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Nuclear Medicine Departments in the Era of COVID-19

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From the outset of the COVID-19 pandemic we, the nuclear medicine (NM) community, expediently mobilized to enable continuity of essential services to the best of our abilities. For example, we effectuated adapted guidelines for NM standard operating procedures (SOPs) and enacted heightened infection protection measures for staff, patients, and the public, alike. Challenges in radionuclide supply chains were identified and often met. NM procedural volumes declined globally and underwent restoration of varying degrees, contingent upon local contexts. Serial surveys have gauged and chronicled such geographical variance of the impact of COVID-19 on NM service delivery and, though it may be too early to fully understand the long-term consequences of reduced NM services, overall, we can certainly expect that this era adversely affected the management of many patients afflicted with non-communicable diseases. Today we are unquestionably better prepared to face unforeseen outbreaks, but a degree of uncertainty lingers. Which lessons learned will endure in the form of permanent NM pandemic preparedness procedures and protocols? In this spirit, the present manuscript presents a revision of prior recommendations issued mid-pandemic to NM centers, some of which may become mainstays in NM service delivery and implementation. Discussed herein are (1) comparative worldwide survey results of the measurable impact of COVID-19 on the practice of nuclear medicine (2) the definitions of a pandemic and its phases (3) relevant, recently developed or updated guidelines specific to nuclear medicine (4) incidental findings of COVID-19 on hybrid nuclear medicine studies performed primarily for oncologic indications and (5) how pertinent pedagogical methods for medical education, research, and development have been re-invented in a suddenly more virtual world. NM professionals shall indefinitely adopt many of the measures implemented during this pandemic, to enable continuity of essential services while preventing the spread of the virus. Which ones? Practices must remain ready for possible new peaks or variants of the roiling COVID-19 contagion and for the emergence of potential new pathogens that may incite future outbreaks or pandemics. Communications technologies are here to stay and will continue to be used in a broad spectrum of applications, from telemedicine to education, but how best? NM departments must align synergistically with these trends, considering what adaptations to a more virtual professional environment should not only last but be further innovated. The paper aims to provide recent history, analysis, and a springboard for continued constructive dialogue. To best navigate the future, NM must continue to learn from this crisis and must continue to bring new

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questions, evidence, ideas, and warranted systematic updates to the figurative table.
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Introduction

Over a year has passed since the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was first isolated in December 2020.[1,2] Since the declaration of a COVID-19 pandemic by the World Health Organization (WHO) on March 11, 2020, the pathogen has caused, through the end of May 2021 (when this manuscript was prepared), over 3.6 million deaths and more than 169 million confirmed infections.[3] In many locations the contagion is not waning. However, there is a glimmer of hope with COVID-19 vaccines being developed in record time, thanks to science and government cooperation, while preserving rigorous development, evaluation, approval, and monitoring processes. Since its introduction to the market, more than 1600 million vaccine doses have been administered.[3] Vaccination strategies have prioritized high-risk groups and health professionals, including the nuclear medicine community, using criteria expediently established by the Ministries of Health of most countries. But herd immunity remains a distant goal, and perhaps even unlikely, as many countries struggle to scale up the vaccination process. According to Dr. Youyang GuHe (an independent data scientist), "Reaching a herd-immunity threshold is looking unlikely because of factors such as vaccine hesitancy, the emergence of new variants, and the delayed arrival of vaccinations for children."[4] Perhaps SARS-CoV-2 is here to stay. *Nature* surveyed more than 100 scientists (eg, immunologists, infectious diseases researchers, and virologists) working on the coronavirus in January 2021.[5] They were asked, *"How likely do you think it is that SARS-CoV-2 will become an endemic virus: that is, one that continues to circulate in pockets of the global population?"* Almost 90% of respondents thought that the coronavirus would very likely, or likely, become an endemic virus. More than half of respondents further believe that waning immunity will be one of the main drivers of the virus becoming endemic.[5]

A significant number of pertinent guidelines were made available to the medical community,[6-8] including some specific to nuclear medicine (NM) centers.[9-14] These primarily aimed to guide how to adjust standard operating procedures (SOPs) to promote *continuity of essential services* while incorporating heightened infection protection and control measures for staff, patients, and the public, alike.

