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- Assisted Dying Survey - Retroperitoneal Sarcoma - Mainstreaming Genomics

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Editorial

Quaerere Verum

David J Armstrong

Quaerere Verum – to seek the truth – is perhaps best known in Northern Ireland as the motto of the Royal Belfast Academical Institution[1], the independent boys' grammar school where Belfast Medical School had its first home until the establishment of Queen's College, later Queen's University, in 1849[2]. It is a quotation from one of Horace's epistles, and is more fully *curvo dinoscere rectum atque inter silvas academi quaerere verum* – to distinguish the straight from the crooked, and among the forests of learning (or 'groves of academia' as it is wont to be translated) to seek the truth[3]. The search for truth has been an obsession of most world religions, philosophies, legal systems and science over the last 5000 years and remains at the heart of medicine in general and every patient consultation in particular.

Pontius Pilate's question to Jesus Christ "What is Truth?" [4] summarises the search for meaning in life which drives much religious inquiry (Christ had already declared 'I am the Truth'[5], and yet in recent times the idea of objective truth itself has oddly come under attack from all angles. The trope that there can be 'my truth' and 'your truth' is often heard in celebrity interviews, and the phrase 'alternative facts' was introduced to mainstream attention by a dispute over the number of people attending the presidential inauguration of Donald J Trump in the USA in 2017[6]. Can there be more than one truth? Can there be alternative facts?

In the clinic, surgery or operating theatre, it would appear not. The patient may feel pain in the shoulder tip, but if the truth is that it is referred from disease of the gallbladder, then injecting the shoulder will not help no matter how much the patient believes that the shoulder is the problem. Many hypotheses conceived in the gloaming are exposed by the bright light of the double-blind randomised control trial. Our Victorian forebearers believed that everything could be observed, described and tested, and that science could eventually conquer most problems. Patients have always liked a clear diagnosis, a label for their symptoms, a foe to fight.

Strangely though, the further we go in science and medicine, the more hazy the idea of absolute truth becomes. No sensible doctor will ever give a patient a 100% guarantee of any outcome (except perhaps the ultimate outcome) and patients now expect to hear "there will a 4 in 10 chance of feeling better from this procedure, a 4 in 10 chance of no change, and a 2 in 10 chance of getting worse" or similar offering. This is of course 'the truth' in an objective sense, but it is not the certainty which in the past patients expected. It does however represent the truth in a much more honest way than the internet charlatan adumbrating '100%' success. But it also depends on a degree of health literacy, and health numeracy, which might not always exist.

And yet perhaps this is the way forward. In my own specialty, the idea of giving a patient a diagnosis of 'osteoporosis' based on a DEXA scan, and prescribing on that basis alone, has moved on to the calculation of a 'fracture risk' using the FRAX algorithm[7], and presenting to the patient, for example "a 35% chance of a major fracture in the next 10 years" on which to base management choices, regardless of what the exact bone mineral density is shown by the DEXA scan. The truth might be that not everyone who has crossed the osteoporosis line on DEXA needs medicine just yet, but that many still on the osteopenia side would benefit from some of the strongest therapies available. The truth is complicated, but remains the truth. Is it too far to stretch the analogy, that the best way to improve local health services might be to close a failing local service, and improve access to a better service elsewhere? Is the best way to reduce pressures on secondary care to increase funding for primary care? What indeed is truth?

The scientist, to confuse things further, might also point out that the further we travel into the world of quantum physics, the more we realise that nothing is really certain. The idea of an atom, first coined by the Greek philosopher Leucippus in the 5th century BC (from a-tomos, not split)[8] has long since given way to a host of particles including neutrinos, charm quarks and the Higgs Boson[9]. But one of the fundamental discoveries of recent years has been the concept that none of these particles are really knowable. From the famous double slit experiment[10], where the beam of light behaves differently depending on how the experiment is set up, as if the light almost knows which outcome the scientist desires, we now realise that any observation – shining light, exposing to radiation – changes the particle itself. We can only give percentages describing where a particle might be found, or how much energy it might have, known as its wavefunction[11]. In the quantum world, which underlies all the observed universe and the direct effects of which are now visible in biological systems[12], is anything truly knowable? Is there any truth?

All this seems a long way away from my clinic tomorrow morning, or the decision on how to fund the health service. But just as the quantum particle can be in two places at once (or can it?) so the doctor must try to present the patient with a

trustworthy, evidence based reliable truth, while maintaining the knowledge that Fate is a capricious mistress, that no outcome can be guaranteed, and that every decision is, in the end, a game of percentages.

Is there therefore such a thing as absolute truth? I am perhaps old-fashioned, but I believe that in terms of religious belief, or in philosophy if you prefer, there is Truth, and the search for truth is something to which we must apply ourselves. In a world of your truth and my truth, lived experience and alternative facts, the doctor must remain, for the patient, someone who tells the truth. The truth may be that the outcome is uncertain, but that will be a lot more truthful than the snake oil seller who promises a cure. The truth may be that we just don't know, but here is what we have tried to find out by honest scientific experiment and fair-minded consideration. The truth might even be that we are sorry, we have got it wrong, we should have done better. A Duty of Candour[13] is a very clear example of truth.

Ultimately, the doctor must be seen as a disciple of Truth. He or she must always be seen as a person of integrity and honesty, who prizes fairness and equality. Who no matter how difficult and contradictory the task may at times appear, searches among the groves of academia and remains a seeker after truth.

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Ulster Medical Society Lecture Programme 2024-2025

Dr Mark Vignesha Roberts

Dr Mark Vignesha Roberts MPH FRCP is a Consultant Physician in Acute and Older People's/Geriatric Medicine since 2011. He grew up in Scotland and then studied at the University of Aberdeen before moving to Manchester and then onwards to Northern Ireland 'in pursuit of the future Lady Roberts'. During the last 13 years in Northern Ireland, as well as Consultant Physician roles, he has been a Clinical Informatics Lead, Training Programme Director at NIMDTA, Clinical Director at the regional Quality Improvement body and most recently as an Acute Care Policy advisor at the Department of Health. He has been a Fellow of the Royal College of Physicians of London since 2013 and in May 2024 took on a Deputy Medical Director and Physician role in South Devon. He is very much looking forward to hosting the UMS evening speaker programme in person in Northern Ireland and hopes to see you and your guests there.

UMS Lecture/Meeting Dates

Date	Lecture	Speaker & Subject	Venue	Time
Thurs 10 Oct	Presidential Address	Dr Mark Roberts *Consultant Physician and Deputy Medical Director Torbay and South Devon NHS Foundation Trust* **A pragmatic optimist's prescription for healthcare for the next 20 years** https://www.eventbrite.co.uk/e/ums-presidential-address-tickets-913932736417	BCH Postgraduate Centre	7.30pm
Thurs 24 Oct	Joint meeting UMS with BCH	Dr Philip Crowley *National Director Strategy and Research, HSE Ireland* **The Irish health service at a crossroads and moving to sustainability** https://www.eventbrite.co.uk/e/the-irish-health-service-at-a-crossroads-and-moving-to-sustainability-tickets-913936778507	BCH Postgraduate Centre	Buffet 6.30pm Lecture 7.30pm
Wed 6 Nov	UMS/QUB/NIMDTA Joint Meeting	Trainee Research Day Professor Peter Cantillon *University of Galway, Department of General Practice* **Research for Clinicians - keynote**	Wellcome Wolfson Institute	9am – 3.00pm
Thurs 14 Nov	Sir Thomas and Lady Dixon Lecture	Dr Eimear Darcy *General Practitioner* **Long Term Condition Management: A Primary Care house with good bones, but in need of a #CVRM renovation.** https://www.eventbrite.co.uk/e/long-term-condition-management-tickets-913937059347	BCH Postgraduate Centre	7.30pm
Thurs 28 Nov	UMS	Terry Irwin *Retired Colorectal/General Surgeon/Author of Medical Presentations: a prescription for success* **Everything we taught you about inguinal hernias was wrong, and why it matters.** https://www.eventbrite.co.uk/e/everything-we-taught-you-about-inguinal-hernias-was-wrong-and-why-it-matte-tickets-913937550817	BCH Postgraduate Centre	7.30pm
Thurs 5 Dec	Gary Love Lecture	Dr Patrick Byrne *Consultant Physician and General Practitioner* **If music be the food of love, play on.** https://www.eventbrite.co.uk/e/if-music-be-the-food-of-love-play-on-tickets-913938493637	BCH Postgraduate Centre	7.30pm
Thurs 16 Jan 2025	Joint Meeting with Ulster Obs & Gynae	Dr Tommy Tang *Consultant Gynaecologist* **Polycystic ovarian syndrome: much more than just a gynaecological condition** https://www.eventbrite.co.uk/e/polycystic-ovarian-syndrome-much-more-than-just-a-gynaecological-condition-tickets-913938794537	BCH Postgraduate Centre	7.30pm
Thurs 30 Jan	UMS	*Professor Frank Casey* *Clinical Professor Paediatric Cardiology, Ulster University and Queen's University, Belfast* **Building a Patient-Centred Clinical Network- Benefits, Challenges and Lessons learnt.** https://www.eventbrite.co.uk/e/building-a-patient-centred-clinical-network-tickets-913939095437	BCH Postgraduate Centre	7.30pm
Thurs 27 Feb	UMS	Sir John Curtice *Senior Research Fellow, Professor of Politics at Strathclyde University and Chief Commentator on the 'What we think' websites* **No space in the waiting room? Why voters are unhappy with the NHS (again).** Mr Hugh McCaughey *Interim CEO Ulster Rugby, Former National Director of Improvement NHS England and CEO South Eastern HSCT* **Dear Mr Bevan, your child is ill. Can I suggest a treatment plan?** https://www.eventbrite.co.uk/e/sir-john-curtice-and-mr-hugh-mccaughey-tickets-913939616997	BCH Postgraduate Centre	7.30pm
Thurs 13 Mar	Desmond Whyte Lecture	Professor Lourda Geoghagen *Deputy Chief Medical Officer, NI* **Improving health and social care - right touch regulation in practice** https://www.eventbrite.co.uk/e/improving-health-and-social-care-right-touch-regulation-in-practice-tickets-913943057287	Centre of Medical & Dental Education & Training, Altnagelvin Area Hospital	Buffet 6.30pm Lecture 7.30pm
Thurs 27 Mar	Robert Campbell Oration	Dr Shobhan Thakore *Associate Medical Director for Quality Management, Clinical Lead Scottish Quality and Safety fellowship* **Realistic Medicine in an Unrealistic World.** https://www.eventbrite.co.uk/e/realistic-medicine-in-an-unrealistic-world-tickets-913943197707	BCH Postgraduate Centre	7.30pm
Fri 9 May	UMS	Annual Dinner	The Great Hall, QUB	7pm
Thurs 22 May	UMS	Annual General Meeting	UMS Rooms and online	5pm

All lectures can be booked via:
Eventbrite https://www.eventbrite.co.uk/o/ulster-medical-society-52479713363 or by emailing administrator@ums.ac.uk

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Clinical Paper

A Ten Year Review Of Management And Outcomes Of Retroperitoneal Sarcoma: A Retrospective Cohort Study

Nicola McKinley[1], Rebekah Wilson[2], Ryan Huddleston[3] Ray Kennedy[4], Julie Reid[5]

Contributorship statement

NM and RW can be considered joint first authors. NM and RW designed the study, collected and analysed the data and drafted the initial manuscript. RH designed the study, collected and analysed the data and revised the manuscript. RK and JR designed the study, analysed the data and revised the manuscript. All authors approved the final version of this manuscript prior to submission.

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Declaration of interest

No conflict of interest to declare by any author.

Data availability

Data available upon reasonable written request to the corresponding author.

Registration of Research and Ethical Approval

The study was preregistered with the Belfast Health and Social Care Trust Quality Improvement and Safety Department (ID number: 6409). No other preregistration exists for the study reported in this article. It was deemed by this department that ethical approval was not required as this was a retrospective service evaluation with anonymised data. No patients or members of the public were involved in the conduct of this research.

ABSTRACT

Background

Retroperitoneal sarcomas (RPS) are a heterogeneous group of rare tumours that require complex surgical management with outcomes tightly correlated to quality of surgery.

This study aimed to examine the determine patient demographics, treatment approaches and outcomes for patients with primary RPS in this single center during the period 2010- 2021.

Methods

All patients diagnosed with RPS from 2010 to 2021 that underwent surgical resection in a single trust in Northern Ireland were identified. Data was collated using histopathology records, electronic care records and retrospective chart review.

