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ORIGINAL ARTICLE

Postgraduate training in Cancer Genetics—a cross-specialty survey exploring experience of clinicians in Ireland

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Abstract

Background As genomic profiling of constitutional and tumour-derived DNA becomes increasingly critical in cancer risk estimation, prognostication and treatment, there is a growing need for clinicians involved in cancer care to up-skill in Cancer Genetics. In the Republic of Ireland (ROI), this is particularly crucial, given a paucity of vocationally trained Clinical Geneticists per capita compared to other European countries.

Aims We aimed to assess the self-reported confidence of postgraduate medical/surgical trainees in ROI in requesting, interpreting, and managing genomic data in patients with cancer, and to assess their selfreported experience, and demand for future training in this area.

Methods A cross-sectional survey of postgraduate trainees in four specialties (Medical and Radiation Oncology, Surgery, and Obstetrics and Gynaecology (O&G)), training in ROI, was undertaken. A bespoke electronic questionnaire was designed to capture data regarding preceding experience, and confidence across several hypothetical clinical scenarios involving genomic testing. The survey was circulated to eligible participants by training programme administrators, after relevant institutional ethical approval. Data was collected anonymously.

Results The study cohort included 62 respondents. A paucity of cancer genetics training at every level was demonstrated, with "hardly any" or "none at all" reported by 47(76%), 62(100%), and 50(81%) during undergraduate, core specialty, and higher specialist training, respectively. A relative lack of confidence in all clinical scenarios was apparent, particularly among Surgery/O&G trainees. Most respondents would value more training in Cancer Genetics.

Conclusions This study demonstrates an unmet need in dedicated Cancer Genetics training for postgraduate specialty trainees in ROI.

Keywords Cancer Genetics · Genomics · Mainstreaming Genetic Testing · Postgraduate Medical Education

Introduction

Medical Genetics is a rapidly evolving area of medicine, in particular when applied to oncological care. Genetic testing is becoming not only a routine part of cancer risk estimation, but also integral to the diagnosis, prognostication and treatment of cancer. Identifying an underlying germline predisposition to cancer may influence clinical decision-making, for example, the surgical decision to perform a bilateral rather than unilateral mastectomy in a carrier of a germline pathogenic *BRCA1* variant.

Many new cancer treatments are now directed towards underlying driver events found on genetic testing of tumour-derived DNA; these targeted agents have significant potential adverse side effect profiles and are costly, and

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so, careful application of these agents is required, utilising genetic medicine expertise. We must take care not to overhype the potential benefit of "precision" or "personalised" medicine, given only a minority of patients with cancer will be eligible for targeted therapies, and not all of those eligible will derive measurable benefit [1]. It is essential that the results of genetic tests in a patient with cancer are carefully interpreted, to ensure the appropriate application of targeted therapies to the patients most likely to derive benefit and avoid inappropriate use in patients that may suffer adverse effects of a therapy that may not benefit them in any meaningful way [1]. Germline genetic testing can also help to identify patients at increased risk of future cancer a—thereby allowing the application of risk-reducing strategies and/or enhanced screening to mitigate cancer risk.

It is becoming increasingly essential that doctors appreciate the utility and limitations of diagnostic germline and tumour-based tests, as well as of direct-to-consumer tests, which are now widely available [2, 3]. There have been, and continue to be, many reported cases where an inappropriate genetic test is ordered, leading to inaccurate medical management and recommendations, as well as unnecessary testing, and cost to the health care system. There are reports of result misinterpretation which has led to unnecessary prophylactic surgery in some cases and diagnosis of cancer at a more advanced stage in others [4]. The main factors that have been found to increase the likelihood of these kinds of errors occurring have been insufficient knowledge or training, inadequate experience, as well as time pressures and case complexity [5]. It is critical that patients with cancer have access to germline and/or tumour-based genetic testing in a timely fashion, in order to provide the best standard of care. It has been proposed in several studies that the most effective way to ensure the integration of genetics/genomics into a health care system is by enhanced specialist training and continuing education for current physicians [6–8]. The barriers to the implementation of genomic medicine into healthcare that have been identified include lack of formal training programmes in genetics and genomics and limited access to educational information [9–11]. Deficiencies in such training, and associated lack of confidence on the part of non-geneticists have also been identified as one of the barriers in appropriate referral of patients to Clinical Genetics services [12, 13].