Concurrently, Surveys have been deployed to understand the impact of COVID-19 on the provision of medical services including nuclear medicine.[15-22] However, it may be too early to fully understand the long-term consequences of reduced provision of diagnostic imaging throughout this period. Nonetheless we can certainly expect that the management of patients with non-communicable diseases, such as cardiovascular diseases and cancer, was adversely affected.[16]

So where do we go from here? Many SOPs were adopted or adapted, and lessons learned after the emergence of SARS-CoV-2. It became clear that maintaining public confidence in the ability of health facilities to provide medical care safely is key to ensuring appropriate decision-making in seeking timely medical care.[13,14]

As a result, today we are better prepared to face unforeseen outbreaks of communicable diseases. The present manuscript presents a revision of recommendations given mid-pandemic to NM centers, some of which may become a mainstay in NM service delivery and implementation.

Impact of COVID-19 on the practice of nuclear medicine

There have been concerted international efforts to assess the impact of COVID-19 on the provision of medical services, the results of which have raised concerns.[15,22] According to a couple of global surveys led by the IAEA,[17,18] conventional nuclear medicine studies decreased by 54% in April 2020 and by 74% in June 2020, with partial restoration to 56% of the pre-pandemic procedural volume average by October 2020. Positron emission tomography (PET) studies in 2020 decreased by 36% in April, 66% in June, and remained 40% below the average volume in October. As for radionuclide therapies, there was a decrease of 46% seen in April, 69% in June, and showed improvement with a 48% decrease in October. Although the October figures were similar to those reported in April, they still represented an almost 50% drop below the standard pre-COVID-19 volume of procedures.

As stated by the respondents, 46% of the centers did not have an adequate supply of technetium generators, and 47% lacked Iodine-131. Regarding therapies, 48% and 50% experienced shortages of Lutetium and Samarium supplies, respectively. Only 21% of the centers reported deficiencies of gallium-68 and [^{18}F]FDG. Among world regions, Latin American (LAC) centers felt the most significant adverse impact, particularly in the availability of I-131 and technetium generators. Paradoxically, the availability of [^{18}F]FDG was higher than 80%; however, the decrease in the number of PET procedures exceeded 60% in LAC. The results mentioned above could reflect the decision of the patients to delay their studies due to COVID fear, and the closure of some centers or postponements of non-urgent procedures.[17]

The IAEA also conducted an international survey to assess the impact of COVID-19 on the diagnosis of heart disease.[20] More than 900 centers in 108 countries participated in the survey, the results of which delineated that the volumes of diagnostic procedures decreased by 42% in March 2020 compared to a March 2019 baseline, and by 64% from March

2019 to April 2020. Transthoracic echocardiography decreased by 59%, transoesophageal echocardiography by 76%, and stress tests by 78%. The stress modalities evaluated were electrocardiography, echocardiography, single-photon emission computed tomography (SPECT), PET, and cardiac magnetic resonance. The cardiac SPECT studies declined by 72%, and cardiac PET by 67%. Coronary angiography (invasive or computed tomography) simultaneously decreased by 55%. These reductions in cardiac imaging were more significant in low- and lower-middle-income countries compared to upper-middle and high-income ones, correlating with lesser availability of both personal protective equipment (PPE) and telehealth.

Dynamics of a Pandemic

An in-depth understanding of the dynamics of a pandemic is of paramount importance towards effecting communicable diseases prevention and control measures. With this aim, the WHO defined pandemic phases in 1999, revised in 2009 during H1N1.[23] These provide a global framework to foster structured pandemic preparedness and response planning.

Indeed, during the COV[[D-19 response, the WHO has applied this 6-phase approach. In phases 1, 2, and 3, animal infections predominate with little transmission to humans. These initial phases emphasize preparedness, including capacity development and early response planning activities. In contrast, phases 4, 5, and 6 incorporate sustained human-to-human transmission, clearly signalling the need for response and mitigation efforts. Further, this schematic approach outlines periods after a first pandemic wave to facilitate structured post-pandemic recovery, having accounted for the possibility of post-peak recurrences or additional waves phenomena[23](Fig. 1).