Results

Fifty-four resections were performed for RPS in a 10 year period. 30 day mortality rate was 3.7%, in-hospital mortality was 1.9% and 90 day mortality was 7.4%. 11.1% of patients were recorded as having a severe postoperative adverse event. 90.4% patients achieved an R0/R1 resection. The 1, 3, and 5-year overall survival were 80% [95% confidence interval (CI) 67-89), 69% (95% CI 53-79), and 62% (95% CI 48-75). The 1 and 5-year crude-cumulative-incidence (CCI) for local recurrence were 32% (95%CI 20, 46) and 55% (95%CI 32,77). 1 and 5-year CCI for distant metastases were 11% (95%CI 4, 23) and 35% (95%CI 15,59). Median overall survival was 6.3 years (IQR 5.0-7.6).

Conclusion

Survival outcomes in this LVH are similar to those reported by a number of HVHs worldwide, with an additional low rate of severe postoperative complication. Given that there are only between 250 and 300 new diagnoses of retroperitoneal sarcoma (RPS) in the UK each year prospective data collection and participation in multi-institution studies, specifically a UK collaboration, is critical to expand upon current knowledge and further improve management, outcomes and follow-up of patients with this rare and complex surgical disease.

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1.1 Introduction

Retroperitoneal sarcomas (RPS) are a heterogeneous group of rare tumours. Approximately 70–80% of primary retroperitoneal soft tissue tumours are malignant; however these only account for 0.1–0.2% of all malignancies[1]. The most common histologic subtypes are liposarcoma (well differentiated/dedifferentiated) and leiomyosarcoma, although rarer subtypes exist[1]. Mean patient age is approximately fifty years, but RPS occur at any age, arising equally in women and men. When symptoms are present, they most often relate to the mass effect of the tumour or to local invasion. Histopathological type and grade as well as complete surgical resection (especially on the first operative attempt) are well recognised as the main prognostic factors[1]. Multifocality is a negative prognostic factor[2].

Treatment of these cancers is complex. Surgery with complete resection of the primary tumour remains the only curative modality[3]. Neoadjuvant chemotherapy or radiation therapy may be considered in patients with technically unresectable or borderline resectable disease, but there is limited evidence to support the use of chemo-radiotherapy as a treatment modality[4,5]. The inaccessible location of the retroperitoneum and the absence of early symptoms often results in a large, locally invasive tumour by the time of diagnosis. This means that complete surgical resection can be difficult. Historically, operative mortality rates were high and complete resection was not possible for the majority of patients[7]. More recently, a multi-disciplinary approach to surgery and clinical decision-making has improved outcomes[4,5,6].

The Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG), first established in 2013 to address challenging management issues surrounding RPS, highlight that resection may require involvement of a urologist, vascular surgeon and general surgeon, in addition to a surgical oncologist with expertise in soft tissue sarcoma[5]. Compartmental resection, en bloc resection of organs and structures adherent to the tumour even if not clearly infiltrated, has become a standard treatment[4,5]. Decision making around preservation of organs and critical structures such as kidney, bladder, duodenum and sciatic nerve, takes into account patient physiology and anatomy, as well as RPS histologic subtype biology[5].

Unfortunately even patients with a R0 resection remain at risk for recurrence. For patients with intermediate- or high-grade sarcoma, this persists beyond 15-20 years, suggesting that patients should be followed indefinitely[5]. The median time to recurrence is less than 5 years; thus, more frequent imaging is indicated during this time frame. TARPSWG consensus guidelines suggest that RPS patients undergo follow up imaging 3-6 monthly for 2 years, then 6 monthly for further 3 years, then annually[5].

Worldwide these cancers are managed by multidisciplinary teams working in specialised centres. Evidence would suggest that outcomes are better at centres managing a high volume (>10 per year) of these cases[4,5]. It is recognised that collaboration of centres in sharing experience and expertise leads to better informed management and improved survival for patients. In the UK there are estimated to be only between 250 and 300 new diagnoses of retroperitoneal sarcoma each year. The Belfast Health and Social Care trust serves a population of 340,000 and provides services for both secondary and tertiary referral in Northern Ireland. In Northern Ireland all cases of RPS are referred to this trust for treatment and subsequent follow-up. This trust established a weekly sarcoma multidisciplinary meeting (MDM) in 2013 to discuss diagnosis and management of patients presenting with this rare and complex disease.

2.1 Aims

This study aimed to examine the determine patient demographics, treatment approaches and outcomes for patients with primary RPS in this single center during the period 2010- 2021.

3.1 Methodology

This work has been reported in line with the STROCSS criteria[6]. The study was preregistered with the Belfast Health and Social Care Trust Quality Improvement and Safety Department (ID number: 6409). No other preregistration exists for the study reported in this article. It was deemed by this department that ethical approval was not required as this was a retrospective service evaluation with anonymised data. No patients or members of the public were involved in the conduct of this research.

Patients diagnosed with the condition from 2010 to 2021 that underwent surgical resection in the Belfast Health and Social Care trust were identified using the trust histopathology database, Labcentre. This database was searched using terms “sarcoma NOS” and “retroperitoneum.” Histopathology reports were reviewed by a pathologist (RM). Intraabdominal and abdominal wall sarcomas were excluded. Ewing sarcomas, alveolar/embryonal rhabdomyosarcomas, desmoid tumours, gynaecological sarcomas and GIST were also excluded. Unfortunately, no histological grading was stated on the histopathology reports for 20 tumours. No patients were lost to follow-up. In order to ensure that the final dataset was complete, the trust sarcoma multidisciplinary meeting (MDM) database (established in 2013) was also reviewed with no further patients identified for inclusion.

Data was collected using electronic care records, histopathological reports and retrospective chart review. Information collated included patient demographics, tumour pathology, treatment and outcomes. Data were collected on Microsoft Excel (Microsoft Corp, Redmond, WA, USA) and then analysed using SPSS (Version 25, SPSS Inc, Chicago, Il, USA). The Kaplan Meier method was used to estimate overall survival and disease free survival. Overall survival was defined as the time between surgery and death from any cause; time was censored at the end of follow-up date of 02.07.2021 for patients who were still alive.

4.1 Results

From 2010-2021 fifty-four resections were performed for RPS in forty-four patients. A further 15 patients were diagnosed with RPS on biopsy but did not proceed to a major surgical resection. Twenty-four male patients and 20 female patients underwent surgery with age range of 18-82 years and a mean age of 58 (SD+/-15) years at time of diagnosis. Forty-three primary resections were performed, 10 subsequent secondary resections and 1 patient underwent a primary, secondary and third resection for local recurrence. Mean length of hospital stay was 9.5 days (SD+/-7.7) with 17 (32%) patients requiring intensive care admission post-operatively.

30 day mortality rate was 3.7%, in-hospital mortality was 1.9% and 90 day mortality was 7.4%. Eighteen patients (33.3%) were recorded as having a post-operative surgical

Table 1 - Post-operative complications

Clavien-Dindo Grade	Number (N)
I	3
II	9
IIIa	2
IIIb	1
IVa	2
V	1
Specific	**N**
Wound complication	5
Collection (Intrabdominal/retroperitoneal)	4
Anastomotic leak	1
Bowel obstruction	1
Ureteric perforation	1
Epidural infection	1
Death	1
Other eg mild AKI, VTE, urinary retention	4

complication with 11.1% of patients having a severe postoperative adverse events (classified as Clavien-Dindo 3 or higher). The most common adverse events were wound complication[5], or intra-abdominal/retroperitoneal collection[4]. Two patients returned to theatre; one with an anastomotic leak following a multi-visceral resection involving a colonic resection, and one patient who deteriorated rapidly in intensive care post-operatively requiring increasing doses of inotropes, and died shortly after surgery.

Forty-seven (90.4%) patients achieved an R0/R1 resection. Five patients (9.6%) achieved an R2 resection. The most common organ resected was kidney (29.6%), followed by

Table 2 - Surgical procedure performed

No organ resected	9
Other	8
Colon + kidney +/- other	2
Colon, kidney, spleen, pancreas +/- other	32
Major vascular resection+/- other	5
Pancreaticoduodenectomy	0

colon (24%) and the combination of colon and small bowel was the most common multi-visceral resection. Nine patients had a retroperitoneal mass that did not require the resection of any organ, five of which involved a major vascular resection. Surgical procedures performed is summarised in table 2. Five (9.3%) of patients went on to have chemotherapy post-operatively. Four (7.4%) patients had subsequent radiotherapy.

Table 3 - Tumour characteristics

FLCNCC histological sub-type	Number (N)	Percentage (%)
Liposarcoma (DD)	15	27.8
Leiomyosarcoma	13	24.1
Liposarcoma (WD)	8	13.0
Perivascular epithelioid cell neoplasm (PEComa)	3	5.6
Undifferentiated pleomorphic sarcoma	3	5.6
Malignant peripheral-nerve sheath tumour	2	3.7
Chondrosarcoma	2	3.7
Fibromyxoid sarcoma	2	3.7
Other	6	11.1
Grade*	**N**	**%**
1	8	23.5
2	5	14.7
3	21	61.7
Multifocality		
Yes	28	51.9
No	26	48.1
Completeness of surgical resection		
R0/R1	48	90.4
R2	6	9.6

*data not available for 20 tumours

Tumour size ranged from 3.8cm to 32.0cm with a median tumour size of 13cm. 51.9% of patients presented with multifocal RPS. The most common histological sub-type was dedifferentiated (DD) liposarcoma. Tumour characteristics are summarised in table 3.

The 1, 3, and 5-year overall survival were 80% [95% confidence interval (CI) 67-89), 69% (95% CI 53-79), and 62% (95% CI 48-75). The 1 and 5-year crude-cumulative-incidence (CCI) for local recurrence were 32% (95%CI 20, 46) and 55% (95%CI 32,77). 1 and 5-year CCI for distant metastases were 11% (95%CI 4, 23) and 35% (95%CI 15,59).

Overall survival (OS) was defined as the time between surgery and death from any cause; time was censored at the end of follow-up date of 02.07.2021 for patients who were

Chart 1- Kaplan–Meier survival curve for overall survival

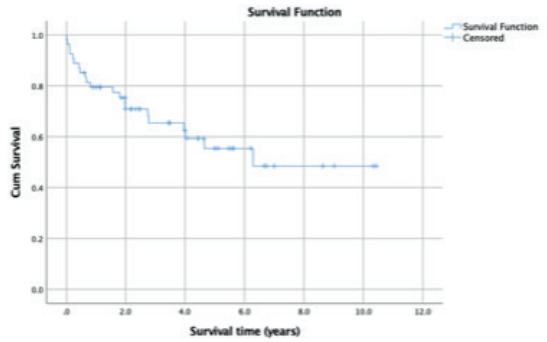


Chart 2- Kaplan–Meier survival curve split by completeness of resection (R0/R1 vs R2)

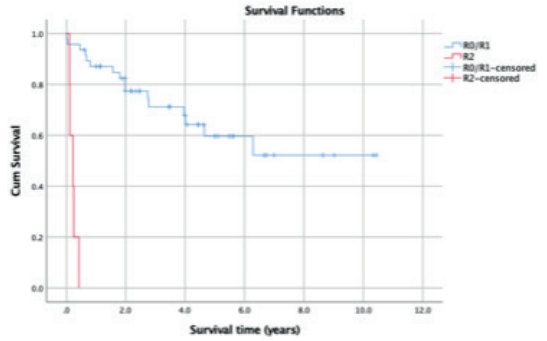


Chart 3- Kaplan–Meier survival curve split by age-group (<65years vs >/=65 years)

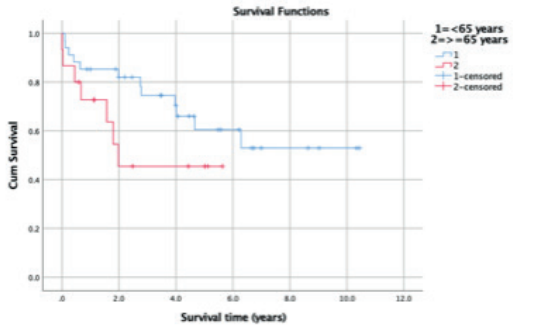
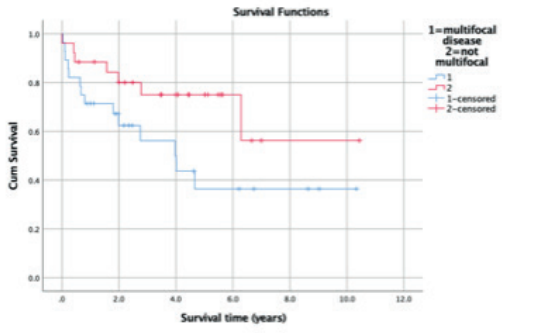


Chart 4- Kaplan–Meier survival curve split by multifocality (multifocal disease vs not multifocal)



still alive. OS curves were estimated using the Kaplan-Meier method. Median follow-up was 4.0 years (IQR: 2.0–5.3). Median overall survival was 6.3 years (IQR 5.0-7.6).

