents are seen as important. The ease of use of competing technologies is however not that often mentioned in Asia, whereas it is the most mentioned driver by respondents from Oceania. An increase in the cost of ^{99m}Tc-based imaging is observed to be a driver for a decrease in use in Europe. Government policies are not often mentioned in Asia (1/3rd) whereas it is relatively important in North America (1/2nd).

Figure 20: Drivers of decreased demand



Summing up the drivers of increasing and decreasing demand, Table 4 shows the top-5 for both categories. It demonstrates that increased demand depends on availability of ^{99m}Tc, improved technology or more efficient use. Both growing wealth and changes in costs of ^{99m}Tc-based imaging were identified as potential demand increasers. The importance of the last two drivers comes partly from the current situation where ^{99m}Tc-based procedures are much cheaper than PET-based imaging.

Changes in cost are also perceived as a relevant driver for decreased demand. If the cost of ^{99m}Tc-based procedures increases in the future, this could drive a shift towards the more expensive PET-based procedures (more on this in section 2.4.5). The first and second drivers for decreased demand are the development of alternative imaging modalities in general and of new radiopharmaceuticals for PET in particular.

Figure 21: Drivers of decreased demand – geographical spread

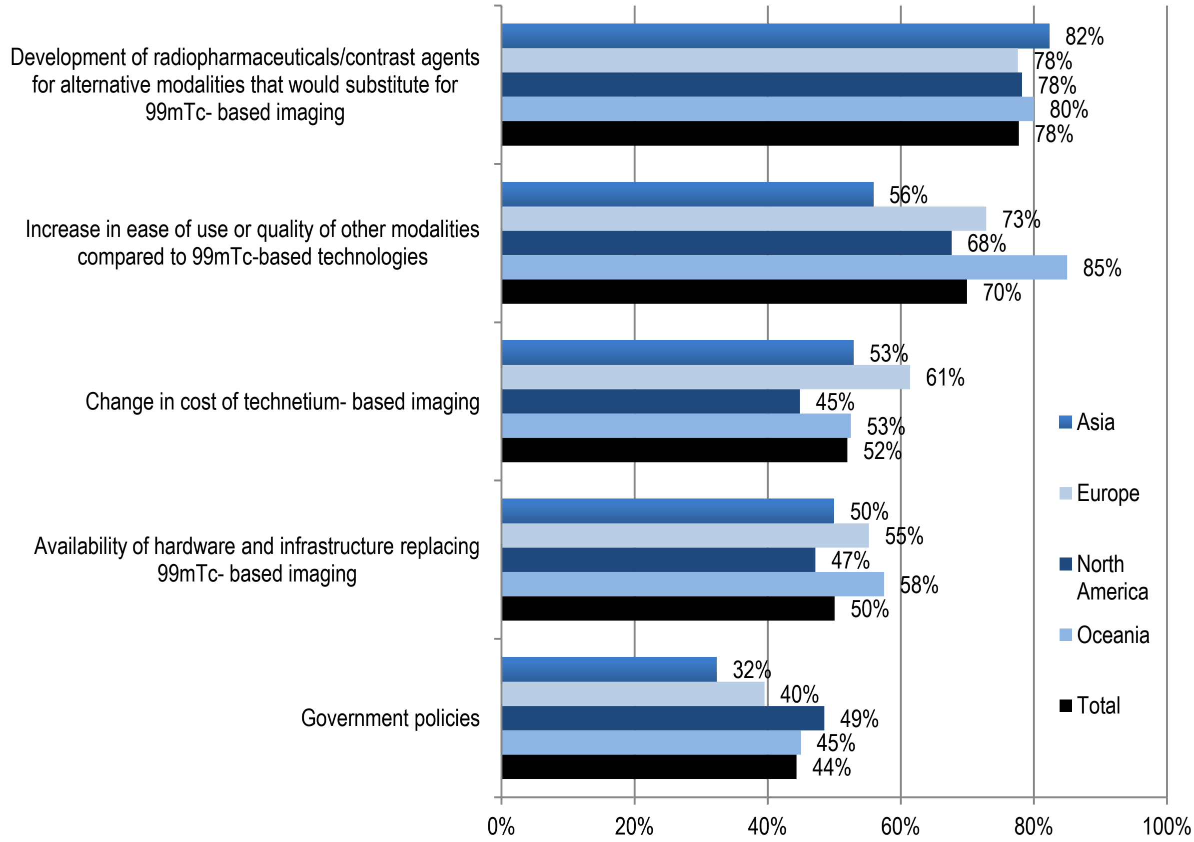


Table 4: Top five drivers of demand- increase and decrease

Increase demand	%	Decrease demand	%
Availability of improved technologies for ^{99m}Tc-based modalities	81	Development of radiopharmaceuticals/contrast agents for alternative modalities that would substitute for ^{99m}Tc-based imaging	78
Stable availability of ^{99m}Tc in future	77	Increase in ease of use or quality of other modalities compared to ^{99m}Tc-based imaging	70
Increased efficiency of use of ^{99m}Tc in clinic/radiopharmacies	60	Changes in cost of technetium-99m-based imaging	52
Changing use of diagnostics due to growing wealth in national economy (patients can afford diagnostics)	41	Availability of hardware and infrastructure replacing ^{99m}Tc-based imaging	50
Changes in cost of technetium-99m-based imaging	41	Government policies	44

2.4.3 Global Trends

Drawing from the results of the global survey, the EAG analysed in more detail some key drivers that represent wider trends. The aim of this discussion was to establish the potential impact of these trends on the future ^{99m}Tc demand and the probability of the impact occurring, in order to validate the survey results. Since the mature and emerging markets are different with respect to these trends, they will be discussed separately when appropriate.

Trend 1: Growing population, urbanisation and wealth increases

According to the United Nations, the world population is projected to reach around eight billion by 2023, from approximately seven billion today (United Nations, 2011). Asia currently accounts for over 60% of the world population with more than four billion people; China and India together have about 37% of the world's population. The growing population is expected to lead to an increase in diagnostic imaging, assuming that access to medical care will not decrease.

This growing population coincides with a growing urbanisation and increasing growth of wealth in low and middle-income countries (World Bank, 2006). Urbanisation generally indicates increased development and growing wealth; by 2030 the middle-class population is expected grow to 1.2 billion people (currently 400 million). However, it is expected that mature markets have already seen the greatest impacts of urbanisation and growing wealth while emerging markets will be most affected by this trend. Therefore the expected impact of urbanisation and growing wealth on ^{99m}Tc demand in emerging markets is a high increase, while mature markets would see a low increase.