The WHO describes 4 transmission scenarios to explain the dynamics of the pandemic,[24] such as 1. no cases reported (either no cases or no detected cases), 2. sporadic cases, 3. clusters of cases, and 4. community transmission. A country or region can go from 1 transmission scenario to another in any direction (Fig. 2).[24]

Adopting restrictive measures must be based on the phase a region is undergoing and should be implemented for pre-established durations in alignment with pre-established local goals. The objective of restrictive measures is to halt or lower transmission. As part of any global, regional, national, or local strategies, it is essential to provide support to health personnel and make available all necessary protective elements.

Concurrent guidelines specific to nuclear medicine

Synergistically, as part of the support provided to the NM community, organizations such as the IAEA developed specific guidelines and recommendations.[10,11]

For example, early during the COVID-19 pandemic, NM departments were advised to adjust their SOPs to minimize the risk of contagion for staff, patients, and family members by following a series of recommendations based on the WHO Minimum Requirements for infection prevention and control recommendations.[25] It was also advised to consider adopting and adapting the 6 operational processes included in the "Coronavirus disease (COVID-19) technical guidance: Maintaining Essential Health Services and Systems" published by the WHO[6] (Table 1). Some of the recommendations could become standard practices to maintain the operation of the NM department and hopefully be better prepared to face the challenges of this or future emergencies. These include appointing a designated focal point to coordinate the operation during emergencies, preparing contingency and business continuity plans, establishing effective patient flow (screening, triage, and targeted referral), and identifying mechanisms to maintain the availability of essential equipment and supplies.

Working together, it did not take long for the scientific community to reveal the characteristics of SARS-COV-2, its routes of transmission, and the magnitude of multi-organ disease manifestations. Specific guidelines were developed to maintain and improve essential service provision while

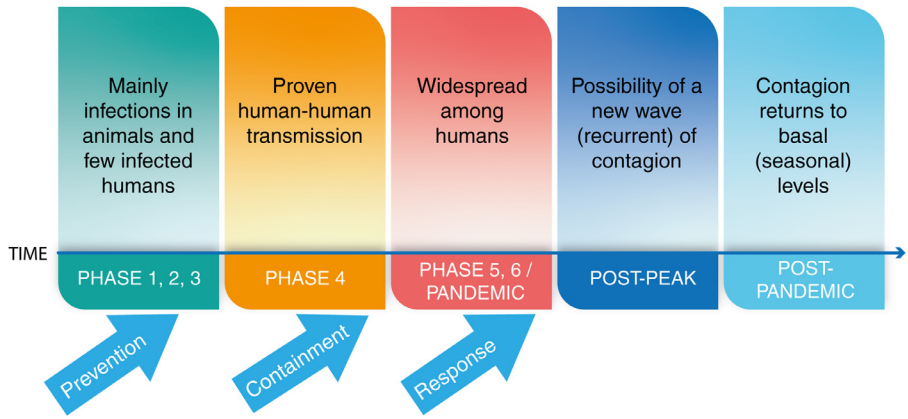

Figure 1 WHO Pandemic Phases. WHO's 6-phase pandemic approach defined in 1999 and revised in 2009 during H1N1 [adapted from 23].

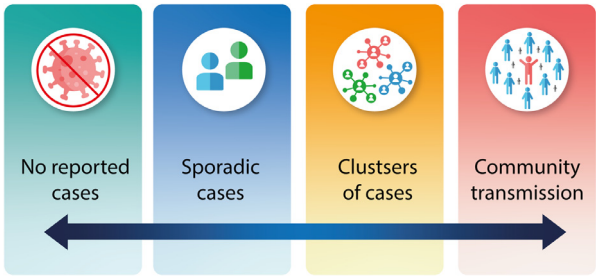

Figure 2 WHO transition scenarios. WHO transmission scenarios. It describes the contagion dynamics of an epidemic with a 4-step approach, from unreported cases to community transmission. A country or region can move from 1 transmission scenario to another in any direction [adapted from 24].