Chart 1 is Kaplan–Meier survival curve for overall survival. In chart 2, survival was split by completeness of resection (R0/R1 vs R2). An R0/R1 resection significantly predicted overall survival (p=<0.01). In chart 3 and 4, survival was split by age-group (<65 vs >/=65) and multifocality (multifocal disease vs not multifocal disease). Despite a clear divergence in the survival plots, the log-rank test comparing the groups was not significant (p=0.13 and p=0.06). Due to the lack of sufficient data to reach significance, no further regression analysis was pursued.

Following its establishment in 2013, TARPSWG recommend follow-up with imaging and clinical review 3-6 monthly for 2 years, then 6 monthly for further 3 years, then annually[5]. When studied from 2010, 52.8% of patients met these consensus guidelines.

5.1 Discussion

This retrospective case series is limited by its small size as is often the case with RPS studies worldwide[8,9]. However, our results show similar demographics to other studies, with a mean age at diagnosis of 58 and a comparable frequency of histopathological type of disease. Tumours were more likely to be multifocal at presentation than in other studies[9,10]**.** OS was 6.3 years (IQR 5.0-7.6) with a 5-year OS rate of 62%. Severe postoperative complication (Clavien-Dindo>/=3) occurred in only 11% of this population and over 90% of patients achieved an R0/R1 resection.

Due to its complexity many groups advocate for performing these resections at high-volume hospitals (HVHs) defined as those performing >10 RPS resections per year[4,5,11]. Several studies have specifically investigated outcomes in HVHs, compared to outcomes in low volume hospitals (LVHs), performing <10 RPS resections per year[12,13]**.** This unit would by definition be deemed a LVH. However, survival outcomes are similar to those reported by a number of HVHs, despite a higher percentage of patients having multifocal disease at presentation in this study. For example, Keung et al's study of almost 7000 RPS patients in the United States, reported an OS of 6.4 years and a 5-year OS rate of 58% for patients managed in HVHs (OS 6.3 years and 5-year OS rate of 62% in this unit)[12]. Villano et al reported an OS of 6 years for HVHs[12] and Maurice et al reported an OS of 5.9 years for HVHs[14]**.** In addition, this unit had a low rate of severe postoperative adverse events; 11% compared with 16.4% in MacNeill et al's TARPSWG study that specifically investigating morbidity following RPS resection[3].

RPS remains predominantly a surgical disease with outcomes tightly correlated to quality of surgery. Complete resection has been repeatedly demonstrated to be one of the most important predictors of local recurrence and overall survival from this disease[1,9-14]. In this study resection rate was the only investigated factor that had a significant impact on overall survival (p=<0.01). We noted a higher rate of multifocal

disease in this patient population than that reported in other studies. Multifocal lesions can be more difficult to resect, resulting in piecemeal or incomplete surgery, possible extension across anatomical borders, and the abutment or involvement of critical structures[2,9,10]. Despite this, the resection rate achieved by this unit was comparable to other centres (92.7% R0/R1 Villano vs. 90%[13]). Within this unit general, vascular, urology and plastic surgeons all attend the sarcoma MDM and these complex cases. This may suggest that the range of surgical expertise in the planning and execution of operative intervention, in addition to the recruitment of surgeons with a specific interest in this disease, results in comparable outcomes for patients.

There are limitations to this retrospective review. These findings, although similar to the those reported worldwide, are only applicable to this single centre that only established a dedicated MDM in 2013. The study was limited by its small size (as is often the case with RPS studies[8,9]). This meant that despite the apparent differences in survival between groups, they did not reach statistical significance, limiting the usefulness of any further regression analysis. Given the small numbers reported here, results are not stratified by demographics. In addition, the grade of 20 tumours was not stated on histopathology reports. However, the results from this single unit are interesting, highlighting that the right expertise from the relevant surgical subspecialities and the appointment of surgeons with specific interest in this complex surgical condition can result in comparable outcomes for patients. It is hoped that sharing the experience of this single unit will lead to better informed management and improved survival for patients.

6.1 Conclusions

In conclusion, surgery continues to be the dominant therapy for RPS with good quality resection at first surgical attempt offering patients the best chance of cure. This small, retrospective study highlights that survival outcomes in this LVH are similar to those reported by a number of HVHs worldwide, with an additional low rate of severe postoperative complication. Given that there are only between 250 and 300 new diagnoses of retroperitoneal sarcoma (RPS) in the UK each year prospective data collection and participation in multi-institution studies, specifically a UK collaboration, is critical to expand upon current knowledge and further improve management, outcomes and follow-up of patients with this rare and complex surgical disease.

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Clinical Paper

The Regional Palliative Medicine (RPMG) Assisted Dying Survey 2024

Matthew Doré [1], Alan McPherson [2]

ABSTRACT

Assisted Dying (AD), the ending of a person's life pre-emptively under a legal criterion is widely debated, both in the United Kingdom (UK) and Ireland. The expectation is often those doctors closest to dying would be both the proponents and facilitators of this action. A survey of Palliative Medicine in Northern Ireland (NI) on this topic has never been previously undertaken.

The Regional Palliative Medicine Group (RPMG) a representative body of all the Palliative Medicine Consultants in NI organised an anonymous 'Google Forms' survey on AD from 3/6/24 to 17/6/24 of all doctors of all grades working within Specialist Palliative Medicine at the time.

The survey had a 69% response rate (56/81) demonstrating 80% of all responding doctors working within Palliative Medicine and 100% of responding Palliative Medicine Consultants and Registrars in Northern Ireland do not favour a change in legislation allowing for AD.

91% (n=51) have concerns that AD will be influenced by a lack of availability of personal care at home. 93% (n=52) are concerned that AD will be influenced by cost-saving for the patient and their family and 82% (n=46) are concerned that AD will be influenced by cost savings for health and social care.

98% (n=55) stated if AD is legalised it should not be 'part of mainstream healthcare' with 45% (n=25) saying it should be 'via the legal system' and 46% (n=26) saying 'via a separate independent facility'. 53% (n=28) 'would not' and 40% (n=21) 'don't know', if they could remain working for an organisation that undertakes AD.

These results clearly show that Palliative Medicine in Northern Ireland will not be part of an AD service model. The question is who will be? Healthcare leaders now need to support their Palliative Medicine workforce by stating there will be AD-free healthcare facilities if AD is legalised.

Introduction

'Assisted dying' (AD) is used in this paper as an umbrella term encompassing both euthanasia (active administration of lethal medications) and physician-assisted suicide (providing the means for the patient to take lethal medications).

There are current debates about the introduction of AD legislation in both the Republic of Ireland and the United Kingdom (UK). If either of these jurisdictions legalise AD there are direct and indirect consequences for the Northern Ireland (NI) population. In particular, the new Irish 'Voluntary Assisted Dying Bill 2024'[1] proposes an eligibility criterion of being a "resident on the island of Ireland and has maintained such residency for not less than one year." Thus, this Bill will legislate for NI adults to access AD across the border.

Background

The views of Palliative Medicine doctors regarding AD are well documented in multiple surveys. The Association for Palliative Medicine of Great Britain and Ireland (APM) members survey in 2015 demonstrated 82% were opposed to changing the law [2]. The Royal College of Physicians (RCP), stratified for Palliative Medicine outlined in 2019, 84.3% opposed a change in the law, and 84.4% were not prepared to actively participate in physician-assisted suicide [3]. The British Medical Association (BMA), stratified for Palliative Medicine in 2020 demonstrated 84% would not be willing to actively participate in the process of administrating life-ending drugs [4]. The APM Scotland survey demonstrated in 2022, 75% would not be willing to participate in any part of the AD process and 98% stated that AD should not be part of mainstream healthcare. However, there has never been a specific survey on the views of Palliative Medicine in Northern Ireland.

The Regional Palliative Medicine Group (RPMG), the representative body of all the Palliative Medicine consultants in Northern Ireland, sought to close this gap by conducting a comprehensive survey of all the doctors working in Palliative Medicine in Northern Ireland. This survey has been conducted by the RPMG.

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This survey was undertaken by the RPMG.

Ethics

Using the UK Medical Research Council website, it is determined this paper does not need reviewed by a NHS Research Ethics Committee. [5]

Methodology

The Palliative Medicine clinical lead in each trust and charitable hospice, community and hospital service throughout Northern Ireland was contacted to provide the name and email address of each doctor (of any grade) who was working in Palliative Medicine between the 2 weeks - 3/6/24 to 17/6/24. This equated to 81 individual doctors.

A 'Google Forms' was set up so that each email was anonymously logged against a response, and although the individual link did not expire once completed, there were no duplicate uses of any individualised link.

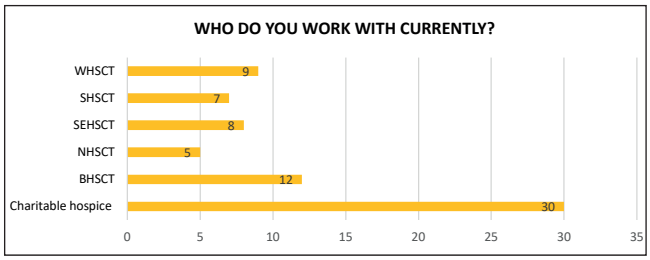
All data was stored anonymously, and password protected on the 'Google Forms', transferred to Excel and analysed. All emails were removed before analysis, thus maintaining anonymity.

Response rate

The survey had an overall 69% response rate (n=56/81) from all medical staff, at all grades, in Palliative Medicine. This represents an 85% (n=23/27) response rate from Palliative Medicine Consultants and an 86% (n=6/7) response rate from Palliative Medicine Specialty Registrars.

Demographics

Out of all the responses (56), 42% (n=23) were Palliative Medicine consultants, 34% (n=19) were SAS doctors / speciality doctors / hospice physicians (non-training), 11% (n=6) Specialty Registrars (in training), 11% (n=6) GP's or GP trainees working in Specialist Palliative Medicine and 2% (n=1) as another junior trainee.



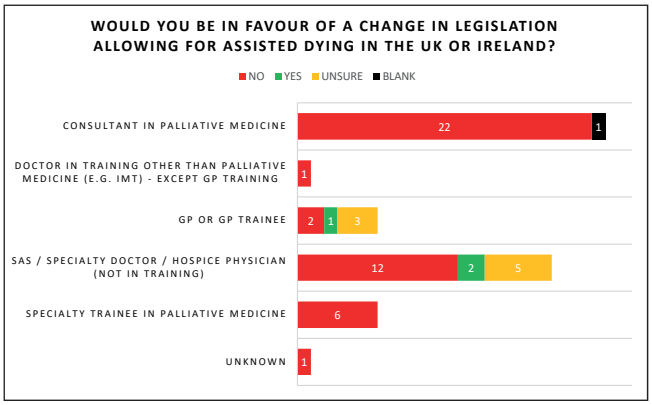
The Palliative Medicine workforce is complex with 27% of respondents (n=15/55) having multiple employers across various trusts and charitable hospices.

77% (n=43/56) of the Palliative Medicine workforce, who responded, provide either a trust or charitable hospice/ inpatient specialist palliative care (SPC) service. The charitable sector hospices are the Foyle Hospice, Marie Curie Hospice Belfast, Northern Ireland Hospice and Southern Area Hospice. The Trust inpatient SPC services include the Macmillan Unit Antrim and the Palliative Care Unit Omagh Hospital and Primary Care Complex.

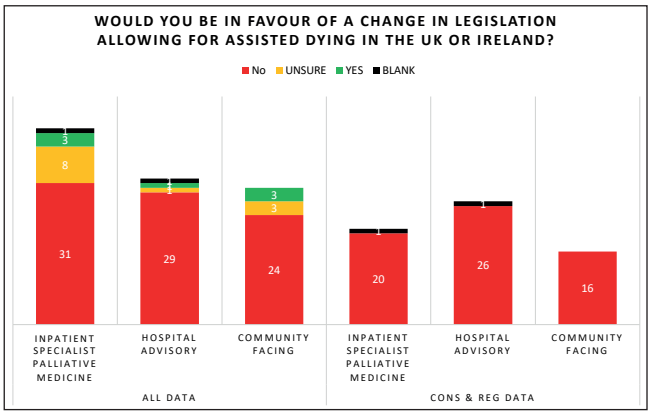
Also, within the responding workforce, 54% (n=30/56) had a community aspect to their jobs. 46% (n=26/56) had a hospital liaison role / cancer centre liaison.