There are fewer vocationally trained medical geneticists per head of population in the Republic of Ireland than most of our European counterparts [14]. The National Cancer Strategy (2017–2026) has acknowledged the acute need for oncologists to up-skill in the area of Genomic Medicine to assist in service provision in the face of increasing demand for genomic testing [11], but up to now, there has been no formal post-graduate training available to clinicians in Ireland.

We aimed to assess the self-reported Cancer Genetics experience of postgraduate trainees in Ireland, as well as their confidence in requesting and managing the results of genetic tests and to assess the demand for formal Cancer Genetics training among this group.

Participants and methods

Participants

A cross-sectional survey was undertaken. The study cohort included postgraduate clinicians across Medical Oncology, Radiation Oncology, Obstetrics and Gynaecology and Surgery. The only specified inclusion criterion was that the participant be undertaking postgraduate medical training in Medical Oncology, Radiation Oncology, Obstetrics and Gynaecology or Surgery within Ireland. A copy of the participant information leaflet and an anonymous web-link to the survey were circulated to eligible participants on Higher Specialist training schemes by the relevant administrator of the training programme. Non-Training Specialty doctors (NTSDs) make up a significant proportion of the clinical workforce in Ireland and are invited to the same study days and are on many of the same mailing lists, as Specialist Registrars. To maximise response rates, we included responses from NTSDs in our analysis, but did not target this group specifically. Participants were excluded from analysis if they were undertaking postgraduate medical training in a programme outside of Ireland, given that their experience would not be representative of Irish training.

Sample size

The average number of recommended individuals to be recruited annually to relevant Higher Specialist Training Schemes include 7 in Medical Oncology [15], 7 in Surgery [16] and 12 in Obstetrics and Gynaecology [17]. In actuality, the numbers recruited each year vary, as does the length of training. Based on current workforce planning documents, the number specialist trainees working in Radiation Oncology in total in Ireland was 15 [18]. We aimed to recruit a representative sample of at least 25% per specialty (total $n = 56$), given that this is the typical response rate to unsolicited web-based surveys [19].

Questionnaire

A bespoke web-based questionnaire (surveymonkey.com, appendix) was designed to capture information regarding participants' clinical and non-clinical formal and

self-directed training in cancer genetics, as well as their self-reported confidence in different clinical scenarios involving handling of genomic data. Data was collected between October and December 2020.

To ensure anonymity of the respondents, we did not collect specific information about gender, age, medical school, sub-specialty interests, or IP address of the participant. To further minimise potential risk of identification of an individual, comparative analyses between specialties were not undertaken if number of responses for each potential option within a question were fewer than 5. Where responses for individual options within a question were fewer than this threshold, comparisons were restricted to "procedure-based" specialties (Surgery and Obstetrics and Gynaecology) versus "Oncology" (Medical Oncology and Radiation Oncology).

Data were collated and analysed using IBM SPSS statistical software package.

Results

Participant characteristics

A total of 62 trainees participated in the study, of which the majority were Specialist Registrars ($n=43$, 69.4%), and smaller proportions of NTSDs ($n=10$, 16%), clinical fellows ($n=8$, 13%) and one consultant. The greatest proportion of respondents were from Medical Oncology ($n=19$ (31%)), 17 (27%) participants from both Surgery and Obstetrics and Gynaecology, and a smaller but representative number from Radiation Oncology ($n=9$, 15%) (Fig. 1).

Cancer Genetics training provided during training programme

Our results revealed a paucity of cancer genetics training, with the vast majority of respondents having "none" or "hardly any" teaching at every stage of medical training, most notably during Core Specialty Training (Fig. 1). There was no statistically significant inter-specialty difference in cancer genetics training provided during Core Specialty Training ($p=0.127$, Fisher's exact test), but there were appreciable differences during Higher Specialist Training ($p=0.009$, X^2), with substantial proportions of specialist trainees in procedure-based specialties declaring "none" with no counterparts in Medical/Radiation Oncology rating Cancer Genetics training at this lowest level ($p<0.001$, X^2). However, the greatest proportion of participants among both Medical/Radiation Oncology trainees ($n=19$) and Surgery/Obstetrics and Gynaecology trainees ($n=16$) selected "hardly any" training at HST level.

