# Key findings

Technetium-99m (Tc-99m) is the most commonly used radioisotope in nuclear medicine (NM) diagnostic scans. It is essential for accurate diagnoses of diseases and effective patient care in health systems of OECD countries. For example, Tc-99m is used for diagnoses of cancer, heart disease and neurological disorders including dementia and movement disorders.

This report presents findings of joint work between the OECD Health Committee and the OECD Nuclear Energy Agency (NEA) on the supply of Tc-99m. The geographic focus is on Australia, Canada, Japan and the United States, the four non-European countries that are the largest end-users of Tc-99m, as well as countries of the European Union and Switzerland. Collectively, these countries account for most of global demand.

## Some health systems rely heavily on Tc-99m and substitution would be costly

Nuclear medicine (NM) diagnostic scans can image and demonstrate the physiology and function of many body parts, including the heart, the skeleton, the thyroid and salivary glands, and the brain, supporting a broad range of medical specialities. NM scans involve the administration of trace amounts of radioactive pharmaceuticals, referred to as radiopharmaceuticals, into a patient's body. Preparation of a patient dose involves the "labelling" of a non-radioactive biomolecule, which is specific to the organ system or anatomical area scanned, with a radioactive medical isotope. Technetium-99m (Tc-99m) is used as the medical isotope in 85% of NM diagnostic scans performed worldwide, or around 30 million scans, every year. Once internalised by a patient, radiopharmaceuticals are physiologically distributed within the body. As they undergo radioactive decay, they emit gamma photons, which are captured by gamma cameras. Each detected photon is registered as a point. Hundreds of thousands of points are collected during a scan to form an image. NM is called a *functional* imaging modality as it visualises normal and abnormal organ and tissue physiology, based on the bio-distribution of the radiopharmaceutical used. It thus allows assessing the function or physiology of various tissues, organs or organ systems. This is in contrast to other common imaging modalities, such as x-ray, computed tomography (CT) and magnetic resonance imaging (MRI), which characterise the body anatomy and structure but not necessarily its functions, and are therefore referred to as *anatomical* imaging.

No comparable substitutes to Tc-99m are available in indications such as breast, melanoma and head/neck cancer sentinel lymph node studies, and in a range of diagnostics in children, in particular for paediatric bone and renal scans. There are also some areas in which Tc-99m-based scans are the preferred standard of care, such as whole-body bone scans to screen for skeletal metastases.

Although substitution of Tc-99m is possible, notably for cardiac and bone scans, which are a large share of all Tc-99m-based diagnostic scans, effective substitution of these scans would require significant long-term investments in alternative scanning equipment and human resources. There is currently insufficient equipment and a lack of trained personnel to increase substantially the use of alternative imaging modalities, including positron emission tomography (PET), computed tomography (CT) and magnetic resonance imaging (MRI). PET scans in particular also tend to be more expensive than Tc-99m-based scans, so that substitution would imply increases in current health expenditures. CT can produce cross-sectional images of tissue density by transmitting x-rays through a patient and registering the “shadows”. In MRI, patients are put into a strong pulsing magnetic field, which causes hydrogen atoms to line up and relax in an orderly fashion with each pulse, changes that are recorded and converted into detailed images. PET, on the other hand, is another form of NM diagnostic imaging, using radioisotopes other than Tc-99m that emit two photons that move in opposite directions and are captured by positron emission tomography – computed tomography (PET/CT) cameras for imaging.