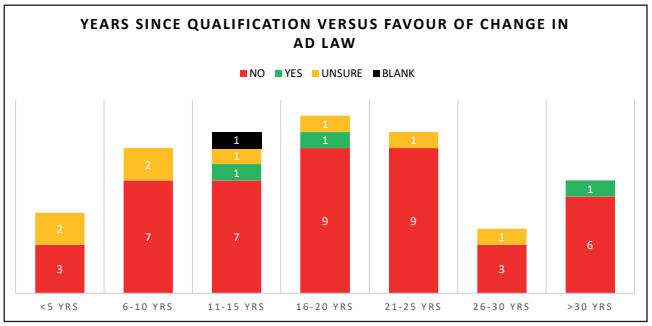
Results

Out of the 69% of respondents, 80% (n=44/55) of doctors working within Palliative Medicine and 100% of Palliative Medicine consultants and Palliative Medicine registrars do not favour a change in legislation allowing for AD in the UK or Ireland. Out of all doctors surveyed, 14.5% (n=8) were unsure and 5.5% (n=3) were for a change in the law to legalise AD.



Breaking the results down by role shows; that 93% (n=37/40) in-patient specialist Palliative Medicine, 96% (n=25/26) hospital advisory / cancer centre , 89% (n=24/27) Community Palliative Medicine would not be in favour of a change in legislation for AD.

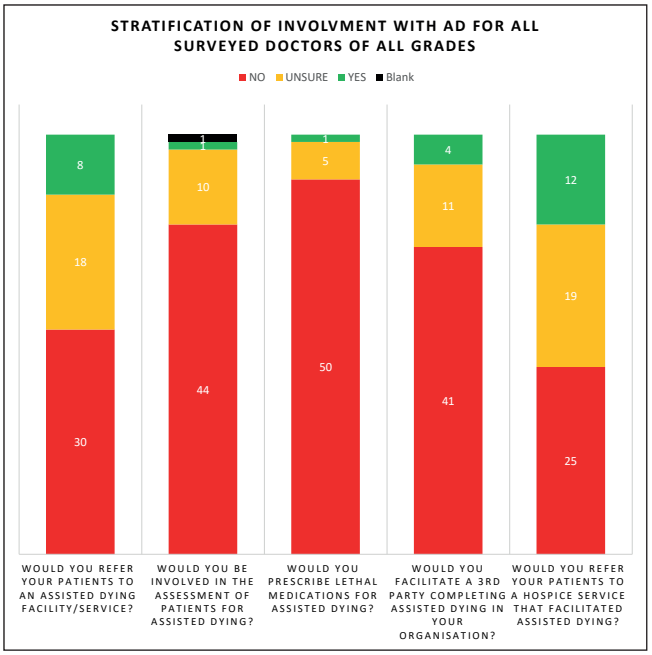


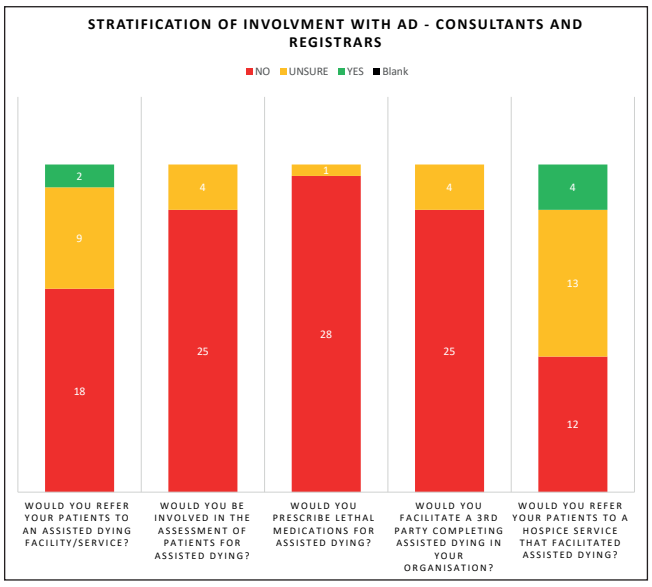


The SAS doctors and GPs were the only 2 groups of doctors to vote unsure or yes to a change in the law. The Hospital advisory (incorporating the Cancer Centres) was the least likely place of work to vote for a change in law.

Years since qualification did not seem to have any correlation with views on changing the AD law.

When asked to consider the legalisation of AD, respondents considered their potential to be involved. 0% of responding Palliative Medicine consultants and registrars would agree to be involved in prescribing lethal medications, facilitate a 3rd party completing AD, or be involved in the assessment of patients for AD (n=29).



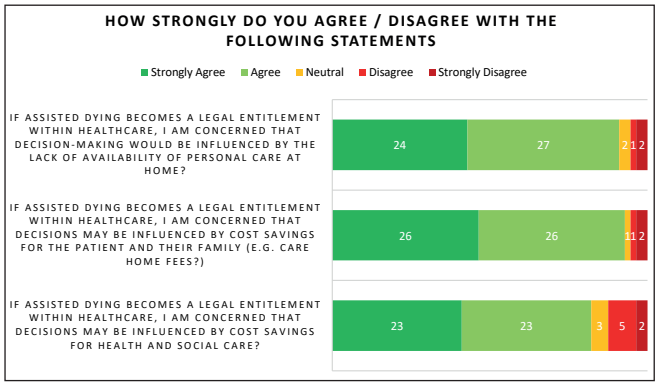


14% (n=8/56) of all the surveyed palliative doctors of all grades would refer a patient to AD services, but only 1 person would prescribe lethal medications. 7% (n= 2/29) of consultants and StRs would refer to an AD service, but 100% (n=29/29) not would be involved in the process. 86% (n=25/29) of consultants and registrars are not convinced they would refer their patients to a hospice/in-patient service that facilitated AD (even if it was not for AD).

To What Extent Do You Agree With The Statement 'Legal Safeguards Will Be Sufficient To Prevent Harm To Vulnerable Patients If AD Were Legalised'

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
Consultant in Palliative Medicine	15	8	0	0	0
Specialty trainee in Palliative Medicine	3	3	0	0	0
SAS / specialty doctor / hospice physician (not in training)	10	4	4	1	0
GP or GP trainee	1	2	1	2	0
Doctor in training other than palliative medicine (e.g. IMT) - except GP training	0	1	0	0	0
Unknown	1	0	0	0	0

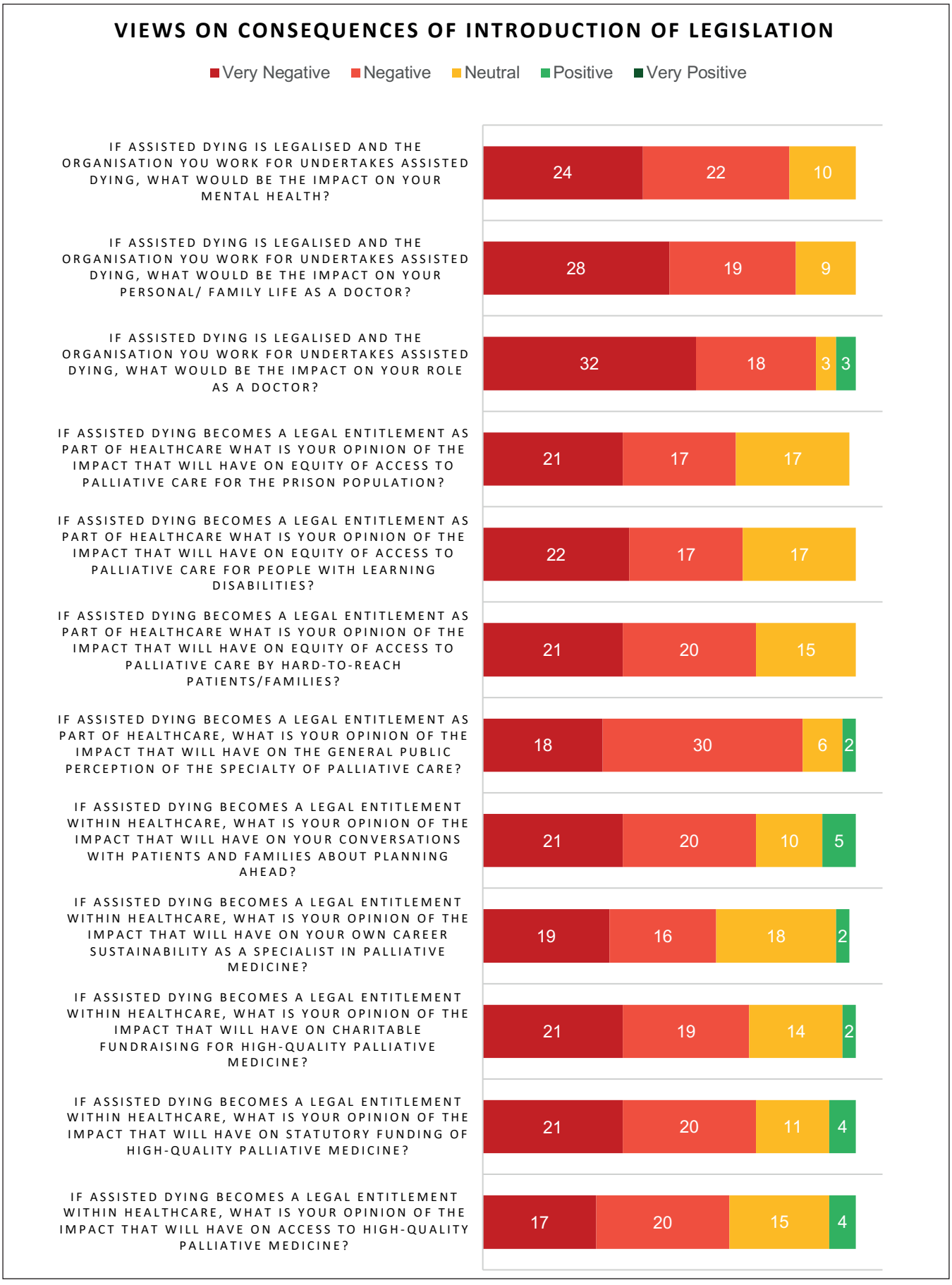
100% of Palliative Medicine Consultants (n=23) and Registrars (n=6) 'Strongly Disagree' or 'Disagree' with the statement "legal safeguards will be sufficient to prevent harm to vulnerable patients if assisted dying were legalised" A total of 3 doctors comprising of 1 SAS doctor and 2 GPs / GP trainees, in the survey agree safeguards will be sufficient. No one strongly agrees.



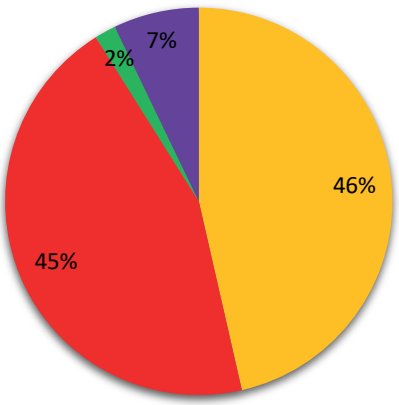
91% (n=51/56) 'Agree' or 'Strongly Agree' in concern that AD will be influenced by the lack of availability of personal care at home. 92% (n=52/56) 'Agree' or 'Strongly Agree' in concern that AD will be influenced by cost saving for the patient and their family and 82% (n=46/56) 'Agree' or 'Strongly Agree' in concern that AD will be influenced by cost savings for health and social care.

The consequences 'If' AD becomes legalised questions when averaged out demonstrate 40% 'Very Negative' (mean 22), 35% 'Negative' (mean 19.8), 22% 'Neutral' (mean 12), 3% 'Positive' (mean 1.8) and 0% 'Very Positive'.

When asked if AD becomes a legal entitlement and what



If AD becomes a legal entitlement, what would be the best way to make this available?

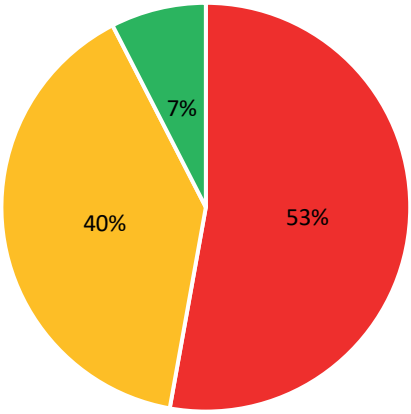


- In separate independent healthcare facilities licensed solely for this purpose and outside of NHS organisations or charitable hospices. (n=26)
- Via the legal system i.e. court authorized decision-making and court directed process. (n=25)
- As part of mainstream healthcare entitlement (including NHS organisations or charitable hospices) and therefore embedded as a duty of care of healthcare providers. (n=1)
- Other (n=4)

'Other' includes: (quoted)

- as a private option
- given the potential for backlash i wonder if a combo of the above eg. independent org plus court assisted decision making although at the same time i see this would be very clunky and potentially expensive for patients. so not ideal
- Ideally to not be within our society, if it is within our society completely out side healthcare. This is not healthcare
- Performed by the specialist with expert knowledge of the condition in question. If cancer causing the suffering - the oncologist should do the assisted suicide, if MND - the neurologist should do the assisted suicide etc etc

If AD is legalised and the organisation you work for undertakes AD would you be willing to continue to work within that organisation?