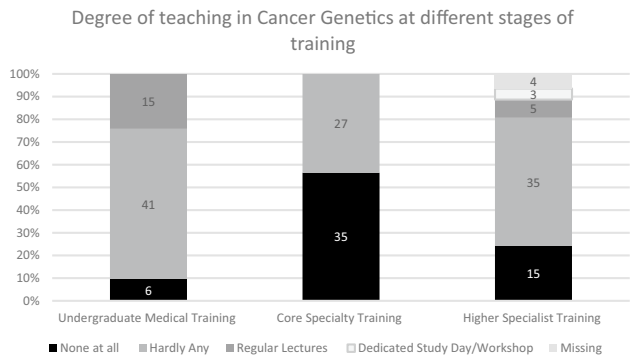

Fig. 1 Cancer Genetics Training at different levels of training

Additional Cancer Genetics training

A small number of trainees ($n=9$) reported additional Cancer Genetics training outside of mandatory training, but the extent of this self-reported expertise ranged from a single masterclass/study day ($n=2$) to higher research degrees (single MSc module ($n=2$), full MSc ($n=4$) and an MD ($n=1$)).

A minority of trainees ($n=12$) undertook a clinical ($n=8$) or research ($n=4$) placement in Cancer Genetics, the greatest proportion of whom were Medical Oncology trainees ($n=6$). In only one instance was the Clinical/Educational supervisor of the trainee during this placement a Clinical Geneticist.

Self-reported confidence in requesting/managing results of genetic tests

In the application of genetics knowledge, the greatest proportion of respondents stated they are "not confident at all" across all of the postulated clinical scenarios, with greatest lack of confidence in managing a variant of unknown significance (VUS) (Fig. 2).

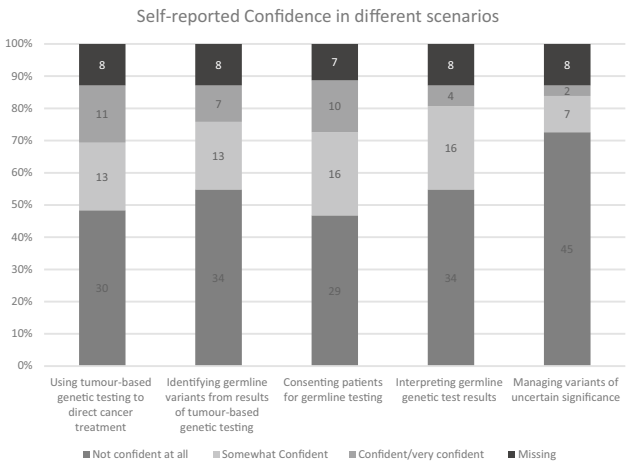

Fig. 2 Self-reported confidence in different clinical scenarios

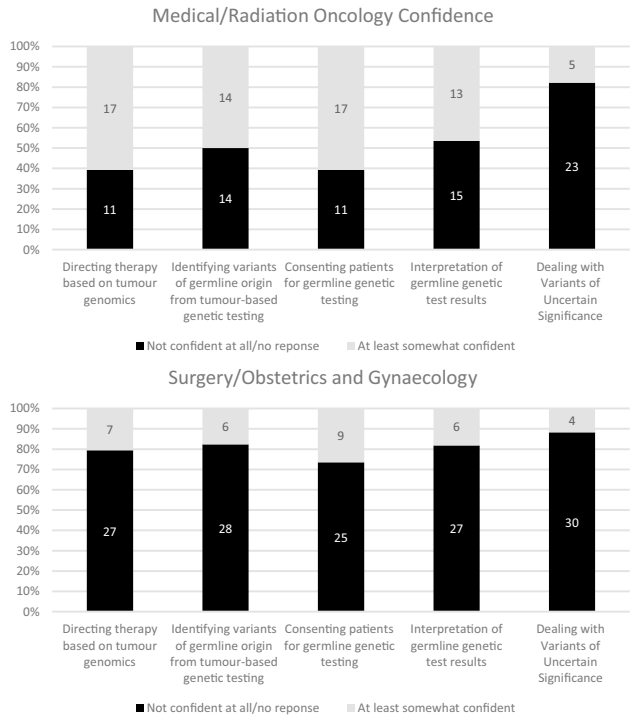

Fig. 3 Comparison of confidence between oncology specialties and procedure-based specialties

Differences between procedure-based specialties and oncology specialties were evident (Fig. 3). Medical/Radiation Oncology trainees were more confident than colleagues in procedure-based specialties in using tumour-based tests to direct cancer treatment (p 0.004, X^2), identifying potential germline origin of variants detected as part of tumour testing ($p=0.037$, X^2), and in consenting patients for germline genetic testing ($p=0.018$, X^2). Differences were less pronounced between procedure-based and oncology specialties in terms of interpreting germline results ($p=0.114$, X^2) and managing variants of uncertain clinical significance ($p=0.883$, X^2).