Table 1 Operational Strategies

I Establish simplified purpose-designed governance and coordination mechanisms
Establish a COVID-19 Incident Management Team
Designate a focal point
II Identify context-relevant essential services
Reallocate financial and material resources
Mobilize additional resources
III Optimize service delivery settings and platforms
Develop a contingency and business continuity plan
IV Establish effective patient flow (screening, triage, and targeted referral) at all levels
V Rapid redistribution of health workforce capacity, including reassignment of tasks
Apply same precautions and screening tests that apply to patients
Stay home if feeling unwell or there is suspicion of COVID-19 infection
Consider segregating staff into teams
Consider re-training of staff to cover other positions within the department
All necessary personal protective equipment available must always be made available for staff at all working sites
Consider providing staff transportation and, if necessary, staff accommodation
Ensure environmental services staff are appropriately trained and protected
Establish periodic virtual staff meetings to update on the local status of the pandemic and to enquire about their well-being
Facilitate psychological consultation for staff
VI Identify mechanisms to maintain the availability of essential equipment and supplies
Identify mechanisms to maintain the availability of essential equipment and supplies
List required supplies and all possible suppliers and distribution channels

Key operational strategies recommended to maintain the delivery of health services during emergencies [adapted from 6]

adopting special protection and control measures.[13,14] But which of the proposed measures should we retain? Not only to continue facing COVID-19 which, as described above, can oscillate between stages of low and high contagion rates, but also to face possible future outbreaks of infectious diseases? It is essential to understand that a situation-based approach should be considered when addressing infectious diseases.

Maintaining a priority-based approach, as proposed by ASNC, IAEA, and SNMMI for the restoration of non-emergency care in nuclear cardiology, 4 clinically-driven categories could be considered appropriate: urgent, higher, lower, and elective (Fig. 3).[14] However, proposing such categorization for non-cardiac imaging and therapeutic procedures is more challenging. NM departments need to have better protocols to decide the priority of studies, including those postponed due to the pandemic. The prioritization should be done in conjunction with the referring physicians to ensure that procedures are performed on time. Contextualized within the 2020 recommendations for the gradual reopening of NM centers, a color-coded scheme based on the status of COVID-19 in the local environment was proposed.[13] This scheme could endure well beyond the roiling pandemic (Fig. 4).

COVID-19 Incidental findings

Several publications have described incidental findings related to COVID-19 on [^{18}F]FDG PET/CT and other hybrid studies performed primarily for oncological indications.[26-29] Among these, a meta-analysis[28] evaluated the role of [^{18}F] FDG PET/CT in patients with COVID-19. The meta-analysis included 11 original studies, 10 of them observational and retrospective, mainly focused on the incidental detection of COVID-19 on [^{18}F]FDG PET/CT, and a prospective analysis of patients with known COVID-19. These aimed to evaluate the inflammatory status of the patient and a possible correlation with the evolution of disease on CT and short-term clinical outcomes.[27] The meta-analysis found that when using a non-diagnostic CT, [^{18}F] FDG PET/CT cannot substitute conventional higher-resolution CT for diagnosing COVID-19 or disease monitoring. However, the PET-CT technique might be helpful in the detection of incidental COVID-19 lesions in patients scanned for other indications, oncological or non-oncological.[28] In the context of the pandemic, it is essential to conduct a systematic analysis of the images, particularly hybrid studies, to assess possible COVID-19 related changes in the lungs or other organs, and to report the findings on a priority basis.

Keeping Education and Research

Medical education is a life-long learning process that accompanies us in earnest from day 1 of medical school until the end of our medical practice.

Without a doubt, innovation in research and development is a driving force in nuclear medicine. New devices, applications, and medical evidence are produced at a fast pace and need to be propagated. New standards of best practices should be emphasized not only as part of training programs, but all efforts should be made to keep the medical