No (n=28) Maybe (n=21) Yes (n=4)

All the reasons given: (quoted)

- I just don't know - I would have to fully appraise how it impacts on my day to day ability to care for the in-patients.
- As long as I can remain apart from it
- If there wasn't a true way to conscientiously object I would have to consider leaving
- Only if I was able to opt out of any involvement in assisted dying
- Depends on what involvement we were expected to have
- Not within a hospice setting. Perhaps if it was performed in the NHS.
- I love working in Palliative Medicine and essentially don't know what other aspect of medicine I would be useful in! But I would be watching very closely to the expectations of organisation and patients in regards to my personal involvement in this. And bottom line, I can and would retrain in something less involved in Assisted Suicide if needed to.
- I do not feel an organisation should be offering both palliative care and assisted dying. Assisted dying should be a separate specialty where people are referred to.

would be the best way to make this available, the answer 'as part of mainstream healthcare' was 2% (n=1). The majority was within an equal split between 'through the legal system' or a 'separate independent licenced facility'.

This last question may help employers understand what their Palliative Medicine staff views are regarding working for an organisation which facilitates AD and thus helps form organisational positions. Indeed, 'Assisted Dying free zones' are now appearing in legalised jurisdictions around the world. Employers will need to seriously consider this approach.

Limitations

The survey was open for 2 weeks and although the response rate was overall 69% this could have possibly been higher if we had the survey open for longer. The survey also selects those who are interested in this topic and debate and therefore there is a non-random selection bias in those who completed this survey. The survey also did not seek the views on this topic from both the wider multidisciplinary team working in palliative care and other professionals in other specialities. We also did not pilot the survey to ensure understanding of the questions, this has resulted in uncertainty regarding one

specific question with four parts which could be interpreted in very different ways and therefore has been omitted from the analysis. This question did not state if the situation was about patients before palliative medicine was involved or after and therefore is impossible to interpret.

Conclusion

This is the first survey of the views of Palliative Medicine physicians in NI about AD. The results are consistent with the wider picture from similar polls in other parts of the UK over the last 9 years. From those surveyed, the majority of NI Palliative Medicine doctors of all grades (80%) are against the introduction of this legislation, and this is unanimous when looking specifically at the consultant and registrar palliative medicine doctors, who are 100% against legalising AD. The survey also demonstrates the view does not change with 'years since qualification' thus it is unlikely to change in the future.

The survey demonstrates serious concern regarding the many consequences legislation of AD would have; on the various groups of patients (the disabled, prisons, vulnerable, learning difficulties), our society (lack of social care, cost-saving for healthcare), the funding (both statutory funding and charity fundraising), the doctors themselves (mental health, family life) and Palliative Care as a whole (reduced access to good Palliative Care).

The current body of legislation (particularly the most recent Voluntary Assisted Dying Bill in Ireland 2024, for the Island of Ireland) being proposed has an expectation of integration into the current healthcare model, with Palliative Medicine integral to its implementation, assessment and safeguarding[1]. However, this will not be a sustainable service model in NI as only 2% (n=1) of Palliative Medicine doctors (0% Palliative Medicine consultants and registrars) are in support of this model.

It is imperative, before any legislation is potentially enacted, that the leadership in both the charitable hospices and Health and Social Care Trust services see the strength of opinion within these results. Indeed, it is clear by some margin that the results of this survey demonstrate the view that AD is not within the remit of Specialist Palliative Medicine. Imposing such controversial and divisive legislation will create risk and division in the already under-resourced Palliative Care services across NI.

Often individual conscientious objection is cited as an answer to varying opinions. However, for AD, this isn't an adequate answer as Palliative Medicine clinicians will invariably face impossible moral and legal situations if legislation is imposed. Indeed, there remains no 'true' conscientious objection as a requirement to refer onwards remains in legislation[1]. There now needs to be a clearly stated and published organisational position from each institution supporting their Palliative Medicine staff. It is stark that 53% (n=28) would 'not' and 40% (n=21) 'don't know' if they could remain working for an organisation that undertakes AD.

These results highlight the large contribution of the charity sector to Palliative Medicine as 55% (n=30/55) have a role in a hospice. Surely the ambition of the government would be to continue the development of Palliative Care services across NI and not abandon such a responsibility to the charitable sector.

If society wishes to pursue AD, this is for society to decide. The consensus from this survey of Palliative Medicine is that although AD legislation is not wanted; if it were to be implemented, the suggested models of implementation strongly favour a model out with healthcare and certainly Palliative Medicine. Individual patient 'Choice' includes not being recurrently asked 'Have you considered AD?' and thus there should be AD free-zones. With the strength of staff opinion outlined, at the very least it should be the specialist palliative care services which provide these AD free-zones. The vast majority of Palliative care physicians in NI believe that when a palliative care specialist comes to see you or your loved one, it should be reassuringly clear their role is to treat you and your suffering and not offer or refer for AD.

We would encourage other medical specialities and the wider multidisciplinary teams to replicate this survey to clearly inform any future decisions.

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The authors would like to thank all the medical professionals who completed this survey, RPMG and the Ulster Medical Journal. Any requests or questions regarding this survey, please contact MD or AM.

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Clinical Paper

Integration of genomic medicine to mainstream patient care within the UK National Health Service

Anhukrisha Karthikeyan[1], Shane McKee[2], Gareth J McKay[1]*

Abstract

The integration of genomic medicine within mainstream patient care promises advances in healthcare and potential benefits for disease prediction and personalised treatment approaches. This paper explores the challenges of integrating genomic medicine within the UK's National Health Service (NHS) and potential solutions for alignment with the NHS's proposed long-term plan and Genome UK strategy.

Critical challenges and knowledge gaps have been identified, including a referral-dependent system, unclear eligibility criteria, lack of policies and guidelines, gaps in clinical genomic competence, genomic sequencing costs, equity issues for genomic testing access across the UK, and data management and patient privacy concerns.

Proposed solutions and future directions include extending genetic test ordering authority to include mainstream clinicians and establishing unambiguous eligibility criteria, policies and guidelines through a developing trained workforce and appropriate patient engagement. Moreover, expanded Whole Genome Sequencing (WGS) and pharmacogenomic testing approaches through up-scaling genomic sequencing capacity and standardising genetic testing across the UK will lower consumable costs. Leveraging artificial intelligence (AI) and data warehousing approaches will improve data management, particularly in the context of integration within electronic health records.

In summary, the successful integration of genomic medicine within mainstream patient care holds transformative potential for healthcare provision. By recognising the challenges identified and embracing the proposed solutions, healthcare systems can revolutionise patient outcomes, advancing precision medicine and shaping the future of genomic-driven healthcare.

Keywords: genomic medicine, mainstream care, Whole Genome Sequencing (WGS), pharmacogenomics, NHS, genetic testing

Introduction

Advances in genomics and genetic testing offer improved disease diagnoses for patients that may also provide additional benefit for family members[1]. Genetic testing within the NHS involves patient genetics service referral if an underlying genetic cause is suspected. Although the current Test Directory now allows mainstream clinicians to order some genetic tests, the system remains mostly referral-dependant from primary or secondary care doctors with limited roles for mainstream clinicians not specialised in genomics that care for patients with genetic-related conditions. A clearer understanding of the referral criteria to identify those patients best suited for genetic testing would be beneficial[2]. A further challenge to the effectiveness of this approach is that genomics traverses multiple clinical specialities and services, often necessitating a 'whole systems approach'[3] to enable successful integration within mainstream patient care and maximise clinical impact and patient benefit[3].

Integration of genomic medicine within mainstream UK healthcare should be considered within the context of balancing capacity and resources. With improved access and integration of genetic testing within the NHS, improved personalised and precision medicine approaches have the potential to move beyond the field of oncology into other medical disciplines. Genetic information can inform decisions around patient care to optimise timely diagnoses and treatments of genetic conditions[2].

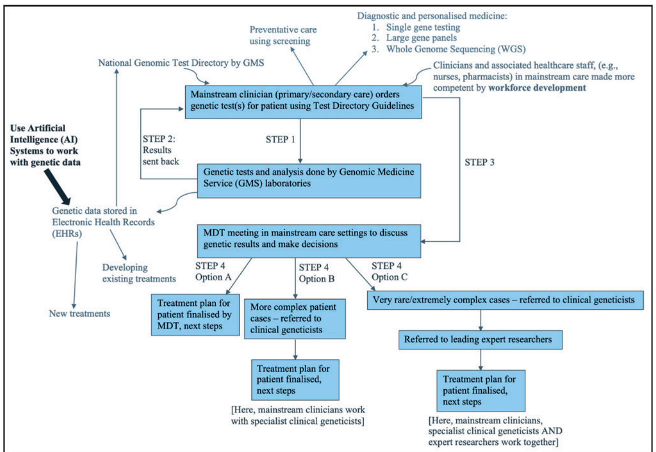

Figure 1. Summary of the Genomic Strategy Framework

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This manuscript aims to evaluate the integration of genomic medicine within mainstream healthcare in line with the principles of the NHS Genomic Medicine Service (GMS) of the NHS long-term plan[3] and Genome UK strategy[4], under the summary framework shown in Figure 1.

Extending Genetic Test Ordering Authority

The NHS workflow is currently challenged by the complex and time-consuming patient pathway to genetic testing. As such, mainstreaming genomic medicine requires a more simplified and efficient approach, to ensure an accelerated and accurate diagnosis. This could be achieved by providing authority to clinicians not specialised in genomics in primary or secondary care to order certain genetic tests without the prior need to refer the patient to a clinical geneticist[5]. This approach has been implemented recently in some NHS specialities such as endocrinology, where an endocrinologist can request a gene panel test for patients with suspected familial hypocalciuric hypercalcaemia[5]. Further extending this authority to other specialities could reduce the burden on specialised clinicians, enabling faster access to genetic testing and improved patient care.

Setting clear eligibility criteria for genetic testing

A key issue faced by clinicians in community and hospital practice lies in the identification of patients most likely to benefit from genetic testing and the appropriate tests to be ordered. Several factors to establish the eligibility criteria were outlined by the Public Health Genomics (PHG) foundation[2]. These include the disease characteristics, frequency within the population, and the clinical setting in which the test will be undertaken[2]. Determination of transparent eligibility criteria is essential to mainstreaming genomic testing as doctors working in primary or secondary care settings lack the expertise of specialist geneticists, and so the establishment of clear guidelines to better inform patient referral for appropriate testing is essential. The National Genomic Test Directory (NGTD)[6] specifies the patient eligibility criteria for access to genetic testing. Expanding and improving this is a starting point for better integration of genomic medicine within mainstream care settings. This initiative has already started within NHS England after the recent formation of the nationally commissioned GMS, which builds upon the existing NHS infrastructure and outcomes from the 100,000 Genomes Project[7]. The GMS recently introduced the rare disease and cancer somatic tissue genetic test directory to enhance the existing NGTD[5].

Setting clear policies and guidelines

A recent systematic review highlighted the importance of policies and guidelines for the successful integration of genomics within mainstream patient care[8]. Clinicians reported challenges arising from insufficient guidelines relating to several aspects, including pharmacogenomic testing, family health history collection, and disclosure of secondary findings. Difficulties have arisen from translating policies and guidelines into clinical practice. For example, in the UK, clinical genetics guidelines consider genetic information as confidential to families, but in practice, decision-making around confidentiality and disclosure tends to follow an individual-based model. Similarly, in the USA, an insurance-mandated requirement for genetic counselling before testing for specific genetic mutations, like BRCA1 or BRCA2, resulted in unintended consequences, with a higher number of individuals opting out of genetic testing after the policy's introduction. These findings underscore the significance of well-designed and effectively implemented policies and guidelines to address the challenges of seamlessly integrating genomics into routine patient care[8]. Notably, the Global Alliance for Genomics and Health (GA4GH) has played a pivotal role in this endeavour by developing comprehensive policies and guidelines. One of its key contributions is the 'Framework for Responsible Sharing of Genomic and Health-Related Data', which outlines a structure for responsible data sharing providing multiple resources around policy guidance, consent tools, and data access standards. These resources serve as a valuable reference for healthcare institutions and professionals seeking to establish and accelerate genomic medicine while ensuring patient-centred and ethically informed practices in the era of precision medicine[9].

Personalised medicine and preventative care

Two main approaches for the incorporation of genomic medicine within routine mainstream healthcare have been proposed: diagnostic and personalised medicine, and preventative care[4] (Figure 1).