The EAG has strong confidence that these impacts will occur. From this, the EAG validates the survey results indicating expectations of increased diagnostic imaging. The EAG also indicated that this supports the expectations of a small increase in ^{99m}Tc demand in mature markets, with a larger increase in emerging markets. The EAG did caution that in mature markets this increase in demand for diagnostic tests may also support substitution to new modalities in the long run; however building infrastructure for PET imaging is much more expensive and complicated than ^{99m}Tc-based imaging (see Trend 4).

Trend 2: Ageing population and changing prevalence of medical conditions

This second trend is partly related to the previous one, but here we focus on the medical consequences of demographic change. In the mature markets, ageing is an important societal challenge, especially with regards to health care impacts. Coupling the effect of ageing populations with effective healthcare systems means that one could expect an increased need for patient care as an ageing population will likely see increased prevalence of cancer or cardiac diseases and a corresponding increase in treatment. This will also lead to an increase of ^{99m}Tc-based SPECT scans. The EAG expects a medium positive impact in the mature markets on ^{99m}Tc demand, with a medium to high probability.

In emerging markets, ageing is not such a challenge as yet, explaining the expectations of a low impact at first (with high probability). However, looking at 2030, the emerging markets' younger populations will have aged (United Nations, 2009) and therefore it is expected that there will be a large impact in the long run. By 2030, both ageing and wealth will have increased significantly in emerging economies. Consequently, more imaging procedures can be expected for diagnostic scans, which would drive an increase in demand for ^{99m}Tc.

Trend 3: Availability of cameras

Use of ^{99m}Tc depends on cameras for imaging. The current sales and expected trends of imaging hardware thus serve as good indicators for both the SPECT/PET shift as well as for whether emerging markets will skip the use of SPECT completely. In general, one could assume that sales of cameras serves as a proxy for demand for radiopharmaceuticals: the more cameras available the more sales will be seen in the related radiopharmaceuticals.

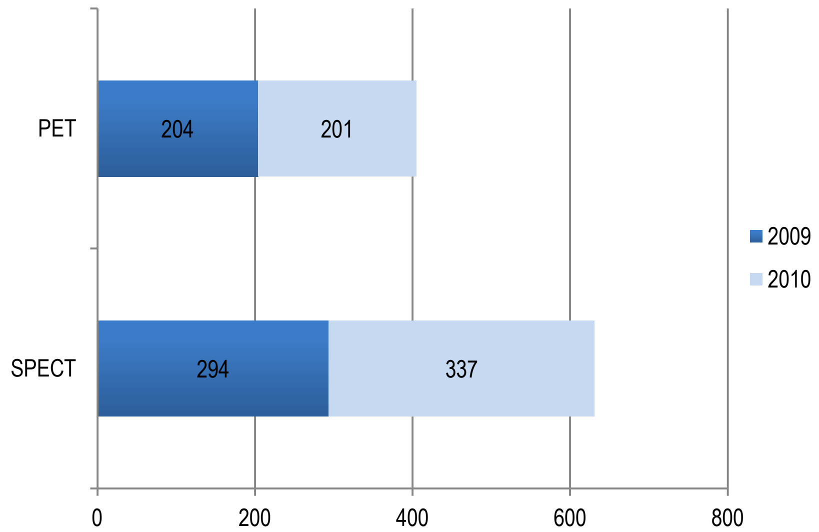
In China and India PET is on the increase, but similar numbers of SPECT cameras are sold as well. India for instance bought 20 PET cameras and 30 SPECT cameras in the last year. Worldwide, there are approximately 2 000 PET or PET/CT cameras compared to about 22 000 SPECT cameras. In some markets (eg, Europe), since 2008 the sales of PET or PET/CT cameras are declining because the market seems to be saturated – at least until replacements after the first life cycle. At the same time, there currently is a growth in SPECT/CT cameras, which is mainly replacement of older SPECT cameras. The view of the EAG is that SPECT cameras are not replaced by PET cameras but rather replaced by a new SPECT or SPECT/CT camera.

A key consideration related to the ongoing availability and growth of SPECT cameras is cost. The costs for PET cameras (EUR 1 million-2 million) are substantially higher than for SPECT cameras (EUR 400 000-800 000). Second hand SPECT cameras are also available, and even cheaper (EUR 150 000-300 000). It is expected that cardiac PET cameras will remain expensive for some time.

In addition, PET cameras have specific infrastructural requirements, as they typically operate with tracers with a very short half-life. In order to be economically viable, a cyclotron needs to be serving four to five PET scanners. This is not much of a problem in denser and wealthy populations, but it is a barrier in more remote and rural areas (i.e. the emerging markets).

As a result of the cost difference and the time required to increase the availability of cameras, provide training and develop the medical infrastructure, the EAG expects that the availability of SPECT cameras will provide a high increase in demand for ^{99m}Tc in emerging markets. The cost impact will be important as SPECT is still the cheapest option and emerging markets (as well as mature markets) are trying to manage the costs of health care. Given uncertainties about the long-term changes, the expected high increase remains for 2030, but with less certainty about the expectation.

Figure 22: Estimated sales of PET and SPECT cameras in the world, except North-America (absolute numbers)



Note: Based on turnover data provided by COCIR – estimation by Technopolis, assuming average cost PET: EUR 1.5 million and SPECT: EUR 0.6 million.

For mature markets there is already a significant number of SPECT cameras in the market; there is a smaller number of PET cameras but purchases are taking place. With the understanding that SPECT cameras are generally replaced by SPECT or SPECT/CT cameras, but with PET cameras resulting in some replacement of SPECT procedures, the EAG expects an ongoing medium growth impact on the use of ^{99m}Tc, but with certainty of this expectation at only a medium level. One key point that leads to additional uncertainty on the impact is that as new SPECT cameras are installed, they will likely be more efficient and thus lead to reduced demand for ^{99m}Tc for the same number of procedures.

Trend 4: SPECT/PET shift

One of the major issues in the discussions on future demand of ^{99m}Tc is whether PET will substitute for ^{99m}Tc-based procedures. From the survey, the top two drivers for decreased ^{99m}Tc demand are related to the use of substitutes (radiopharmaceuticals/contrast agents and modalities). More than 75% of the survey respondents expect that PET and combined PET modalities will eventually be more dominant and will replace SPECT procedures.

The EAG believes that PET modalities will take over a small share of the SPECT procedures between now and 2020/2030, although the level of this shift is expected to be low. However, they do indicate significant uncertainty around this prediction, as there are a number of factors that could impact the substitutability of modalities.

Although the expectation of low substitutability is slightly contrary to the survey results, the EAG provided a critical analysis of the issues facing potential substitutions, which are discussed below. In addition, they recognised that a key uncertainty is related to the timing and pace of substitution; therefore substitution may occur, but likely at a pace slower than predicted by the survey respondents.