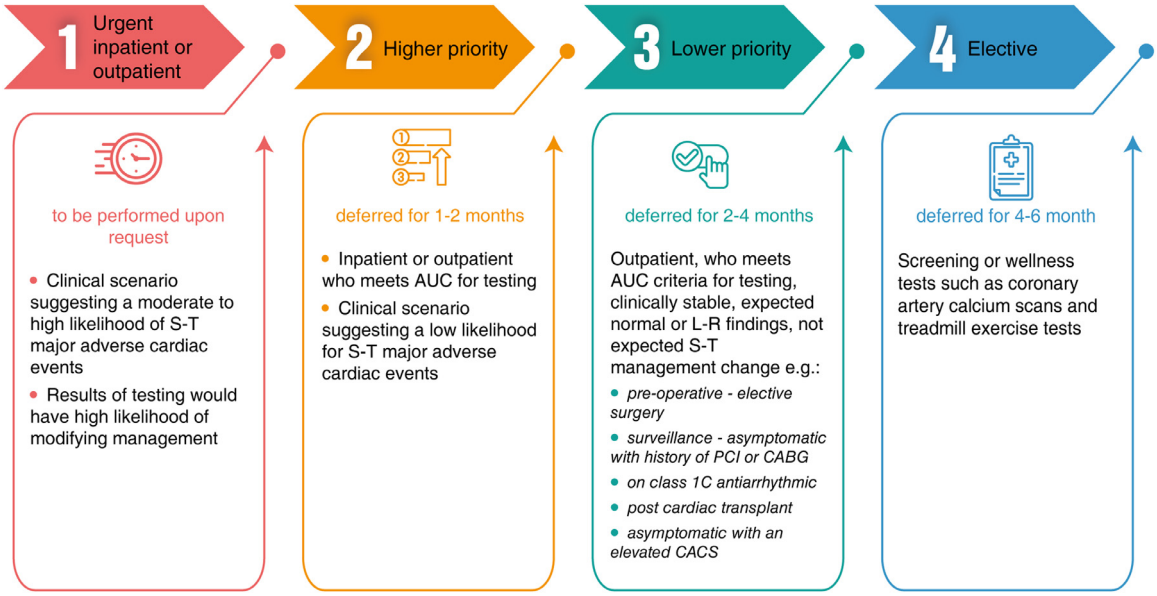

Figure 3 Nuclear cardiology prioritization scheme. Prioritization scheme for nuclear cardiology studies based on the perceived clinical urgency of the study [adapted from 14].

community abreast of developments to provide the highest possible level of patient care within a framework of safe and quality clinical practices and promote professional growth.

The COVID pandemic has affected every aspect of our lives and education is no exception. In a matter of weeks, how education was delivered around the world transformed, including for healthcare professionals. These changes have allowed a futuristic glimpse at how education and training could metamorphose sustainably for the better and for the worse. On the positive side, communications technologies have enabled greater access to eLearning materials and more virtual events. Multidisciplinary meetings have continued and, in many cases, expanded. These virtual platforms will likely be permanently incorporated into educational processes in the future. For example, traditionally, in-person conferences may become entirely virtual or convert into combined face-to-face and virtual gatherings, thus getting the best of both worlds.

The negative side includes the loss of hands-on, face-to-face training essential in medical education; the relocation of trainees in clinical wards and intensive care units largely or entirely devoted to COVID-19; and the social isolation associated with remote work.[30]

Towards reducing disruptions in medical education and training, genuinely innovative and inspiring pedagogical research has started of late. For example, virtual clinical experiences and augmented reality modules have been further developed and applied to an unprecedented degree. While these measures anticipate a smooth transition back to hands-on clinical experiences in a post-pandemic environment, some such tools may endure as complements to traditional medical education. Furthermore, the suddenly increased availability of such educational modules and platforms may enable more excellent capacity building in lower resource settings, where telemedicine has yet to be potentiated. Modern telecommunications facilitate health care delivery and sharing of medical knowledge universally, from teleradiology to the remote planning and guidance of radiotherapy. Notable is the emerging branch of general telemedicine dubbed "tele-nuclear medicine" by the Union Européenne des Médecins Spécialistes.[31]

Concluding remarks

Since SARS-CoV-2 was isolated, we have lived in a world full of uncertainties with many intriguing questions and mixed opinions. The same questions are being asked. Where did it come from? How is it transmitted? Which subset patient populations are at heightened risk of severe disease sequelae or mortality? What are the associated short and long-term complications? Which treatments work, do not work, or are still being tested? Although we have learned many lessons, many more remain to be learned from this pandemic. Will SARS-CoV-2 become endemic? How long will the immune memory of people who have had COVID-19 last? Could cold virus-type mutations undermine the success of COVID vaccines?

Amid so much uncertainty, what is certain is that we have to learn to live with this new coronavirus, and we must be prepared for possible new peaks of the infection and even for the emergence of new viruses that may cause outbreaks or pandemics. Nuclear medicine departments must remain vigilant and permanently adopt many of the measures implemented during this pandemic to continue providing essential services while preventing the spread of the virus.

Communications technologies are here to stay and continue to be used in a broad spectrum of applications, from telemedicine to education.