Dealing with uncertain results

When asked if predictive testing of familial variants of uncertain significance should be offered to unaffected at-risk relatives, the greatest proportion of respondents did not know/respond ($n=24$, 39%). A minority ($n=5$, 8%) would inappropriately offer predictive testing in this instance, while a larger proportion ($n=18$, 29%) would offer predictive testing in certain circumstances. Fifteen respondents (24%) would not offer predictive testing in this instance.

When asked how unaffected carriers of a VUS should be managed, a minority ($n=7$, 11%) would consider risk-reducing surgery in such patients. Most respondents ($n=6$) selecting this option were trainees in procedure-based specialties. Nine (15%) respondents would offer enhanced surveillance but not risk-reducing surgery based on a VUS result, while seventeen (27%) would base screening recommendations on the family history irrespective of the patient genotype. The greatest proportion ($n=29$ (27%)) selected "I don't know" or did not respond to this question.

When asked regarding management of unaffected *non*-carriers of familial VUS, a minority of respondents ($n=10$, 16%) would be reassured by a negative result and would discontinue enhanced surveillance, while a greater proportion ($n=30$, 48%) would appropriately continue screening guided by family history of cancer. Over a third of respondents ($n=22$, 36%) selected "I don't know" or did not respond to this question.

Demand for additional training in Cancer Genetics

The majority of those surveyed ($n=52$, 83.8%) would value more training in Cancer Genetics. Most felt expertise in this area was fundamentally required in their specialty ($n=45$, 72.6%). A small minority ($n=3$, 4.8%), all of whom were surgical trainees, felt training in Cancer Genetics was not relevant for their specialty.

A significant proportion of respondents stated that online forms of training, including webinars ($n=15$, 24.2%) and online resources for self-directed learning ($n=12$, 19.4%), would be the most helpful types of additional training, while smaller proportions would prefer face-to-face workshops ($n=11$, 17.7%), clinical placements in Cancer Genetics ($n=11$, 17.7%) or lectures ($n=6$, 9.7%).

Discussion

The concept of precision/personalised medicine has long since been touted as the holy grail of cancer treatment, particularly as our knowledge of the complexities of the genomic evolution of cancer becomes more refined, and as genomic testing becomes cheaper and more readily available. Although a significant proportion of genomic aberrations within cancer are "undruggable" (at present), treatment of certain cancer types, such as melanoma or lung cancer, has been revolutionised by molecular profiling and development of targeted agents, and cancer care is increasingly moving away from organ-specific to more molecularly driven, tumour-agnostic approaches. It has been estimated that ~7% of patients with metastatic cancer will have an identifiable FDA-recognised molecular biomarker to direct application of an FDA-approved drug for the cancer in which the variant has been identified; and the tumours in an additional 29% of patients have biomarkers for which compelling clinical evidence exists to support their use as a clinical biomarker, or which are already used to direct targeted therapy in another

tumour type [20], supporting use of molecular profiling as part of routine assessment [21, 22].

Requesting and interpretation of tumour-based molecular profiling and subsequent prescription of targeted agents are primarily undertaken by Medical and/or Clinical Oncologists. This may explain, in part, the relative confidence we have identified among trainees in Medical/Radiation Oncology compared to their procedure-based peers in directing therapy based on tumour genomics. Over half of Medical/Radiation Oncology trainees surveyed were at least somewhat confident in this scenario, despite the majority having declared having "hardly any" cancer genetics training during their specialist training. This may reflect provision of "on the job" training as part of the hidden curriculum of continuing medical education. Peers in procedure-based specialties would not necessarily be exposed to such training. Recognition that a substantial proportion of Medical/Radiation Oncology trainees admitted a lack of confidence in using tumour-based testing to direct therapy supports implementation of more equitable and consistent training to support this skill. The clinical significance of a genomic aberration must be considered in relation to pathogenicity, availability of a targeted agent and licencing of that agent for treatment of the cancer type in which the variant has been identified. These complex discussions, as with most discussions impacting treatment decisions, are best undertaken within the context of a multidisciplinary meeting—ideally a "molecular tumour board" (MTB), with input from Clinical Scientists, Geneticists, Molecular Pathologists and appropriately trained Oncologists. Access to such MTBs is suboptimal within Ireland, and internationally, particularly outside of academic institutions [23, 24], such that trainees may miss the opportunity to observe such discussions depending on their clinical rotations. Medical Oncology trainees were generally more confident than peers in the three other specialties, which is not unexpected given that Medical Oncologists are more likely to request tumour-based and germline genetic tests and to prescribe targeted therapies than other cancer specialists in Ireland [25, 26]. Furthermore, five of the 19 participants from this group had undertaken a clinical placement in Cancer Genetics.