There are a number of factors that would prohibit or hinder the substitution of SPECT procedures by other modalities in the next decade or so. First of all, SPECT has particular functionalities that PET does not offer. Moreover, SPECT infrastructure and procedures are generally much cheaper than PET infrastructure and procedures. In addition, PET based infrastructure requires a larger team at the hospital or clinic compared to SPECT infrastructure. Related to this is the level of education and training that is available; in general there is a large SPECT installed base and much experience, whereas PET still has a small installed base and therefore there is less experience with the technology. This will encourage the ongoing use of SPECT procedures and the infrastructure, especially in emerging markets.

In addition, there are only a few PET radiopharmaceuticals approved for use, and the EAG indicated that the development and approval process of new radiopharmaceuticals is difficult and expensive. Coupling this restriction with the fact that not all the current SPECT procedures can be replaced by currently available PET radiopharmaceuticals, again supports the view that substitution of SPECT procedures will not be rapid.

In general, the EAG noted that SPECT provides high quality scans, so there is not an obvious incentive for a quick replacement with other, some currently not-available, PET procedures.

The EAG did recognise that the medical community is looking towards PET as a key modality for the future, but other imaging techniques such as MRI, stress-echo, and functional imaging with PET/CT, are key modalities as well. However, it is expected that all these techniques will be used in a balanced way. PET will replace some SPECT procedures, but will not be able to replace all. PET and other modalities will likely supplement the current SPECT procedures, moving into different areas, but not directly replacing SPECT. In addition, they recognise that some of the PET growth will capture the expected growth in overall diagnostic imaging, meaning that SPECT will have a smaller share of the overall market, but will not see an overall decline in absolute terms.

A note of caution to this assessment is the fact that stability of supply is key to ongoing support for using a certain technology or radiopharmaceutical. If the $^{99}Mo/^{99m}Tc$ supply faces challenges like they have faced recently, this could increase the pace towards technology substitution. A perception of long-term unreliability could have the same effect; however, the survey indicated that most respondents indicated a confidence in having stable supply moving forward.

Taken these issues together, substitution of SPECT by PET would have a negative effect on ^{99m}Tc demand, but in the context of the different issues above the impact will be low.

However, all it takes is one paradigm shift and the system could completely change. If new PET-based radiopharmaceuticals can come onto the market or if there is a breakthrough in the costs of PET infrastructure, there could be a significant substitution of SPECT. For this reason, the EAG noted that there was a great deal of uncertainty related to the issue of substitution and they provided a low certainty related to their prediction of low substitutability.

Trend 5: New radiopharmaceuticals

As indicated by the respondents, the development of new radiopharmaceuticals for PET for studies that are currently done by SPECT or planar, could have a significant negative impact on ^{99m}Tc demand. This expectation is partly based on the fact that there has not been any development of new radiopharmaceuticals based on ^{99m}Tc, while there has been a lot of attention given to the development of new PET tracers. PET always had a different approach; since the early nineties there has been considerable development of tracers.

However, the actual uptake of new radiopharmaceuticals could be quite limited as health regulatory approvals take time and are seen to be quite difficult. Taking a radiopharmaceutical to the market reportedly takes up to EUR 15 million in investment and not many players are willing to take such a risk. This may explain why from the 20 tracers that were in development 10 years ago none has made it to the market. Now only a few are in development for market entry, one of which is a PET tracer for cardiac disease that is in phase 3 clinical trials. If this is approved, there could be a shift to PET for cardiac perfusion. In addition, in some jurisdictions it is difficult to get new radiopharmaceuticals approved for reimbursement through health care systems, supporting the ongoing use of ^{99m}Tc-based radiopharmaceuticals that have already been approved.

The development of other new radiopharmaceuticals, such as for the detection of Alzheimer disease, might increase demand. However, there is still significant uncertainty as to whether radiopharmaceutical companies will invest the necessary funds to develop and approve new radiopharmaceuticals, especially if they are only for detection and not for therapy of the conditions. In addition, there is significant uncertainty as to whether the new radiopharmaceuticals will be for SPECT or other modalities (e.g. PET).

Taken together, the EAG expects a negative impact of new (PET) radiopharmaceuticals on ^{99m}Tc demand, having a medium probability up to 2020, which is related mainly to the new cardiac PET tracer. In the long run, the development of new PET-based radiopharmaceuticals would significantly reduce demand for ^{99m}Tc in mature markets; however, there is still significant uncertainty on whether new radiopharmaceuticals will actually be developed and approved. In emerging markets, the effect of new radiopharmaceuticals is expected to have less of a negative impact on ^{99m}Tc demand between now and 2030 as mature markets are expected to lead the development of new radiopharmaceuticals, with emerging markets picking up the product later.

2.4.4 Assessment of global trends

The EAG made an assessment of the impact and the probability (or certainty) of the five major trends having the impact predicted on the demand for ^{99m}Tc. The impacts and probabilities differ largely in different jurisdictions, especially between emerging and mature markets. Table 5 summarises the assessment of the experts for mature markets; Table 6 for emerging markets.

For mature markets, the EAG expects ageing and prevalence of associated health issues and availability of (improved) SPECT cameras to have a medium positive effect on ^{99m}Tc demand, with medium/high certainty by 2020-2030. Availability of new radiopharmaceuticals may have a large negative impact on ^{99m}Tc demand, but the certainty is rather low as the actual amount and type of new PET tracers is unknown. A shift from SPECT to PET is considered to be unlikely and low-impact: new imaging technologies are expected to be an add-on to the existing set of imaging procedures, rather than replacements for established (and cheaper) technologies. Growing wealth and ongoing urbanisation is expected to have a minor positive effect on demand in mature markets, as they are already reasonably wealthy and urban.

Table 5: Global trends and the expected impacts on ^{99m}Tc demand in mature markets

Trend	Mature markets			
	2020		2030	
	Impact	Probability	Impact	Probability
Growing wealth and urbanisation	+ Low	High	+ Low	High
Ageing prevalence	+ Medium	Medium/High	+ Medium	Medium/High
Availability cameras	+ Medium	Medium	+ Medium	Medium
SPECT/PET shift	- Low	Low	- Low	Low
New radiopharmaceuticals	- Medium	Medium	- High	Low

Note: 2011 EAG workshop: *Impact*: indicates weight (high, medium, low) as well as direction (+/-) that EAG expects the trend to have on ^{99m}Tc demand if it were to occur; *Probability* represents the degree of certainty that the predicted impact will occur.