"Learn from yesterday, live for today, hope for tomorrow. The important thing is not to stop questioning."- ALBERT EINSTEIN

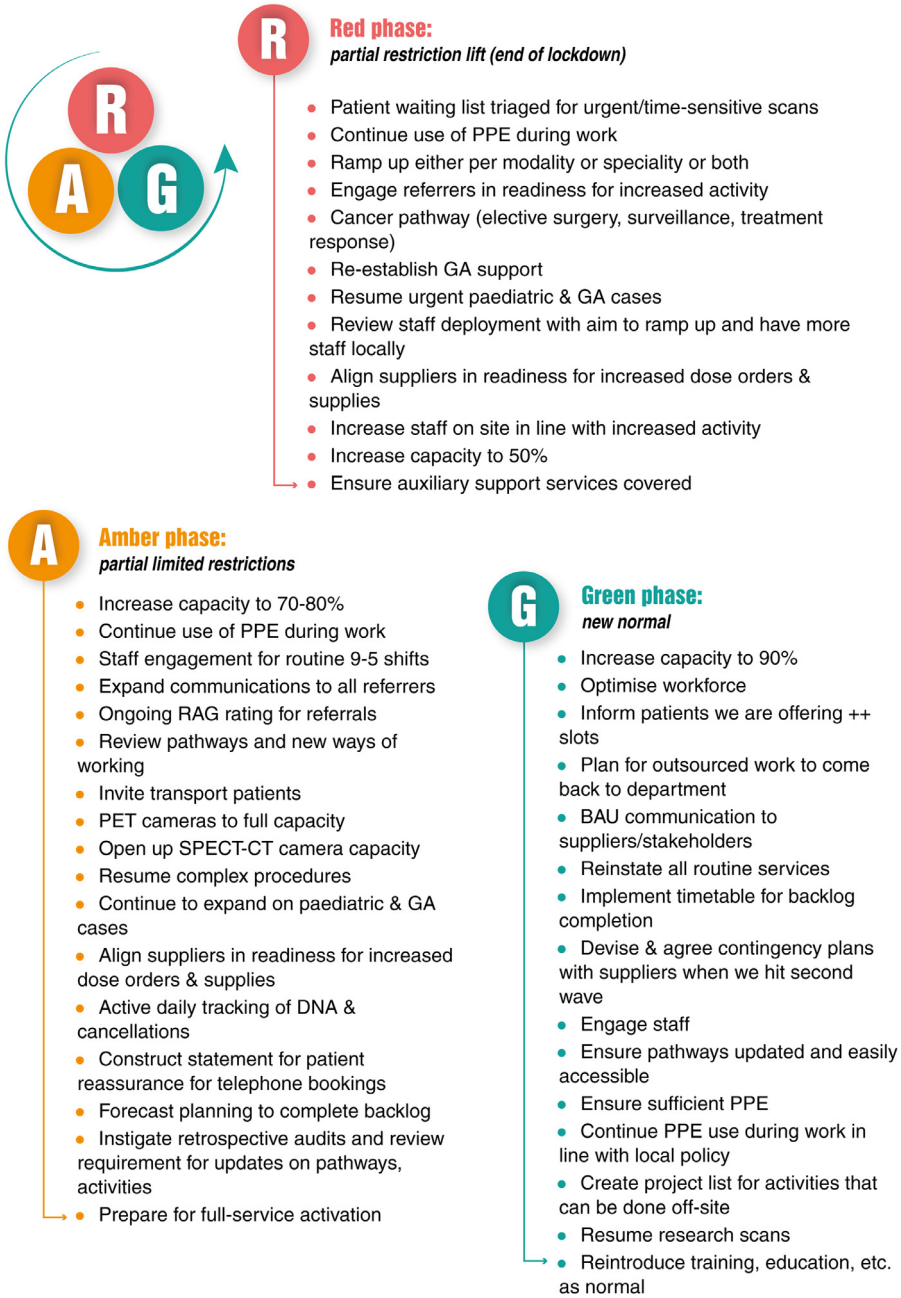

Figure 4 Gradual reopening of NM departments. GA, anaesthesia; RAG rating, R (red) A (amber) G (green); ++slots, additional slots; BAU, business as usual; WFH, work from home; DNA, did not attend. Proposal for a gradual reopening process of nuclear medicine departments presented in the publication [Adapted from 13].

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