Diagnostic and personalised medicine

Firstly, in terms of diagnostic and personalised medicine, a wide variety of genetic tests are available, such as single gene testing for cystic fibrosis, *BRCA1* breast cancer etc, as well as large gene panels and Whole Genome Sequencing (WGS)[3]. As outlined by Genome UK, pharmacogenomics provides an important opportunity for incorporation within routine care. Pharmacogenomics is the study of the role and influence of genetic variants on an individual's response to drugs and can guide prescribing practice and likely responsiveness to a particular drug[10]. Therefore, incorporating routine genomic testing within the NHS would inform medication prescribing and dosing regimens for individual patients, expanding the concept of personalised medicine. In addition, pharmacogenomic testing offers the potential to limit adverse drug reactions (ADRs). A recent systematic review and meta-analysis in 2021 revealed that more than 8% of patients in receipt of primary care developed ADRs[11]. Furthermore, a large prospective observational study within a UK teaching hospital reported ADRs contributed to, or directly caused, 16.5% of all admissions with an associated mortality rate of 0.34%. The projected annual cost of ADR admissions to the NHS in England was estimated at £2.21 billion in 2021, with almost 40% of ADRs identified as avoidable or potentially

avoidable[12]. There is increasing evidence that genetic variants are associated with ADRs[13]. For instance, the presence of the HLA-B*15:02 allele was reported to significantly increase ADR risk in individuals receiving the antiepileptic drug carbamazepine[14]. Thus, genetic variants detected through pharmacogenomic testing can be used to predict the potential for ADRs to minimise such events in patients through tailored medication prescribing or recommendation of alternative drug classes[3]. The recent prospective, multi-centre Pre-emptive Pharmacogenomic Testing for Preventing Adverse Drug Reactions (PREPARE) study investigated the clinical benefits of a pre-emptive genotyping strategy using a 12-gene pharmacogenetic panel to limit clinically relevant ADRs. This ground-breaking study reported pharmacogenomic-guided treatment significantly reduced ADR incidence. Specifically, in patients with actionable genetic variants related to their prescribed drugs, the incidence of ADRs was significantly lower in the pharmacogenomic-guided group compared to standard care, with an odds ratio of 0.70 (95% Confidence Interval 0.54–0.91)[15], highlighting the potential of pharmacogenomic testing for improved medication safety and best clinical practice.

WGS involves sequencing the entire patient genome within a routine clinical care and genomic medicine service. The completion of the NHS 100,000 Genomes project provided a platform for the routine use of WGS as a diagnostic service. This initiative provided improved clinical care and research opportunities by revealing new diagnoses for many patients across a wide range of rare diseases[7]. A study investigating 4,660 participants from the 100,000 Genomes Project found that WGS was successful in the identification of disease-causing variants present in genomic regions not commonly considered using other testing approaches[16].

Diagnostic medicine in cancer and rare diseases

The benefits of genomic medicine approaches are evident in cancer studies. For instance, 36 non-consecutive paediatric patients with 23 different solid tumour types representing over one-sixth of all cases nationwide were recruited to the 100,000 Genomes Project and analysed using WGS. Remarkably, clinically informative driver variants were identified in 70% of central and peripheral nervous system tumours. Additionally, WGS identified potential new therapeutic opportunities in 8 out of 36 cases (22%) that would not have been routinely detected through current NHS practice[17]. Identification of these genetic risk variants provided information on the cancer's pathogenesis and type, which refined and/or changed the diagnosis and identified associated hereditary cancer risk. This provided crucial insight for tailored treatment plans that improved patient outcomes although turnaround times were protracted, and issues associated with variant cataloguing and interpretation, and national data-sharing opportunities for benchmarking exercises, were recognised[18].

Genomics has emerged as a valuable tool for the detection of cancer relapse, and one promising approach involves the use of circulating tumour DNA (ctDNA), fragmented DNA from tumour cells that circulate in the bloodstream. This enables doctors to identify the recurrence of a patient's cancer more rapidly and accurately than traditional methods like imaging[19]. A recent study investigated the relapse of early-stage non-small-cell lung cancer (NSCLC). Among the 28 patients who experienced clinical recurrence during the observation period, ctDNA was detected in samples collected before recurrence in 12 cases. The median lead time between ctDNA detection and clinical recurrence in these cases was 212.5 days. Additionally, in 8 of the 20 patients who had clinical recurrence more than 200 days after the end of treatment, ctDNA was detected before recurrence, providing a median lead time of 402.5 days. These findings highlight the significant benefits of ctDNA detection in extending lead time for identifying cancer recurrence and timelier intervention to improve patient outcomes[20].

Beyond the sequencing of the tumour genome to uncover actionable characteristics informing treatment and detect relapse, genomic testing also plays a pivotal role in identifying potential germline variants associated with genetic predisposition. This knowledge is not only crucial for the patient but also has implications for other family members who may share these genetic risk factors. A recent study investigated the impact of germline mutations on lung cancer susceptibility and their correlation with somatic mutations. This study involved the analysis of germline mutations from 1,026 patients using a 58-gene next-generation sequencing (NGS) panel containing known hereditary cancer-related genes. The results revealed plausible genetic susceptibility in 4.7% of lung cancer patients, identifying 14 patients with pathogenic mutations and 34 patients with likely-pathogenic mutations. This insight into germline risk variants provides an opportunity for targeted screening and early intervention to mitigate cancer risk within affected families[21].

Rare diseases collectively affect ~7% of the UK population with more than 80% subject to an underlying genetic component[22]. Accurate diagnosis and treatment for patients with rare diseases remains challenging despite extensive testing[22,23]. Delays in reaching an accurate diagnosis [the "Diagnostic Odyssey"], as well as misdiagnoses of patients with rare diseases often result in missed opportunities for beneficial and timely intervention[22]. Thus, accelerating pathways that include WGS may improve access to timely and effective treatments and shorten the Diagnostic Odyssey. Recent research on the clinical utility of rapid whole genome sequencing (rWGS) in critically ill infants with congenital heart disease highlighted the potential for improved genetic diagnostic rates compared to standard microarray ± gene panel testing. Furthermore, a 2023 retrospective, population-based cohort study evaluated the effect of rWGS in children presenting with acute liver dysfunction reporting higher diagnostic rates that led to a change in clinical management for one-third of patients[24]. rWGS not only offers timely and actionable information that may influence treatment options

but could also reduce associated longer term patient care costs. This evidence supports the premise that implementing WGS, particularly through rWGS approaches, can expand access to timely and life-saving treatments for patients with rare diseases[25]. In recognition of the potential for genomics to improve patient care, the NHS Long Term Plan has outlined goals to expand the use of WGS and genomic testing to cancer patients and those with genetic disorders such as familial hypercholesterolemia. Healthcare systems can enhance diagnostic capabilities, facilitate personalised treatments, and improve outcomes for patients with rare diseases by embracing these strategies[3].

Nevertheless, the use of WGS remains somewhat controversial as the technology remains expensive, and the diagnostic success is largely dependent on the accuracy of detailed phenotypic information. The process of ordering appropriate tests can be challenging for clinicians balancing a busy workload. Consequently, automated methods to extract phenotypic information in a structured format from clinical notes and Electronic Health Records (EHRs) have included the use of Natural Language Processing (NLP) algorithms[26,27]. In addition, although WGS provides a comprehensive overview of individual genomes, the vast majority of data generated is irrelevant to the patient's presenting complaint or health prospects. This can lead to false-positive or spurious findings, where a variant with no clinical relevance is erroneously flagged as significant. Thus, to ensure the accuracy and clinical integrity of the data generated and minimise the reporting of spurious findings, it is essential to focus on the genes or genomic regions known to be associated with the patient's specific condition[28].

Preventative care

Accelerated use of genomic-based screening within routine care would expedite its incorporation within mainstream preventative care. This could potentially benefit patients and healthcare providers through reduced adverse events and longer-term healthcare costs. One example is the provision of Non-Invasive Prenatal Testing (NIPT) as a more accessible approach for the screening of fetal genetic conditions. Between 10-20% of cell-free DNA (cfDNA) within maternal blood contains a fetal component known as cell-free fetal DNA (cffDNA) during pregnancy[29]. NIPT can be used to test for fetal aneuploidies like Down Syndrome (DS) by analysing maternal blood[29] replacing invasive tests that require the collection of amniotic fluid. NIPT could improve earlier DS diagnoses and inform parental decisions regarding the continuation or potential termination of the pregnancy given its high sensitivity and specificity of 99% and 99.5% respectively[29,30]. Given that almost 75% of rare diseases affect children, early diagnosis could enable health professionals to support families about the associated risks of having further children – thus, early genetic testing could prevent families from potentially having additional children with the same genetic condition[22]. Furthermore, the introduction of NIPT for the detection of fetal aneuploidies in Wales has shown significant cost efficiencies and reduced risk of miscarriage[4]. In addition, current new-born screening involves a heel prick blood test to detect rare diseases. Introducing WGS to new-born screening could expand the scope for earlier detection of a much wider array of rare diseases and genetic conditions. This could facilitate early intervention ultimately enhancing long-term health and quality of life with associated cost benefits for healthcare provision[31].

Nevertheless, the logistical challenges and costs associated with introducing genomic medicine approaches such as pharmacogenomics, WGS or screening into mainstream care, remain significant, possibly necessitating prioritisation of pharmacogenomic testing to the most commonly prescribed medications. This includes drugs associated with the highest prescription volumes, costs, health burdens, and ADRs. Further, ensuring quick turnaround times for test results is crucial for the successful implementation of pharmacogenomic testing in prescribing practices. Given current resource constraints, modifying existing workflows to accommodate frequent prescription changes based on additional pharmacogenomic information is often impractical. Moreover, delays in test turnaround times could undermine the potential benefits of utilising pharmacogenomics data, particularly since many ADRs occur shortly after initiating a new medication. A potential solution to this is implementing a system that allows clinicians to specify the timeframe for patients to begin drug treatment enabling laboratories to prioritise sample analysis before treatment initiation. By facilitating timely decision-making based on pharmacogenomic information, this approach would minimise the risk of ADRs and suboptimal treatment outcomes[32].

Another approach includes the concept of sequencing first and asking questions later. Storing genomic data in EHRs would allow for its retrieval for analysis each time a patient is prescribed a new drug. A recent study explored the utility of ClinPharmSeq, a targeted sequence panel specifically designed for pharmacogenomic testing that focused on a select set of genes associated with drug response. This approach combined cost-efficiency with significantly reduced data storage and computational capacity for analysis needs compared to the more comprehensive approach of WGS. It informs prescribing practice by employing genomic data that is not exhaustive but rather focused exclusively on genomic facets pertinent to drug metabolism[33].

Costs associated with genomic sequencing

The costs associated with WGS represent a significant implementation barrier within mainstream genomic medicine. Despite significant cost reductions from $3 billion for the first human genome sequenced to approximately $200 today[34], these figures largely reflect only the actual sequencing costs. A 2019 UK-based study reported total costs for WGS and clinical analysis for a cancer case or rare disease trio at £6,841 (£3,420 per genome) and £7,050

(£2,350 per genome), respectively[35]. These costs also reflect sample processing, associated bioinformatics analyses, and infrastructure requirements for the interpretation and storage of results. The study recommended that associated consumable costs need to be reduced considerably, with sequencing performed at scale to lower overall costs per genome[35]. In contrast, a recent microcosting systematic review identified consumables as the largest cost component of genomic sequencing, potentially accounting for up to 78% of total sequencing costs[36]. By addressing these cost factors and increasing the volume of sequencing performed, the overall cost per genome can be lowered, facilitating integration of personalised and diagnostic genomic approaches like WGS within mainstream care settings[35].

Furthermore, despite high initial costs, centralising WGS within the NHS could shorten the 'diagnostic odyssey' experienced by patients with rare diseases. This odyssey typically involves multiple consultations, repetitive tests, and invasive procedures, leading to increased healthcare costs over time. For instance, WGS has significantly improved the diagnostic process for mitochondrial disease identification, facilitating better family planning, prenatal diagnosis, and targeted surveillance for known complications. Thus, a crucial component of integrating genomics within mainstream care includes incorporating WGS approaches to minimise unnecessary and costly investigations, ultimately reducing overall healthcare expenditure associated with managing these complex cases in the longer term[37].

The initiative for adopting rapid WGS testing and screening in England was announced in December 2022 with a £175 million funding boost for genetic services. This will support genomics research and the application of mainstream genomic medicine via the introduction of a WGS service within the NHS to expedite rare genetic disease diagnosis in new-born infants[31].

Regional disparities with access to genomic testing

There are equity concerns regarding access to genetic tests across the four devolved UK nations leading to regional disparities in the availability and range of tests offered. Despite these disparities, the recently commissioned GMS seeks to address these shortcomings through the standardisation of genomic testing across England[5], although access for patients from other devolved nations remains uncertain[38]. For instance, the implementation of WGS in Northern Ireland has been largely limited to the Public Health Agency Health Protection Surveillance of SARS-CoV-2 genomic variants to track the prevalence of different genomic lineages to guide public health measures to mitigate COVID-19 spread. WGS of viral genomes has become a valuable Public Health surveillance tool to enable timely identification of infectious diseases[39]. While WGS has been introduced in Northern Ireland for specific purposes, it has yet to be fully commissioned and routinely used as a clinical diagnostic tool to treat patients[40]. Therefore, integration of genomics within mainstream healthcare requires a comprehensive strategy that standardises accessibility of genetic testing services across all regions of the UK to ensure equitable access for all citizens.