Table 6: Global trends and the expected impacts on ^{99m}Tc demand in emerging markets

Trend	Emerging markets			
	2020		2030	
	Impact	Probability	Impact	Probability
Growing wealth and urbanisation	+ High	High	+ High	High
Ageing prevalence	+ Low	High	+ High	Medium
Availability cameras	+ High	Medium	+ High	High
SPECT/PET shift	0	Low	- Low	Low
New radiopharmaceuticals	- Low	Medium	- Low	Medium

Note: 2011 EAG workshop: *Impact*: indicates weight (high, medium, low) as well as direction (+/-) that EAG expects the trend to have on ^{99m}Tc demand if it were to occur; *Probability* represents the degree of certainty that the predicted impact will occur.

In emerging ^{99m}Tc markets, the EAG expects global trends to have more impact. Demographic changes, such as growing population, urbanisation and ageing are important trends with a positive effect on the demand for ^{99m}Tc. Growing wealth and urbanisation will certainly have a large positive impact on ^{99m}Tc demand. In the longer term, a high positive impact of ageing and the increased prevalence of related diseases will amplify this predicted growth, with medium probability. The growing availability of cameras (both new and second hand)[9] will have a large impact on the ^{99m}Tc demand by 2030, with a high degree of certainty. In emerging markets, no impact is expected from a shift from SPECT towards PET cameras by 2020, for which the EAG has low certainty on the

[9] The shift from single SPECT cameras to multiple modality cameras (i.e. SPECT/CT and SPECT/MR) may play a significant role in the emergence of a second hand market. An EAG participant stressed that even today second-hand cameras with relatively high quality can be obtained.

prediction. A low impact is expected from a shift from SPECT towards PET cameras and use of new radiopharmaceuticals in emerging markets by 2030; for the former, the EAG has low certainty on the prediction while they have more certainty on the latter prediction.

2.4.5 Price elasticity

In relation to the impact of changing costs on demand, we sought further information through the survey on how the respondents see price as influencing their choice. We asked them at what price increase of a ^{99m}Tc-based radiopharmaceutical (of which the ^{99m}Tc is often only a minority component) they would decide to move to alternative modalities. The responses indicated that a price increase of 230% *of the radiopharmaceutical* would lead to 1/3 decrease in ^{99m}Tc-based radiopharmaceuticals compared to current demand, while a 500% price increase would result in a 2/3 decrease, and a 1000% increase would be necessary to decrease demand for ^{99m}Tc-based procedures to zero (see Table 7). From these results, ^{99m}Tc demand appears to be quite inelastic – meaning that changes in price have smaller changes in the overall demand of the product.

However, we recognise that these figures should be treated with care, as a more elaborate study would be required to accurately determine the price elasticity of ^{99m}Tc demand. Such a study may be directed at a different audience that was not well represented in this survey, i.e. the economic decision makers within hospitals, clinics, insurance companies, Medical Directors, CFOs, administrators, etc.

Table 7: Price elasticity

Price increase	Decrease of procedures compared to current level
230%	33%
497%	66%
999%	100%

3. Demand Scenario

3.1 Discussion

In this document we have gathered the expectations of over 700 experts in diagnostic imaging. The results from the survey and the views of the Expert Advisory Group have allowed for an educated analysis of the long-term future demand for ^{99m}Tc. The EAG analysis of the key drivers of change has validated the survey results, recognising the significant uncertainty when discussing future demand almost 20 years out.

The EAG was not able to arrive at unanimous agreement on whether ^{99m}Tc would be replaced in the very long run. However, given the uncertainties around substitution, the expert panel believes that the pace of change is slow and before 2030 there will not be substitution at such a level to actually reduce ^{99m}Tc demand. In addition, the other external factors potentially affecting ^{99m}Tc demand will slow historical growth, but will not remove its overall demand.

Another key element of the survey results, and one agreed to by the EAG, is the conclusion that the majority of the actions taken during the 2009-2010 shortages will not be permanent. The exception seems to be some cases where more efficient elution from the generator and more efficient patient scheduling may remain. Again, these results may change in the future if there is pressure from tightening reimbursement rates or increased costs; for example, better use of generators may result in cost savings. However, expectations today are that the majority of changes have or will return to pre-shortage practices.

Given its analysis, the EAG endorsed the results of the survey, and found it probable that ^{99m}Tc demand will grow approximately 20% between 2010 and 2020, and 25% between 2010 and 2030 in mature markets; 40% between 2010 and 2020, and 50% between 2010 and 2030 in emerging markets. This represents an average annual growth rate of approximately 1.1 to 1.85% in mature markets and 2 to 3.4% in emerging markets, assuming straight-line growth from 2010 for both 2030 and 2020 (respectively). Incorporating the two points in the same growth line provides a representative annual growth for the mature markets as 1.84%/a from 2010 to 2020 followed by annual growth of 0.4%/a from 2020 to 2030; for emerging markets, this is 3.42%/a to 2020 followed by 0.69%/a between 2020 and 2030. It should be noted that the later periods are subject to more uncertainty.

The EAG furthermore concluded that unexpected changes of any kind could have large effect on demands, especially if changes take place in jurisdictions where demand is currently large (i.e. Europe and North-America). The EAG recognised the importance of costs of ^{99m}Tc with regard to this, and emphasised that reimbursement rates for technetium-based procedures and competing imaging modalities play a crucial role.

With regard to the results concerning subsets of the total survey sample size, it should be noted that the results of smaller subsets of respondents (i.e. emerging markets and division towards expertise) is subject to higher uncertainty, because of smaller sample size. As a result, the observed variations in answers of the different populations within the sample (i.e. maturity of markets, expertise) were most often not statistically significant[10].

[10] Using a 95% confidence interval.

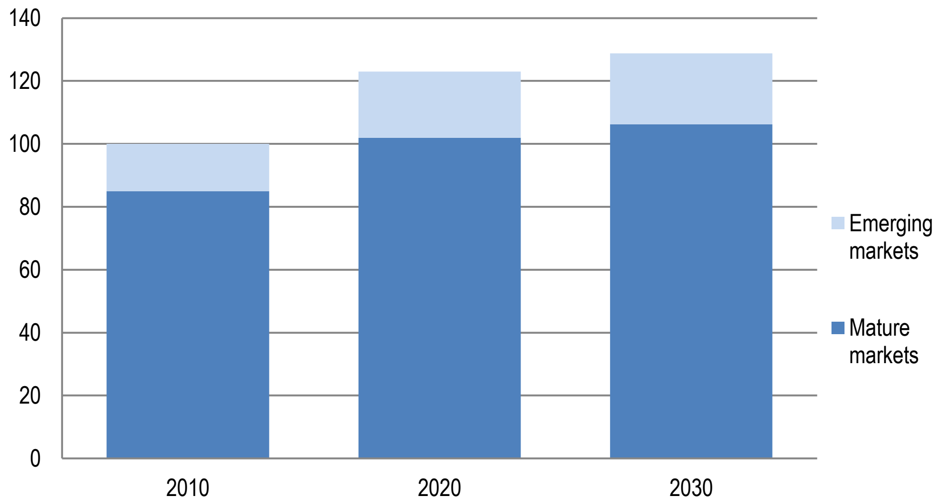
3.2 Scenario of ^{99m}Tc demand

To construct a quantitative future demand scenario based on the results of the survey and the input of the EAG, we would require a solid baseline on use in the various regions in the world. Although efforts were made, data on ^{99m}Tc consumption was not available for all regions. Various (sometimes conflicting) figures exist on the number of procedures undertaken annually, and these are not provided for all the various regions examined in this global survey.