The results of tumour-based genomic profiling may have implications beyond treatment decision-making. Unless germline subtraction is undertaken during analysis, genetic testing of tumour-derived DNA may lead to inadvertent detection of constitutional variants [27, 28]. This has implications for the affected patient, but also for their blood relatives. Although factors such as variant allele frequency, patient phenotype and family history are helpful to consider, it is not always immediately obvious if a variant is of somatic or germline origin, and indeed may be impossible to determine without paired analysis of constitutional DNA. Half of Medical/Radiation Oncology trainees felt at least somewhat confident in identifying variants of germline origin from tumour-based testing, but over a third of such trainees did not feel confident at all in this scenario. A lack of confidence was more pronounced among procedure-based specialist trainees, with 71% selecting "not confident at all" in this context.

Germline genetic testing has traditionally been undertaken only after pre-test counselling with a Clinical Geneticist or Genetic Counsellor, but implementation of "mainstreaming" of genetic testing through routine Oncology and/or Surgical clinics is happening at pace internationally. In Ireland, germline and/or tumour-based *BRCA1/BRCA2* testing may now be requested by Medical Oncologists in Ireland for those patients with ovarian cancer likely to benefit from treatment with (Poly (ADP-ribose) polymerase PARP) inhibition [25, 26], and a pilot study of mainstreaming of such testing by surgical and oncology physicians in patients with breast and/or ovarian cancer in three Irish cancer centres was also met with enthusiasm [29]. Mainstreaming of other types of germline tests, and extension to other clinical specialists, may well be implemented in the future, in line with other countries. A recently published report by Hegarty et al. examining the unmet need in Cancer Genetics Services in Ireland has highlighted the role of mainstreaming genetic testing to ensure provision of standardised access for all patients with cancer to germline genetic testing [30]. However, the report equally outlines challenges to broader implementation of mainstreaming in the Irish system, considering the relative lack of genetics expertise among non-geneticists in the country, in combination with the low number of vocationally trained specialists available to provide requisite support to such schemes. Due consideration needs to be given to up-skilling of non-geneticist clinicians working in cancer care in tandem with investment in over-stretched existing Clinical Genetics services. This issue is not restricted to the care of patients with cancer—indeed, genomic testing is increasingly becoming a fundamental component of patient care across almost all specialties. Ideally, education in Genomic Medicine should be embedded in undergraduate as well as postgraduate medical training—which will require time and significant investment.

This study demonstrates that 61% of Medical/Radiation Oncology trainees working in the Republic of Ireland are at least somewhat confident in consenting patients for germline genetic testing, but a substantial proportion, (25%) and a greater proportion (65%) of procedure-based specialist trainees are not confident at all. A considerable number of patients for whom genetic testing may be appropriate may not come under the direct care of an Oncologist, meaning that all clinicians involved in the care of patients with cancer should be trained to at least recognise such patients, and ideally, to be able to provide pre-test counselling where mainstream genetic testing is appropriate. This study represents