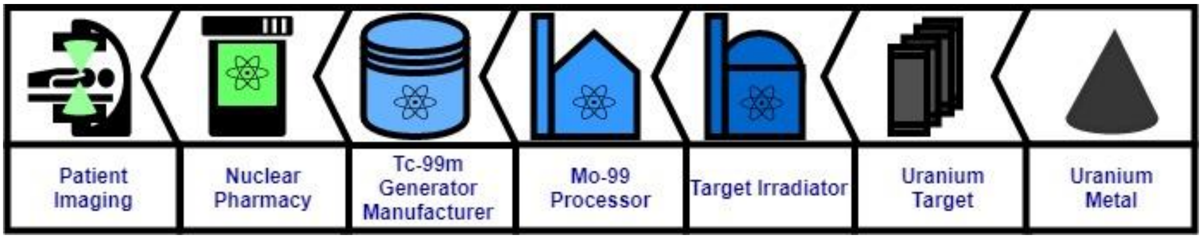
As in other domains of medicine, NM practice patterns and the use of Tc-99m-based diagnostic scans vary markedly between countries. This is true in terms of the numbers of Tc-99m scans performed relative to the population and in terms of the share of each organ system in the total number of scans. While the reasons for this variation are multiple and sometimes unclear, it means that the potential impacts of future shortages of Tc-99m and the scope for substitution are not the same across countries. Scan rates vary from nearly 50 scans per 1 000 people in Canada and between 30 and 40 scans in Belgium and the United States to as few as 2-3 scans per 1 000 population in Estonia and Poland. Among five of six countries for which data are available, bone and cardiac scans are the most common types of scan, collectively accounting for between 60% and 76% of all scans. Bone scans are more common than cardiac scans in all countries for which data are available, except in the United States, where cardiac scans are 55% of the total and bone scans only 14%. Germany is another notable exception, where endocrine scans are more than 40% of the total while this share is less than 10% in all other countries.

## Technetium-99m supply is a complex and just-in-time activity, and supply remains unstable

The supply of Technetium-99m (Tc-99m) requires continuous production in a complicated and aging supply chain that combines a mix of governmental and commercial entities. Governments essentially control both ends of the supply chain, i.e. uranium supply and policy on health care provider payment, as well as the regulatory framework. The central steps of the supply chain are mainly commercial. Tc-99m is obtained from radioactive decay of its parent isotope, Molybdenum-99 (Mo-99). While Mo-99 has a half-life of 66 hours, the half-life of Tc-99m is only six hours. Therefore, these products cannot be stored and supply is a just-in-time activity that requires sufficient capacity for ongoing production plus a reserve in case of unplanned outages.

To prepare doses for patient scans, specialised pharmacies, called nuclear pharmacies, elute Tc-99m daily from Mo-99 containers. These containers are called *Tc-99m generators* and their manufacturers require marketing authorisation by the pharmaceutical regulatory authority responsible for each jurisdiction to sell them. Pharmaceutical companies, which include firms specialised in nuclear medicine as well as large and diversified firms, manufacture and sell Tc-99m generators commercially. They buy Mo-99 in bulk from processing entities that transform irradiated uranium into a Mo-99 liquid used to fill Tc-99m generators. Processors procure uranium as a raw material and contract with nuclear research reactors (NRRs) that perform irradiation services. Figure 1 shows the main steps in the supply chain. NRRs, also referred to as irradiators, have a range of purposes aside from medical isotope production and were not originally designed for the commercial supply of medical isotopes. Their activities include nuclear technology testing, fundamental scientific research and industrial isotope production. Some of these activities are undertaken on a commercial basis; however most commonly they are funded by governments, in part or in full.

#### Figure 1. Simplified structure of the Mo-99/Tc-99m supply chain




Note: Technetium-99m (Tc-99m) generators are specialised containers of Molybdenum-99 (Mo-99) from which nuclear pharmacies elute Tc- 99m to prepare patient doses.
Source: Authors

Supply of Tc-99m to health care providers has been unreliable over the past decade due to unexpected shutdowns and extended maintenance periods at several of the facilities in the supply chain. Many of these facilities, including NRRs and processors, are relatively old. In response to the severe supply crisis in 2009-10, the OECD Nuclear Energy Agency (NEA) established the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) to help secure stable and economically sustainable supply of these products in the short- and long-term. In a 2010 economic study of the supply chain, the NEA concluded that supply was unreliable because prices of Mo-99 were too low to allow NRRs to cover their full costs of production and to invest in sufficient production and reserve capacity. Government funding of NRRs allowed Mo-99 production to continue despite unsustainably low prices but also distorted price signals in the supply chain. The HLG-MR has since made efforts to encourage price increases in the supply chain, a policy principle referred to as full-cost recovery (FCR) in the framework for supply security developed by the HLG-MR.

While progress has been made since past supply crises, the inability of NRRs to increase prices sufficiently and the resulting lack of reserve capacity at various steps of the supply chain leave supply vulnerable and the market economically unsustainable. Supply frailty was demonstrated between late 2017 and early 2019, with chronic shortages occurring regularly due to unplanned outages.