Yet, recognising the uncertainties inherent in a long-run future forecast, a general direction and size of changes in demand are sufficient. The scenario in Figure 23 provides that direction and size of change taking 2010 as 100 and then applying the growth rates from the survey: approximately 20% between 2010 and 2020, and 25% between 2010 and 2030, in mature markets; 40% between 2010 and 2020, and 50% between 2010 and 2030 in emerging markets. These growth rates were applied based on data that mature ^{99m}Tc markets represent 85% of the total market and emerging ^{99m}Tc markets represent 15%.[11]

The scenario does not provide a growth path for ^{99m}Tc demand as the survey only provided data on two distinct points: 2020 and 2030. We did not want to provide a growth path in this document that may be misleading to readers.

Figure 23: Expected future demand of ^{99m}Tc, 2010 = 100



3.3 Scenario of ^{99}Mo demand

The original purpose of the overall project was to understand the impacts of future demand on the need for new ^{99}Mo-producing infrastructure. This question is important given the required level of investment and decision makers need to have information to allow them to assess whether or not the investment will be used in the future, at least for a period long enough to make the investment worthwhile.

From the results, it is clear that there will be an ongoing demand for ^{99m}Tc at least until 2030. Although views among survey respondents varied, the overall results show continued, albeit slow, growth. The share of ^{99m}Tc-based procedures within the overall imaging diagnostic market is expected to fall, but the absolute demand for ^{99m}Tc will not decrease between now and 2030.

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[11] Derived from data presented by Natural Resources Canada during NEA Workshop on Security of Supply of Medical Isotopes, 29-30 January 2009, and updated with information on Australian demand.

Given that the majority of global ^{99m}Tc supply comes from ^{99}Mo produced by the irradiation of targets in research reactors, we can derive a reasonable idea of the expected future need for ^{99}Mo from our results. Based on the survey results, we can assume that the same amount of ^{99}Mo is required to produce the ^{99m}Tc used globally (i.e. elution efficiencies are not sufficiently applied to result in less ^{99}Mo being required for the same amount of ^{99m}Tc).

Prior to the 2009-2010 shortages, the global demand for ^{99}Mo for ^{99m}Tc production was approximately 12 000 6-day curies per week. Although revised demand numbers are not currently available, it has been reported that following the shortages, world demand was approximately 9 000 6-day curies per week. More recent information from the supply chain has indicated that demand may be returning closer to pre-shortage levels. Looking at both a 12 000 and 9 000 starting point, Figure 24 and Figure 25 show the forecasted demand of ^{99}Mo for 2020 and 2030.

Figure 24: Forecasted Demand of ^{99}Mo; 2010 demand=12 000 6-day curies of ^{99}Mo per week

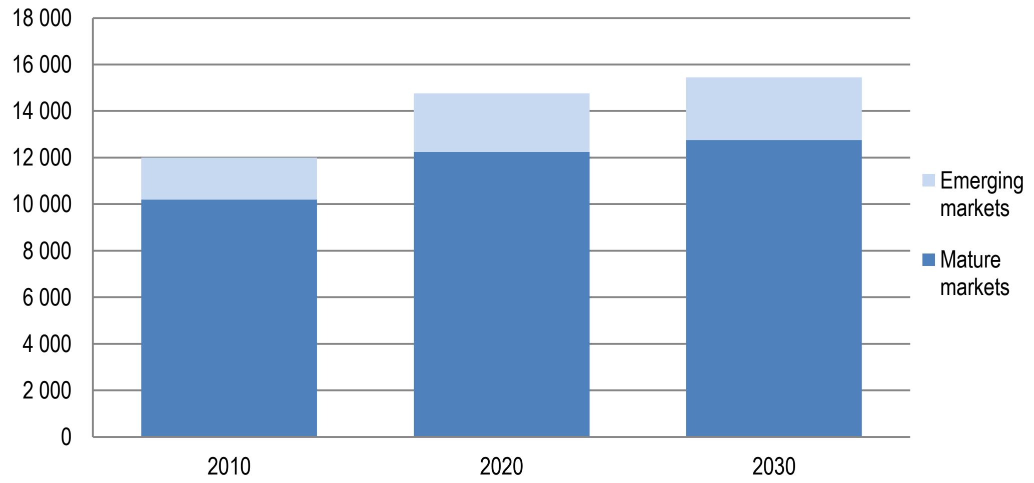
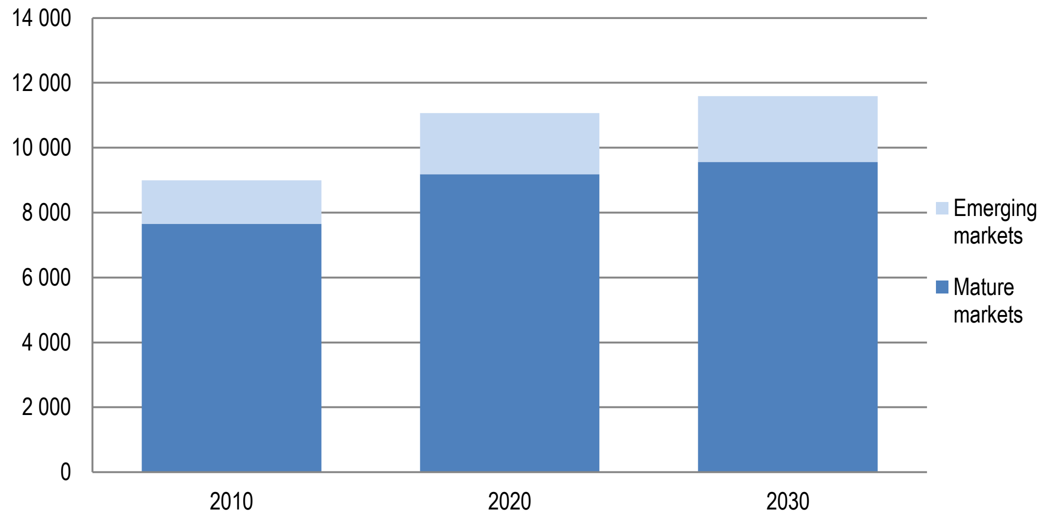


Figure 25: Forecasted Demand of ^{99}Mo; 2010 demand=9 000 6-day curies of ^{99}Mo per week



4. Conclusions

The HLG-MR requested that a demand study be undertaken to provide an indication of the long-term demand for ^{99}Mo/^{99m}Tc. This request was based on significant uncertainty in the industry as to the future of these isotopes, with supply chain participants suggesting different futures.