Enhancing Clinician Competence and Collaboration

Mainstreaming genomic medicine within NHS primary and secondary care may be limited by insufficient genomic knowledge among healthcare professionals, necessitating enhanced training in genetic test provision[3]. As shown in the hypothetical framework model (Figure 1), tests ordered by mainstream clinicians will be sent to GMS laboratories for testing and analyses with results returned to requesting clinicians. Therefore, if clinicians have the authority to order genetic tests, they will also likely need appropriate knowledge to interpret, understand, action and communicate the findings. The NHS will require significant bioinformatic support to develop analysis pipelines for the interpretation of data to inform clinicians with the appropriate genetic information to guide personalised treatment plans[5].

Targeted workforce development plays a crucial role in balancing resources, capacity and managing expectations, particularly in the face of financial constraints. Targeted educational programs and continuous professional development opportunities are essential to equip primary care clinicians with the necessary knowledge and skills for appropriate test ordering, interpretation and actioning of reported findings and workload management[32]. Furthermore, decision-making for complex patient cases often requires input from a multidisciplinary team (MDT) to discuss genetic findings (Figure 1) in combination with associated detailed clinical and phenotypic information. Here, the MDT may comprise healthcare professionals from various backgrounds, such as nurses, pharmacists, GPs, etc.

Grade and position	Required transformation
Medical student	Updated and taught undergraduate genomics curriculum reflecting transformation in quantity and diverse clinical application of genomic data.
Foundation years and core medical trainees	Updated junior doctor training curricula. 'On the job' training in pharmacogenomics and prescribing. Clear pathways for requesting advice from clinical genetics services.
Specialty training and middle grade clinicians	Specific genomics curriculum and integrated training as relevant to specialty. For example, oncology trainees receiving cancer genetics training attachments in the identification, investigation and management of patients at increased risk of genetic predisposition to cancer. Clear pathways for requesting advice from clinical genetics services.
Consultants and associate specialists	Reactive training programmes in genomic data and clinical applications. Novel, efficient pathways for receiving specialist genomic advice from both clinical genetics services and genomic laboratory hubs. Implementation of new testing and management pathways due to mainstreamed genetic testing.

Table 1. Educational and support requirements for medical students and doctors[5]

Therefore, incorporating genomics into mainstream care in the longer term requires substantial clinical transformation to develop a broader, better informed, multi-professional workforce with suitable support from Clinical Genetics specialists, Regional Genetics and Genomic Laboratory Services. Notably, a recent study investigating the competence and confidence levels of UK practising nurses and midwives reported relatively low confidence levels of 2.07 ± 0.47 (measured on a 5-point Likert scale) in all areas of genomic medicine, with 1 being low confidence, and 5 being high confidence. These findings highlight the

urgent need to address this knowledge gap among nurses and midwives, as they constitute the largest professionally qualified workforce in the NHS[41]. Table 1 summarises recent findings for workforce development[5], including additional genomics teaching across undergraduate and post-graduate medical curricula.

Nevertheless, mainstreaming genomic medicine also requires the interaction of physicians in different medical specialities with genetic services and clinical geneticists/counsellors to guide accurate interpretation of genetic data and support patients. As shown in Figure 1, an efficient strategy could see discussion of genetic findings in MDT meetings in mainstream care settings to develop a treatment plan for less-complex cases. If the patient case is more complex, it could be escalated for clinical genetics support. It is important to highlight that Clinical Genetics specialists and Genetic Counsellors are an integral component of the broader MDT and key to providing improved treatment outcomes for patients. Their specialist expertise would be crucial for the interpretation of complex test results for patients with multiple genetic variants associated with rare diseases or unknown cancers[42]. Therefore, this strategy would enable clinicians in mainstream care to work with geneticists to diagnose and develop more robust treatment plans.

It should also be acknowledged that genetic reports will require some degree of interpretative and actionability information to guide mainstream clinicians. This would require major resourcing of Regional Genetics and Genomic Laboratory services. Thus, incorporating genomics into mainstream care requires not just workforce development, but also a fully resourced Clinical Genetics Service accessible to MDTs to guide the translation of genetic findings from complex cases to inform patient management decisions.

Patient education and engagement

The successful integration of genomics within mainstream patient care also depends on effective engagement through public health education and genomics promotion programmes. Various approaches, such as educational events, online platforms, and social and mass media, offer effective knowledge dissemination about the potential benefits of genomics. Some countries, including the UK, have already taken initiatives to incorporate genomic education into primary and secondary education curricula. These efforts aim to equip individuals with the necessary understanding to make informed choices about their healthcare, including whether to undergo genomic testing and how to interpret the results. Educated patients are more likely to recognise the value of participating in research initiatives, contributing to the advancement of genomic medicine and the broader healthcare field[43]. In addition, patient portals in EHR systems are integral to improved patient engagement[44]. The PennChart Genomics Initiative (PGI) operationalised the American College of Medical Genetics and Genomics (ACMG) guidelines to optimise EHR patient access for the delivery of precision medicine. The PGI provided patients access to their genomic test results through a secure patient portal, accompanied by annotated educational information in simple, medical jargon-free language to improve communication between patients and healthcare providers, reducing the risk of misinterpretation and confusion around complex genomic data[45].

Data management in genomics

A major issue with expanding and integrating genomics into routine mainstream healthcare is managing large volumes of genetic data. For example, each human genome consists of three billion nucleotides, which are typically stored as plain text files and can occupy several gigabytes of storage space[46]. Beyond the challenges and costs of data storage, data analysis and interpretation are complex. Artificial intelligence (AI) approaches for the development of bioinformatic pipelines may mitigate this issue through 'deep learning' of neural networks to identify features, such as mutations, from large and complex databases. These approaches focus the search for associated genetic disease variants and reduce clinical analysis time[47]. In addition, access to genetic information raises the issue of patient privacy and data protection. Recently, various AI techniques have been developed to preserve privacy, such as cryptographic methods, differential privacy, federated learning, and hybrid approaches. Thus, developments in AI and the future implementation of these data-protection strategies could potentially benefit mainstream care and genomic medicine[48]. The issue of privacy and access to patient data for employers, insurance companies etc. is also a key concern as this may compromise patient confidentiality.

Furthermore, incorporating genomic medicine into mainstream care presents challenges in prioritisation and data handling. The IGNITE projects conducted in the United States identified concerns for the integration of genomics data into EHRs. Appropriate data warehousing techniques involve data extraction from multiple sources for integration within a central repository to enable the customisation of genomic innovations to suit different contexts[49]. Genomics England currently stores participant data in a dedicated centre, the National Genomic Research Library[50], although a recent report by the Science and Technology Committee outlined plans for the establishment of a new data warehouse, consolidating data from various UK laboratories. These developments aim to enhance data management and accessibility within the UK healthcare system[51]. It is important to emphasise that storing and linking patients' genomic data to EHRs (with the aid of effective data warehousing strategies) can be extremely beneficial, as it can allow the data to be reused to inform lifetime care. Nevertheless, connecting these datasets represents an immense challenge and requires health systems and suppliers to commit to open standards for data persistence and communication.

Conclusion

In conclusion, integrating genomic medicine within mainstream healthcare is well-developed within the NHS. The process of mainstreaming genomics can be accelerated through the implementation of a robust framework (Figure 1). This includes making a wider variety of genetic tests available to patients in routine care, such as WGS, more genetic tests to aid drug prescribing, additional genetic screening for new-borns, etc. Furthermore, increasing the level of workforce training for non-genetic specialists will enable a broader range of genetic-related conditions to be diagnosed and managed by clinicians in mainstream care settings. Although some level of an integrated healthcare system already exists within the NHS, creating a system where mainstream clinicians and health professionals can work more closely with clinical geneticists will offer significant advances in preventative medicine, improved diagnoses, and ultimately better patient outcomes[52].

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Systematic Review

Simulate to stimulate? A systematic review of stress, learning, and performance in healthcare simulation

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Abstract

In recent years, simulation has come to prominence as an educational method within the healthcare professions, aiming to shield learners from real-world consequences. However, the associated risks of this educational method have largely remained unaddressed. One of the most potent risks of simulation is felt to be the experience of psychological stress. Over the last two decades, researchers have suggested that an increase in simulation-related stress goes hand-in-hand with diminishing performance, but the evidence base for this claim is lacking. A medical educator thus has no robust scientific steering on which to gauge how 'hard to push' a trainee in a simulation environment to best assist their learning. In this review we systematically analyse the literature to further understand the impact of simulation-related stress on learner performance and report that inducing a high-stress environment during simulation is generally associated with impaired performance.

Keywords

Simulation, Education, Stress, Psychological.

Key Practice Implications
Simulation is used extensively as a tool in medical education.
Psychological stress may be induced during a simulation.
An educator has some control over the degree of stress experienced by a trainee during a simulation, so robust data on how stress impacts learning in such settings would be especially useful.
The literature on this subject is sparse and heterogeneous, but in most circumstances, increasing stress seems to impair performance.
Further research into the optimal means for tracking stress in simulation and studying the effects of stress-reducing interventions would be welcomed.

Introduction

In recent years, simulation has become increasingly employed as a training modality within the field of healthcare professions education by virtue of creating an environment where errors do not have the same clinical implications as in the real world[1]. Nevertheless, simulation has the distinct potential to arouse a multitude of biological responses, which may not only impact learning and performance[2], but also the wellbeing of the individuals involved. The word 'stress' is often used as an umbrella term, aiming to portray the complex relationships between the environmental demands, resources, perceptions, and responses of an individual or group[3-5], with acute psychological stress commonly reported after simulation. Stress may, however, be more simply defined as the situation arising when one's resources are insufficient to meet the demands placed upon them. Stressors acting as stimuli for more salutary outcomes are the aim when it comes to optimising the processes of learning and performance. However, straying into the realms of under- or over-stimulation can expose the learner to a range of increasingly deleterious effects[6], not conducive to either of the aforementioned processes. Current evidence concerning the impact of simulation-related stress on learning and performance is ambiguous, leaving fertile ground for educationalists to debate the optimal level of stress for an effective healthcare educational experience. If these concepts continue to be incompletely understood, we can never be confident that we are doing all in our power to develop educational practices that will equip today's students with the resources to meet tomorrow's demands. The aim of this systematic review is to investigate the relationships between simulation-related stress, learning, and performance, offering readers a new perspective on an old issue.

Methodology

Search Strategy

This systematic review did not place limitations on language and was conducted in line with PRISMA guidelines[7]. The question of interest was, "What impact does simulation-related stress have on learning and performance?" After consultation with a subject librarian, a combination of subject headings (/) and keywords ("") were utilised. Search terms were categorised into three fields: (i) Simulation, (ii) Stress and (iii) Health Professions Education. Terms within the

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same field were combined via the 'OR' function (Simulation Training OR Patient Simulation). Fields were combined via the 'AND' function (Simulation terms AND Stress terms AND Health Profession Education terms).

Eligibility Criteria

Studies were included if they covered all of the following:

1. Population: Healthcare students or professionals involved in simulation-based healthcare exercises that monitor participant stress, learning outcomes and/or performance.
2. Exposure: Variables that contribute to participant stress.
3. Outcome: Level of participant performance, as defined by the study.
4. Study types: Crossover, cross-sectional, observational, randomised control.

Information Sources

EMBASE (Reed Elsevier PLC, Amsterdam, the Netherlands), Ovid MEDLINE (US National Library of Medicine, Bethesda, Maryland, USA), and PsycINFO (American Psychological Association, Washington, DC, USA) were searched for relevant studies from journal inception to the 14th of November 2023. Reference lists from all selected studies were screened for relevant literature not captured by the original search strategy.

Study Selection

On completion of the search, duplicates were removed, then titles and abstracts independently assessed for eligibility by two authors (AV and ADS). Studies deemed eligible were subject to full text review, to evaluate appropriateness of inclusion. The aforementioned process was repeated when hand-searching reference lists of included studies. Disagreements were addressed through inter-reviewer discussion (AV and ADS) with a third reviewer available (PKH) to ensure consensus, if required.

Extraction and Analysis of Data

A data extraction form was developed following pilot on three included studies. Where available, extracted data included: methodology, participants, study environment, stressors, and performance outcomes. Qualitative data were assessed for common themes (e.g., perceived anxiety level during high-stress simulations). Quantitative data (e.g., low- vs. high-stress simulation performance score) were evaluated for statistical significance ($p < 0.05$) and trends obtained from correlation analyses.