## The main barrier to price increases is found in the supply chain

The main barrier to full-cost recovery (FCR) is found in the current structure of the supply chain, the cost structure and funding of NRRs and in the resulting behaviours of supply chain participants. NRRs are capital-intensive enterprises that have high fixed costs while irradiation services for Mo-99 production have low marginal costs. Due to transport constraints and radioactive decay, NRRs are captive to local processors and have little choice but to continue supplying irradiation services even at prices that are too low to cover fixed and marginal costs, while continued government funding allows their operations to be sustained. Downstream, competition creates a disincentive for each supply chain participant to increase prices unilaterally as this might result in losing business to a competitor. Processors compete globally for business from Tc-99m generator manufacturers, which are commercial organisations that in turn compete for business from nuclear pharmacies and health care providers.

## Health care provider payment must not be neglected, but provider incentives to contain the cost of Tc-99m are likely to be weak in most cases and are not the main barrier to price increases

Although the responsiveness of payment mechanisms and financial incentives to health care providers must not be neglected in further efforts to increase prices, health care provider payment is not the main barrier. Tc-99m represents a small item in the overall cost structure of nuclear medicine (NM) providers. The price increase necessary to achieve FCR is currently estimated to be less than USD 1 per patient dose on average, a 4% increase of the average price of Tc-99m at the point of dispensing. Health care providers could absorb such a price increase in most cases.

Providers of NM diagnostic scans are usually paid prospectively fixed amounts for their services, rather than being reimbursed for costs actually incurred. They therefore bear the financial risk related to differences between payments and their input costs. This means that they have an incentive to control input costs, including the cost of Tc-99m. Such incentives are stronger where payments are low relative to input costs and where providers have little scope to substitute activities towards more profitable ones, which can allow them to cross-subsidise activities that incur losses.

Three types of health care providers deliver Tc-99m-based scans to patients: office-based physicians, other types of outpatient providers (such as diagnostic centres and radiological clinics) and hospitals (to in- and out-patients). Outpatient scans represent the majority of all scans. While payment amounts for all provider types are set prospectively, payments cover service bundles of varying breadths. Outpatient providers are typically paid fee-for-service (FFS), i.e. a fixed fee that applies to the entire diagnostic service and covers all provider costs related to that service. The breadth of bundling tends to increase with the provider size and scope of activities. Hospitals are often paid for broad service bundles, such as all services related to a diagnosis-related group (DRG) for inpatient care or through global budgets. Providers are required to cover their costs for procuring Tc-99m from these payments in all countries, except some providers in four countries. All providers in Belgium and Japan, outpatient providers paid FFS in Germany, and specialists paid FFS by Medicare in the United States receive separate payments for radiopharmaceuticals used. Increases in Tc-99m prices may be more difficult to absorb for small providers, such as office-based NM specialists, who rely exclusively on NM scans for revenue and whose FFS payments are not responsive to input costs. Hospitals that generate revenue from a wide range of activities may be able to absorb cost increases more easily.

While a detailed analysis of the strength of financial incentives for providers to contain costs of Tc-99m is not possible with the data available, such incentives are probably relatively weak. The average cost of an individual patient dose at the point of dispensing of Tc-99m is estimated to be around 21 USD, which is small relative to the broader provider payments for the diagnostic service, the DRG or the global budget. Where providers receive unbundled payments that specifically cover the cost of Tc-99m, providers have a weak incentive to contain costs when such payments are sufficient to cover actual costs of purchasing Tc-99m, but may resist cost increases where such payments are insufficient. In most countries, outpatient provider fees are revised annually, allowing providers to negotiate payment increases if costs increase. There are however, exceptions, for instance in Australia and France, where fees have not been increased for several years. At the same time, data on the actual cost of purchasing Tc-99m is often not taken into account when determining provider payments. Provider payment can therefore also be relatively unresponsive to increases in the cost of Tc-99m.

## Policies could catalyse price increases in the supply chain

This Report presents five main policy options that could help increase the prices of Molybdenum-99 (Mo-99) in the supply chain to achieve full-cost recovery (FCR) and improve the reliability of Mo-99/Tc-99m supply (see Options 1 to 5 in Figure 2).

A phased and co-ordinated discontinuation of funding of the commercial production of Mo-99 and other medical isotopes by governments of producing countries would likely be necessary to catalyse price increases (Option 1). This would compel nuclear research reactors (NRRs) to increase prices of irradiation services, while not requiring direct government intervention in the supply chain and leaving the adjustment of supply contracts and prices along the supply chain to market forces.