The uncertainty came from whether changes in ^{99m}Tc use during the 2009-2010 shortages would remain after supply returned to normal. In addition, there are a number of recognised external forces that could affect future demand, including the development of other modalities, emerging ^{99m}Tc markets, the effects of changing reimbursement rates in some jurisdictions, expectations of future stability of ^{99m}Tc supply and demographic trends.

The results from the survey and the EAG analysis has provided a better understanding of the possible long-term effects of these changes, resulting in an expected steady growth of ^{99m}Tc demand, at a slow pace. Demand is expected to grow faster in emerging markets, but from a smaller base. The results show that substitution of ^{99m}Tc-based procedures by alternative modalities or isotopes will likely have an impact on the overall share of ^{99m}Tc in diagnostic procedures, but will not reduce the absolute amount of ^{99m}Tc being demanded.

This forecast for ^{99m}Tc growth translates reasonably to a similar situation for ^{99}Mo demand, although it is recognised that increased direct production of ^{99m}Tc may also occur. If the changes seen during the 2009-2010 shortage related to efficient use of ^{99m}Tc were predicted to continue, there would have been a greater impact on ^{99}Mo demanded. However, survey results indicate that most of the pre-shortage practices returned to normal after the shortages ended. Based on these results, it is reasonable to predict that ^{99}Mo demand will continue to grow at levels equal to approximately two percent annually until 2020 and then levelling off to a growth rate of less than one percent annually until 2030.

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Appendix A

Expert Advisory Group

Table 8: The Expert Advisory Group

Name	Organisation/company
Prof. Dr. med. Jörg Mahlstedt	Vorsitzender des Vorstandes des BDN, Germany
Prof. Dr. Aleander McEwan	Director of Oncological Imaging at Cross Cancer Institute; Professor and Chair, Dept. Oncology, University of Alberta, Canada
Richard J. Flanagan, PhD	Ex-CEO Draximage, Canada
Dr. Fred Verzijlbergen	European Association of Nuclear Medicine (EANM); St. Antonius Hospital, Netherlands
Prof. Richard Underwood	Professor of Cardiac imaging, Imperial College, London, United Kingdom
Dr. Maurizio Dondi	Head of Nuclear Medicine Section, International Atomic Energy Agency (IAEA), Vienna, Austria
Dr. Steven M. Larson	Memorial Sloan-Kettering Cancer Center, United States
Marc Gheeraert	Philips Healthcare International; President of AIPES
Prof. Dr. Tomio Inoue	Yokohama City University, Graduate School of Medicine, Japan

Appendix B

Survey design

1. Technetium-99m Demand Assessment Survey

Welcome to the survey site where you can answer the questionnaire regarding the global future demand for technetium-99m (^{99m}Tc) for medical use.

The OECD Nuclear Energy Agency (NEA) has become involved in global efforts to ensure a reliable supply of molybdenum-99 (^{99}Mo) and its decay product, ^{99m}Tc. The NEA is seeking to better understand future demand for ^{99}Mo/^{99m}Tc and/or related nuclear medicine procedures, given the uncertainty in future ^{99m}Tc demand and the lack of a long-term comprehensive demand overview that includes recent changes in the supply chain. As a result, the NEA has partnered with the Technopolis Group to assess future demand of ^{99}Mo/^{99m}Tc out to 2020 and 2030.

Forecasting is not easy, especially when the future horizon is far ahead in time. However, forecasting is important to get an understanding of what actions need to be taken today to meet tomorrow's demand. Therefore, we are seeking your expert opinion about the future medical demand for ^{99m}Tc. Your answers will be important for policy and decision making processes that can affect the future production of ^{99m}Tc.

To ensure the best forecast possible, we are inviting experts from a wide range of related disciplines to respond to the survey (such as nuclear medicine practitioners, users of alternative imaging modalities, and others involved in ^{99m}Tc-based medical imaging). We would be grateful if you could take approximately 15-20 minutes to complete the following survey.

Each page has a status bar indicating your progress. It is possible to browse between pages, but please make sure that you answer as many questions as possible. The survey addresses the following topics:

- General information about you.
- Drivers of change of ^{99m}Tc demand.
- Price elasticity and supply.
- Strategies to deal with the ^{99m}Tc shortage.
- Imaging technologies in your country.
- Future of diagnostic imaging.
- Future of ^{99m}Tc-based imaging.

This survey is being sent to a broad audience. As a result, there may be some questions that you will not be able to answer based on your experience. In this case, please feel free to leave the question unanswered; however, please answer all the questions where you have experience/knowledge.

It is OECD/Technopolis policy to protect the privacy of the respondents to this survey at all times. Therefore, results will not be connected to individuals or institutions. Any reference to survey results will only include a list of participating disciplines and countries.

In case you still have questions, please do not hesitate to contact us. For more information about the NEA's work related to medical isotopes, click here.

Thank you very much for your cooperation.

Kind regards,

Chad Westmacott
www.oecd-nea.org

2. Personal details

Please fill in your personal details. This information will be kept confidential; it will only be used in case of a technical problem and to be able to send you the final report.

1. Your personal details:

Name:

Title:

Organisation:

Main job role/function

City:

Country:

Email Address:

2. Your medical or imaging speciality (multiple answers possible)

- ☐ Medical Doctor: Imaging specialist: Nuclear Medicine
- ☐ Medical Doctor: Imaging specialist: Radiology
- ☐ Medical Doctor: Imaging specialist: Both
- ☐ Medical Doctor: Clinical specialist: Oncologist
- ☐ Medical Doctor: Clinical specialist: Neurologist
- ☐ Medical Doctor: Clinical specialist: Cardiologist
- ☐ Medical Doctor: Clinical specialist: Internist
- ☐ Medical Doctor: Clinical specialist: Other
- ☐ Medical Physicist
- ☐ Physicist
- ☐ Pharmacist
- ☐ Pharmacologist
- ☐ Radiochemist
- ☐ Biochemist
- ☐ Imaging analyst (ICT)
- ☐ Chemical technician
- ☐ Radiology technologist
- ☐ Nuclear medicine technologist
- ☐ Researcher

Other (please specify)

3. Your expertise in specific imaging modalities

- ☐ Nuclear imaging based on ^{99m}Tc, including planar and SPECT, SPECT/CT, and SPECT/MRI
- ☐ Nuclear imaging based on other isotopes, including PET, PET/CT and PET/MRI
- ☐ Other types of imaging, including X-Ray, CT, MRI, Ultrasonography
- ☐ User of medical diagnostics, e.g. doctors of Internal Medicine, cardiologist, oncologist, etc.
- ☐ None

Remarks

3. Drivers of Change in ^{99m}Tc Demand

There are many parameters that will influence the future use of ^{99m}Tc. We have identified a list of drivers that may change the future demand for ^{99m}Tc. These drivers can have both positive and negative effects on the demand for ^{99m}Tc in your country.