the largest survey of specialty trainees in the Republic of Ireland addressing their experience and knowledge on genetics and precision medicine. We have identified a paucity of Cancer Genetics training at undergraduate and postgraduate levels. This is not unique to Ireland [31–34]. In a UK study, gastroenterology trainees felt ill-equipped to practice personalised medicine and genomics as consultants, and further education and better defined pathways for referral to local genetics services were highlighted as the best ways to address this issue [31]. Detection of constitutional variants of uncertain significance may cause significant clinical challenges. Misinterpretation of the significance of a variant may lead to misdiagnosis, inaccurate risk estimation, inappropriate management and/or unnecessary surgical/chemoprophylaxis. Furthermore, it can lead to delays in further investigation for and detection of a causative pathogenic variant. Although current UK best practice guidelines for reporting of VUS recommend reporting only those variants for which a high degree of suspicion exists, many laboratories continue to report all detected VUS. In a large retrospective analysis of 1.45 million people undergoing testing for cancer predisposition, in whom 26,670 VUS were identified between 2006 and 2016, only 7.7% of VUS were ultimately reclassified, of which 91.2% were downgraded to benign/likely benign [35]. For the most part, VUS are not considered clinically actionable, and detection of VUS should not be used as a factor in treatment planning or surgical decision making. Predictive testing of affected relatives may be offered on occasion, if the data from such tests would be useful to support reclassification. However, testing of unaffected relatives for uncertain variants is not recommended. In this study, a significant proportion of respondents would not only consider predictive testing for familial VUS in unaffected at-risk relatives, but would also consider risk-reducing surgery in unaffected carriers of a VUS, as well as removal of enhanced surveillance to non-carriers of a familial VUS. Undertaking surgical prophylaxis in a carrier of a variant for which pathogenicity is unclear has been the focus of medicolegal cases, and may be considered somewhat analogous to giving chemotherapy without a definite histological diagnosis of cancer. A lack of confidence or over-interpretation of the relevance of a variant of uncertain significance is not unique to Irish clinicians [36–38], nor is this unique to cancer genetics [39].

In the era of COVID-19, medical and surgical trainees have had to adapt to remote learning for continuing medical education. Furthermore, given the paucity of trained Clinical Geneticists available to provide face-to-face teaching and/or supervision of trainee placements, online resources are more feasible to develop and roll out. There are a number of relevant courses or postgraduate qualifications that would be suitable to provide trainees with foundational knowledge and skills in Cancer Genetics. A substantial proportion of such courses consist of blended learning methods or are fully online, for example resources created by the Genomics Education Programme of Health Education England, or Massively Open Online Courses certified by major UK- or USA-based universities, available through websites such as Futurelearn or Coursera. In response to the identified area of unmet need in Ireland, a fully online Postgraduate Certificate in Cancer Genetics has been developed by the authors in collaboration with the Royal College of Physicians of Ireland and commenced its inaugural run in January 2021 (after completion of this survey) [40]. The authors will also continue to work with both of the respective colleges, to help build educational content and develop training opportunities in this area.

Limitations of the study

All trainees on Higher Specialty Training Programmes in Medical Oncology, Radiation Oncology, Surgery and Obstetrics and Gynaecology were invited to participate in this study. Participation was voluntary and respondents self-selected. Response rates were sub-optimal, but sample size was greater than minimum intended cohort, and was representative considering the relatively small number of maximum eligible participants.

We do not believe that trainees who responded are any more or less likely to be concerned about their lack of training in Cancer Genetics compared with the total trainee population, but it is possible that those who did choose to respond were motivated to do so because they are more concerned about their lack of confidence and/or knowledge on this topic than the general trainee cohort. There was no information on non-respondents due to anonymous nature of this online survey. In order to maximise response rates, we did not undertake a formal assessment of knowledge, and asked trainees to self-report their confidence in clinical scenarios. While it is possible that those trainees that lack confidence have high levels of competence in Cancer Genetics, formal assessment of performance was not possible. Similarly, although some trainees declared confidence in various scenarios, it is impossible to determine if this is misplaced or justified based on available data.

Conclusion

Our study clearly identifies the need for further training in cancer genetics for postgraduate clinicians who treat patients with cancer. There is an unmet need for post-graduate training in Cancer Genetics to be made available to clinicians across specialties in Ireland.

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Author contribution The study was conceived and designed by Dr Jana McHugh and Dr Terri McVeigh. All authors contributed to and approved of the survey design. Dr El Beltagi, Professor Barry, Professor O'Reilly and Professor Daly provided approval as Programme Directors for circulation to trainees of their respective programmes. All authors reveiwed and approved the final manuscript.

Data availability A bespoke web-based questionnaire (surveymonkey.com) was designed to capture information for the study and data were collated and analysed using IBM SPSS statistical software package.

Declarations

Ethics approval The study was approved by the Research Ethics committees in the Royal College of Physicians of Ireland (REC SAF 133) and the Royal College of Surgeons in Ireland (record ID 212533170). The study was performed in the accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments and comparable ethical standards.

Consent to participate Informed consent was obtained from all individual participants included in the survey.

Consent for publication The participants consented for submission for publication in a journal.

Conflict of interest The authors declare no competing interests.

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