Because a policy of withdrawing government funding of the production of medical isotopes could further destabilise supply in the short-term, it would need to be accompanied, at least temporarily, by one or several other measures that would help ensure that price increases are passed on through the supply chain. One option to achieve this would be to increase price transparency (Option 2), to provide a mechanism of peer-pressure among supply chain participants to comply with commitments to increase prices. Price regulation for irradiation services (Option 3) would be another option and the most direct means of ensuring that prices increase. A price floor could be imposed temporarily along with the withdrawal of government funding to ensure that NRRs are able to make up for the reduction of government funding through additional revenue. The establishment of a commodities trading platform for bulk Mo-99 (Option 4) could be another option, to make prices more responsive to supply and demand and thereby help ensure that the appropriate level of production capacity is made available.

As an alternative to market-based approaches, governments could maintain funding of irradiation services but have end-user countries bear the costs in proportion to the share of total supply they consume, based on an new inter-governmental agreement between producing and end-user countries (Option 5).

The Report also presents two options for governments to reduce the reliance on the current supply chain, through substituting Tc-99m with alternative isotopes or diagnostic modalities, or by investing in alternative means of producing Mo-99/Tc-99m (Options 6 to 7). However, these last two options could be costly.

### Figure 2. Overview of policy options

***Policies to move towards full-cost recovery within the current Mo-99/Tc-99m supply chain***

*Policy to catalyse price increases of irradiation and downstream supply chain activities*

1. Phased and co-ordinated discontinuation of funding of NRR costs attributable to Mo-99 production by governments of producing countries

*Policy options that could accompany withdrawal of government funding for Mo-99 production by NRRs*

2. Increasing price transparency in the supply chain
3. Setting a temporary price floor for irradiation
4. Introducing a commodities trading platform for bulk Mo-99

***Possible alternative to a market-based approach***

5. Direct funding of Mo-99 production by end-user countries

***Policies to reduce the reliance on the current Mo-99/Tc-99m supply chain***

6. Increasing use of substitute diagnostic imaging modalities or substitute isotopes
7. Move towards alternative methods to produce Mo-99/Tc-99m

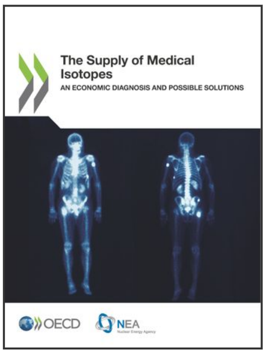
Based on the analyses presented in this report, no single option can be recommended as the preferred solution to current issues with the reliability of supply. Each option has a number of strengths and weaknesses. The main contribution of this report is to explore the issue of the reliability of Mo-99/Tc-99m supply from a health system perspective and it concludes that the main barrier to price increases is not in health care provider payment but rather *within the supply chain*. However, data on the structure of the supply chain, such as ownership, revenue and cost structures of players, their respective market shares and prices of intermediary Mo-99 products, are limited. The discussion of policy options is therefore inevitably superficial and may not exhaustively identify all strengths and weaknesses across all countries.

While governments of producer and end-user countries need to co-ordinate their efforts, they should also evaluate each option locally in more depth and in co-operation with all stakeholders, to identify the most acceptable solutions in their respective jurisdictions. In particular, the choice and implementation of policies that could help achieve FCR should be informed by a more detailed study of NRR- and processor specific production costs, the extent and purpose of current government funding, and the magnitude of price increases that would be necessary to achieve FCR at each facility.

## Notes

[1] Available at https://www.oecd-nea.org/med-radio/supply-series.html

[2] Respondents of 13 of 23 countries that are members of the European Union and the OECD responded to the OECD Health Division Survey on Health Care Provider Payment for Nuclear Medicine Diagnostic Services: Belgium, the Czech Republic, Denmark, France, Germany, Latvia, Lithuania, Luxembourg, the Netherlands, Poland, Slovenia, Sweden, United Kingdom (England only).




**From:**

# The Supply of Medical Isotopes

## An Economic Diagnosis and Possible Solutions

**Access the complete publication at:**

https://doi.org/10.1787/9b326195-en

**Please cite this chapter as:**

OECD/Nuclear Energy Agency (2019), “Key findings”, in *The Supply of Medical Isotopes: An Economic Diagnosis and Possible Solutions*, OECD Publishing, Paris.

DOI: https://doi.org/10.1787/469d59a2-en