4. Please choose drivers that will lead to increasing or decreasing demand for ^{99m}Tc in your country.

Mark the five (5) strongest drivers that will lead to increased demand for ^{99m}Tc (1st column), and the five (5) strongest drivers that have a negative effect on demand for ^{99m}Tc (2nd column). You may choose drivers twice; both as positive or as negative driver.

	Strong driver leading to increased demand for ^{99m}Tc	Strong driver leading to decreased demand for ^{99m}Tc
Change in cost of technetium-based imaging	☐	☐
Change in income received for diagnostic procedure	☐	☐
Stable availability of ^{99m}Tc in future	☐	☐
Increased efficiency of use of ^{99m}Tc in clinic/radiopharmacies	☐	☐
Increase in ease of use or quality of other modalities compared to ^{99m}Tc-based technologies	☐	☐
Development of radiopharmaceuticals/contrast agents for alternative modalities that would substitute for ^{99m}Tc-based imaging	☐	☐
Changing prevalence of medical conditions (e.g. heart disease) or move towards personal medicine	☐	☐
Changing use of diagnostics due to growing wealth in national economy (patients can afford diagnostics)	☐	☐
Government policies	☐	☐
Regulatory limitations to approving new radiopharmaceuticals	☐	☐
Concerns related to radiation doses (both public opinion and regulatory actions)	☐	☐
Availability of improved technologies for ^{99m}Tc-based modalities	☐	☐
Availability of hardware and infrastructure replacing ^{99m}Tc-based imaging	☐	☐

4. ^{99m}Tc Supply

5. Could you indicate in qualitative terms how stable you expect the supply of ^{99m}Tc to be between now and 2020/2030 in your country?

	Extremely unstable	Unstable	Moderately unstable	Moderately Stable	Stable	Very stable	No opinion
2011 to 2020	○	○	○	○	○	○	○
2021 to 2030	○	○	○	○	○	○	○

6. During the past 2 years ^{99m}Tc supply has been under pressure. Did you experience any effects of the shortage of ^{99m}Tc in your day-to-day activities?

○ yes

○ no

7. Would you be able to indicate the impact of any strategies or actions undertaken at your institution to cope with the low supply of ^{99m}Tc?

○ yes

○ no

6. Strategies to deal with Technetium-99m shortage

8. What was your strategy to cope with the low supply of ^{99m}Tc during the shortage period? Please indicate the degree of the reduction of ^{99m}Tc used in your institution as a result of the following strategies, when compared to normal operations before the ^{99m}Tc shortages in 2009/10.

	Great reduction (>30%)	Large reduction (16-30%)	Smaller reduction (0-15%)	No reduction (0%)
More efficient elution from generator	○	○	○	○
More efficient patient scheduling	○	○	○	○
Reduction of doses in procedures	○	○	○	○
Sourcing from centralised radiopharmacy/sharing generators	○	○	○	○
Use of alternative isotopes using planar or SPECT cameras	○	○	○	○
Use of alternative modalities	○	○	○	○
Lost procedures: no diagnostics used	○	○	○	○
Other strategies (specify the strategy or strategies below)	○	○	○	○

Please specify "other"

9. Do you expect that the changes that were made during the recent supply shortage will continue, resetting demand for ^{99m}Tc at a lower level than before the recent shortage?

	Practices have returned to normal	Some changes will likely remain, but not all	Most changes are permanent	Don't know
More efficient elution from generator				
More efficient patient scheduling				
Reduction of doses in procedures				
Sourcing from centralised radiopharmacy/sharing generators				
Use of alternative isotopes, using planar or SPECT cameras				
Use of alternative modalities				
Lost procedures: no diagnostics used				
Other strategies (specified in previous question)				

7. Future of diagnostic imaging and use of ^{99m}Tc

The questions on this page will address your expectations with regard to the use of diagnostic imaging and ^{99m}Tc in the future.

10. Do you think that for your country the total number of diagnostic imaging procedures(including SPECT, CT, MRI, PET, etc.) will increase, remain the same or decrease in the future compared to the end of 2010?

Please fill in the relative change, compared to 2010. For example, if you think that the total number of scans will double, select: "+81-100%".

	% change in total number of procedures (compared to 2010)
Mid-term (2020)	
Long term (2030)	

11. What do you estimate the future medical use of ^{99m}Tc-based procedures will be as compared to the current use (end of 2010) in your country?

Please fill in the relative change, compared to 2010. For example, if you think that the total number of ^{99m}Tc-based procedures will double, select: "+81-100%".

	% change in total number of ^{99m}Tc procedures (compared to 2010)
Mid-term (2020)	
Long term (2030)	

12. Do you foresee substitution of ^{99m}Tc (at least partially) by alternative imaging isotopes or modalities?

yes

no

8. Substitution of ^{99m}Tc

13. How likely do you think it is that the medical use of ^{99m}Tc will be substituted (at least partially) by other imaging modalities in your country?

	Possibly	Probably	Very probably	Definitely	Don't know
Mid-term (2020)					
Long term (2030)					

14. How large do you think that the substitution of ^{99m}Tc-based procedures will be in your country?

	0-10%	10-25%	25-50%	>50%	Don't know
Mid-term (2020)					
Long term (2030)					

15. Given your previous answers on the substitution of ^{99m}Tc. What alternatives will substitute for ^{99m}Tc by 2020 and 2030 in your country? Please mark the substitutes you expect to replace, at least partially, ^{99m}Tc.

	2020	2030
CT		
MRI (incl. fMRI)		
Ultrasonography		
Optical imaging		
Planar imaging using alternative isotope (not ^{99m}Tc)		
SPECT using alternative isotope (not ^{99m}Tc)		
SPECT/CT using alternative isotope (not ^{99m}Tc)		
SPECT/MRI using alternative isotope (not ^{99m}Tc)		
PET		
PET/CT		
PET/MRI		
Other (Please specify below)		

Please specify "other"

9. Price elasticity

16. Suppose that the price of radiopharmaceutical was the only changing variable (reimbursement rates/price of procedures remaining constant). Could you please indicate at what price increase you would expect a reduction in the number of ^{99m}Tc-based procedures at your facility at the increments presented below.

Example: In practice X, we would reduce procedures by 1/3rd if the price was 2.5 times higher than at the current situation; by 2/3rd if the price was 5 times higher; and we would stop using ^{99m}Tc-based procedures if the price was 10 times higher. Accordingly, we fill in the table: 2.5 in the first row, 5 in the second and 10 in the third.

If you are unable to make an estimate, please ask the management of your institution to do so, if possible. If you are unable to answer the question, please leave it unanswered.

Reduction of 1/3rd of the total number of procedures	
Reduction of 2/3rd of the total number of procedures	
Stop using ^{99m}Tc-based procedures	

10. Conclusion: THANK YOU

This is the end of the questionnaire. Thank you very much for your cooperation.

The results of this survey will serve as input for the development of future demand scenarios for ^{99m}Tc (and its parent isotope ^{99}Mo). This information is important for determining the best approaches to addressing the issues related to security of supply of these vital medical isotopes. Your input helps us develop the best possible assessment of future demand.

If you provide us with your e-mail address, we will send you a final copy of the report that will be developed. This report is expected to be completed by mid-2011.

If you have any overall comments that you would like to provide either on future demand or on this survey, please do so in the box below.

17. Any Comments?

Appendix C

Respondents per country

Country	# of respondents
Algeria	1
Argentina	1
Australia	40
Austria	2
Belgium	16
Brazil	1
Canada	25
Chile	1
China	12
Croatia	4
Czech Republic	2
Denmark	4
Egypt	1
Finland	6
France	52
Germany	18
Hungary	7
Iceland	3
India	3
Indonesia	1
Iran	1
Ireland	5
Israel	5
Italy	23
Japan	7
Korea, Republic of	3

Country	# of respondents
Latvia	1
Malaysia	1
Malta	1
Mongolia	1
Morocco	2
New Zealand	3
Norway	10
Poland	4
Portugal	4
Puerto Rico	9
Romania	7
Russian, Feration	2
Saudi Arabia	2
Singapore	2
South Africa	1
Spain	22
Sweden	1
Switzerland	4
The Netherlands	12
Turkey	2
United Kingdom	23
Ukraine	1
Undefined	49
United States	304
Vietnam	1
Total	**713**

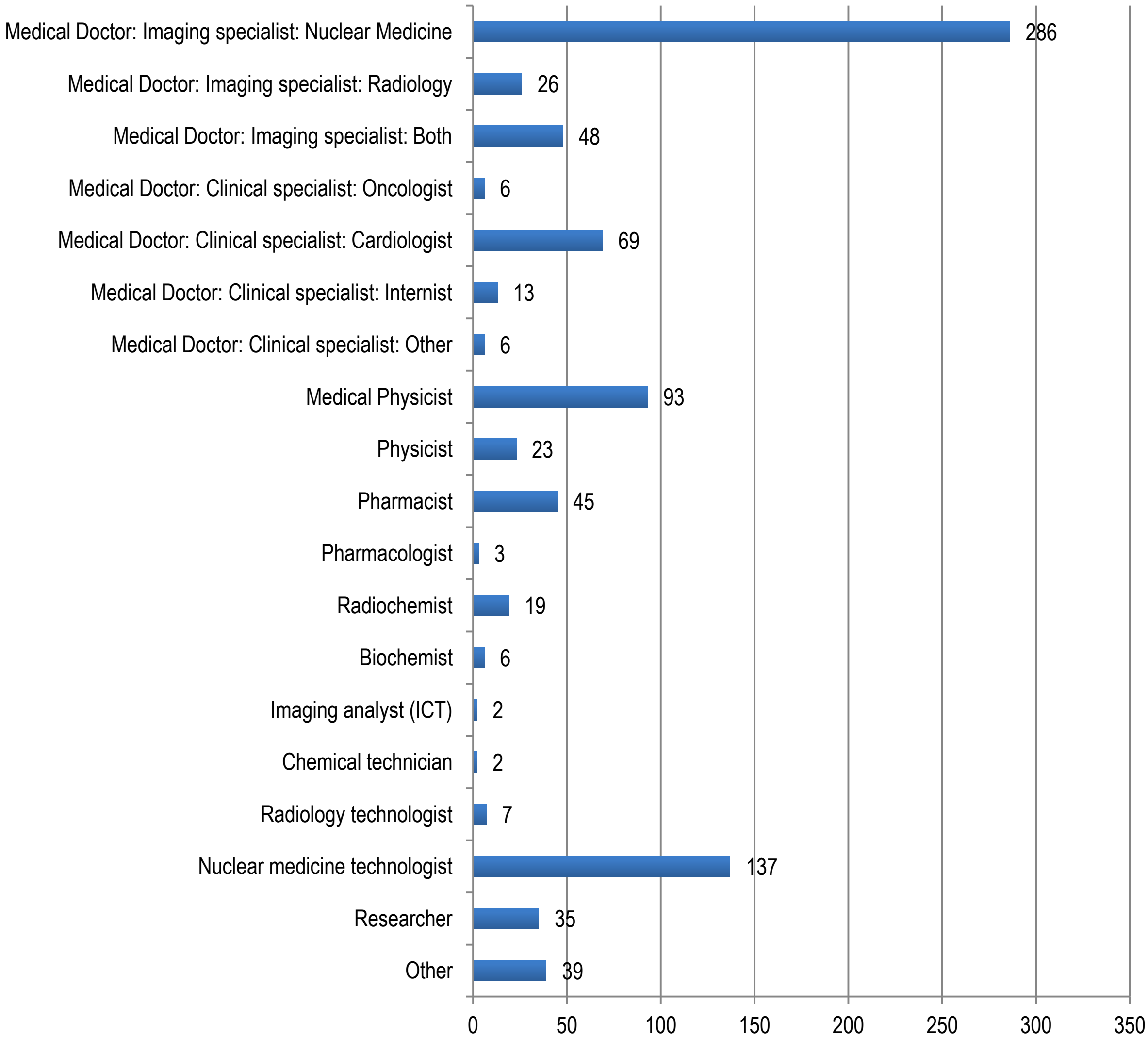
Appendix D

Backgrounds and expertise in the sample

Professional background of respondents

In the survey we have asked the interviewees to indicate what their professional background is. The figure below shows the distribution of the respondents over professional backgrounds, in absolute terms.

Figure 26: Professional background



Expertise of the repondents

In the survey we have asked the interviewees for an indication of their expertise with regard to diagnostic imaging. The figure below shows the distribution of the respondents over the expertises, in absolute terms.

Figure 27: Imaging expertise