Assessment of Study Quality

In accordance with National Health and Medical Research Council (NHMRC) guidelines, we used the Cochrane risk of bias tool version 2.0 (RoB 2.0) for randomised control trials[8]. Two authors (AV and ADS) independently evaluated the risk of bias concerning the five domains of potential bias. Results were compared and a consensus achieved.

Results

Study Selection

In total, database searches yielded 836 studies. On removal of duplicates, 434 studies were eligible for assessment. Abstracts from all 434 studies were assessed against predefined eligibility criteria, leaving 49 full text studies for review; of which 15 studies were included. An additional five studies were identified from the reference lists of included studies (Figure 1). Studies were excluded if they (i) were in the wrong setting (e.g., non-healthcare simulation environment, or (ii) were article types of high bias risk (e.g., reports and case series, as well as editorials, letters and conference abstracts).

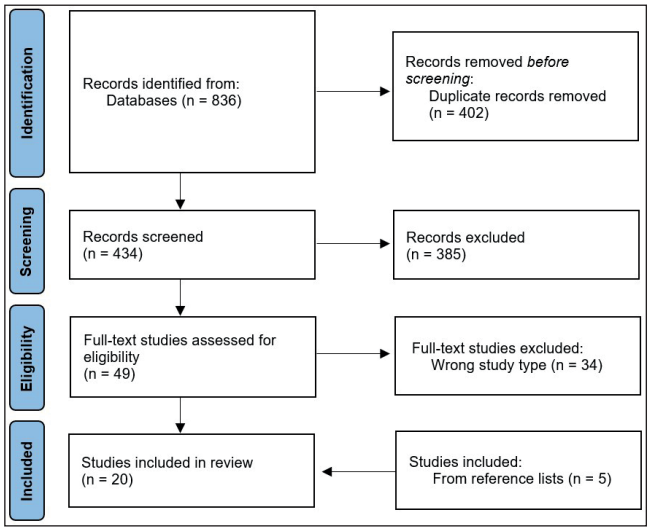

Figure 1: PRISMA flow chart of study selection process.

Study Characteristics

The final number of studies for inclusion was 20. The total number of participants in these studies was 926. Studies were published between 2005 and 2021, with individual study sizes ranging from 13 to 120. Studies were conducted in several countries: seven in Canada, four in the USA, and two in Australia. The remaining studies were conducted in France, Switzerland, and the UK (Table 1).

Individual Study Results

Of the 20 included studies, seven were randomised control, seven were observational, five were crossover, and one was cross-sectional (Table 2).

Risk of Bias Within Studies

The risk of bias was assessed regarding individual studies.

Table 1: Study Characteristics

Study	Year	Country	Participants	Study Population (n)	Age Mean (SD) or range
LeBlanc et al.[9]	2005	Canada	Paramedics	30	N/A
Arora et al.[10]	2010	UK	Trainee surgeons	18	N/A
Hunziker et al.[11]	2011	Switzerland	Medical students	120	23 (22 – 24) *
Harvey et al.[12]	2012	Canada	Medical residents	13	N/A
Hunziker et al.[13]	2012	Switzerland	Medical residents	28	29 (4.9)
LeBlanc et al.[14]	2012	Canada	Paramedics	22	N/A
Pottier et al.[15]	2013	France	Medical students	41	23 – 30
Fraser et al.[16]	2014	Canada	Medical students	116	N/A
Piquette et al.[17]	2014	Canada	Intensive care unit residents	53	29.8 (3.8)
Pottier et al.[18]	2015	France	Medical students	109	21.6 (0.8)
DeMaria et al.[19]	2016	USA	Medical students	26	SG: 25.1 (1.9) DG: 26.5 (5.6)
Mills et al.[20]	2016	Australia	Nursing students	70	28 (10.1)
Mills et al.[21]	2016	Australia	Paramedicine students	31	27.6 (8.4)
Bajunaid et al.[22]	2017	Canada	Neurosurgeons, neurosurgical residents and medical students	24	NS: 42.2 (7.3) SR: 31.5 (2.1) JR: 28.5 (1.9) MS: 24.8 (3.6)
Geeraerts et al.[23]	2017	France	Critical care residents	27	27.7 (1.8)
Lizotte et al.[24]	2017	Canada	Pediatric trainees	42	N/A
Moawad et al.[25]	2017	USA	Obstetrics/ gynecology residents	31	N/A
Bakhsh et al.[26]	2019	UK	Surgeons, residents, nurses and medical students	35	N/A
Anton et al.[27]	2021	USA	Emergency medicine residents	49	N/A
Anton et al.[28]	2021	USA	Medical students	41	25.98 (2.7)

** Median (interquartile range); N/A – Nonapplicable; TG – Test Group; CG – Control Group; SG – Survival Group; DG – Death Group; NS – Neurosurgeons; SR – Senior Residents; JR – Junior Residents; MS – Medical Students.*

Table 2: Study Type, Simulation and Associated Stressors, Assessment, and Performance

Research group	Study type	Simulation and/or Associated Stressors	Assessment	Performance
LeBlanc et al.[9]	Prospective, crossover	High-/low-stress, respiratory failure	Drug calculations	Impaired
Arora et al.[10]	Cross-sectional	Laparoscopic exercises	Facilitator criteria	Impaired
Hunziker et al.[11]	Prospective, observational	Cardiac arrest	Hands-on time	Impaired
Harvey et al.[12]	Prospective, crossover	High-/low-stress, trauma exercises	Global rating scale and check list score	Impaired
Hunziker et al.[13]	Prospective, observational	Cardiac arrest	Time to start resuscitation; Hands-on time	Unaltered
LeBlanc et al.[14]	Crossover	High-/low-stress, cardiac arrest	Global rating scale	Impaired
Pottier et al.[15]	Prospective, randomised	High-/low-stress, ambulatory consultation	Diagnostic accuracy	Unaltered
Fraser et al.[16]	Randomised, control	High-/low-stress, cardiac arrest, simulated patient death	Objective structured clinical examination	Impaired
Piquette et al.[17]	Crossover	Respiratory failure	Global rating scale	Unaltered
Pottier et al.[18]	Prospective, randomised, crossover	Severity of disease, patient aggression	Clinical abilities and communication score	Enhanced
DeMaria et al.[19]	Randomised, control	Cardiac arrest, simulated patient death	Written test	Unaltered
Mills et al.[20]	Randomised, control	Intravenous drug administration, multiple onlookers	Clinical assessment checklist	Impaired
Mills et al.[21]	Randomised, crossover	Multiple trauma exercises, instructor presence	Clinical assessment checklist	Unaltered
Bajunaid et al.[22]	Prospective, crossover	Brain tumour resection, uncontrollable bleeding	NeuroTouch metrics	Impaired
Geeraerts et al.[23]	Observational	Multiple trauma exercises	Technical/nontechnical skills criteria	Unaltered
Lizotte et al.[24]	Randomised, parallel	Pulseless neonate, survived or died	NRP megacode assessment form	Unaltered
Moawad et al.[25]	Prospective, observational	Laparoscopic exercises, audiovisual stressors	Facilitator criteria	Impaired
Bakhsh et al.[26]	Prospective, observational	Thoracic endovascular aneurysm repair	Global rating scale	Unaltered
Anton et al.[27]	Prospective, observational	Multiple trauma exercises	Trauma-nontechnical skills criteria	Impaired
Anton et al.[28]	Prospective, observational	Surgical trauma	Global rating scale	Impaired

NRP – National Resuscitation Program.

Table 3: Risk of Bias Assessment for Randomised Control Studies

Research Group	Study Type	Domain 1: Risk of Bias Arising from Randomisation Process	Domain 2: Risk of Bias Due to Deviations from Interventions	Domain 3: Missing Outcome Data	Domain 4: Risk of Bias in Outcome Measurement	Domain 5: Risk of Bias in Reported Results	Final Risk of Bias Assessment
Pottier et al.[15]	Prospective, randomised	Low	Some concerns	Low	High	Some concerns	High
Fraser et al.[16]	Randomised, control	Low	Some concerns	Low	Low	Some concerns	Some concerns
Pottier et al.[18]	Prospective, randomised, crossover	Low	Some concerns	Low	High	Some concerns	High
DeMaria et al.[19]	Randomised, control	Low	Low	Low	Low	Some concerns	Some concerns
Mills et al.[20]	Randomised, control	Low	Some concerns	Low	Low	Some concerns	Some concerns
Mills et al.[21]	Randomised, crossover	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Lizotte et al.[24]	Randomised, parallel	Low	Some concerns	Low	Low	Some concerns	Some concerns

Of the seven randomised control studies, two were deemed to have a high risk of bias (Table 3).

Stress and Performance

The stressors evaluated within the studies were heterogenous. High-/low-stress versions of simulation scenarios were used in the majority of studies (17/20 studies), with psychosocial stress in the form of noise, simulated relatives, presence of faculty, and simulated patient death often used to embellish high-stress environments.

LeBlanc *et al* (2005)[9] analysed paramedic drug calculation performance following a stressful simulation, where the high-stress scenario involved a mannequin that had to be diagnosed with respiratory failure and intubated by the participants. Paramedic performance (assessed by 'calculation proficiency') was diminished following the high-stress scenario. LeBlanc *et al* (2012)[14] evaluated the impact of stress on paramedic performance during simulated cardiac arrests. The high-stress scenario incorporated noise (two-way radio) and interpersonal (simulated relative) stress into the situation. Paramedic performance (assessed by a 'global rating scale') was reduced during the high-stress scenario. Harvey *et al* (2012)[12] assessed the effect of stress on resident performance during simulated resuscitation. The high-stress scenario involved management of a polytrauma victim, where the resident may have reasonably expected the victim to die. Resident performance (assessed by a 'global rating scale') was impaired during the high-stress scenario.

Mills *et al* (2016: I)[20] analysed the effect of social evaluation anxiety on nursing student checklist performance. The high-stress scenario involved the addition of a simulated nurse and inquisitive relative. Student performance (assessed by a 'clinical checklist') showed a decline during the high-stress environment.

Simulated cardiac arrest as a stressor was used in three studies, one of which included a high-/low-stress structure featuring simulated patient death. Hunziker *et al* (2011)[11] evaluated the impact of a simulated cardiac arrest on the resuscitation performance of medical students. Students reported an increase in perceived stress/overload and negative emotions, whilst resuscitation performance (assessed by 'hands-on time') was diminished. Hunziker *et al* (2012) [13] assessed the effect of a simulated cardiac arrest on the resuscitation performance (assessed by 'time to start' and 'hands-on time') of medical residents. Residents reported an increase in perceived stress/overload, with the trend towards a decline in resuscitation performance not reaching statistical significance.

Laparoscopy simulation as a stressor was used in two studies, one of which included a high-/low-stress structure. Arora *et al* (2010) [10] analysed the effect of stress on the simulated laparoscopy performance of trainee surgeons. Trainees reported elevated anxiety levels during the simulations, showing significant correlations with increases in both error frequency and uneconomical movement, resulting in diminished surgical performance. Moawad *et al* (2017) [26]

evaluated the impact of stress on the performance (assessed by 'exercise time and accuracy') of both obstetrics and gynecology residents during laparoscopic exercises. During the high-stress exercises (consisting of increased time pressure), participant task completion time was reduced, whilst accuracy declined in three of four tasks.

Discussion

This systematic review has identified studies investigating the association between stress and healthcare simulation performance. Whilst stress research within the field of health profession education is developing, only twenty studies satisfied the inclusion criteria. There is therefore a paucity of research in this area, and much remains to be learned. The identified studies have shown that exposure to high-stress simulation scenarios, consisting of noise, simulated patients, the presence of faculty, and increased task difficulty can elicit a variety of effects on participant performance, 11 (55 %) detailed impaired performance, eight (40 %) reported no effect on performance, and one (5 %) reported enhanced performance.

We feel that learning and performance are two sides of the same coin. It could be argued that performance is the metric by which learning is measured. To learn, one must perform – be that a task or a test. Learning involves the absorption, processing and recall of information, whereas performance encompasses the absorption, processing and recall of information conducive to successfully addressing a demand[34].

Stressors

The nature of the stressor used within the simulation is a potential area for dispute. For example, cardiac arrest is often described as a stressful event, often resulting in this endpoint being employed within many healthcare simulations. However, the way in which a healthcare professional is taught to deal with cardiac arrest is very much algorithm based. So, whilst the event may be deemed as 'stressful,' it may not actually be perceived so, as the healthcare professional will likely be assigned a role and specific tasks, often mitigating the impact of stress on the outcome. Stressors that remove the locus of control from an individual have the potential to be a profound source of stress. A prime example would be the human factors aspect of dealing with an unexpectedly irritated relative in a simulation setting. Therefore, one may find that the type of stressor selected for a simulation may have a considerable impact on the stress responses, and thus performance, of the individuals involved. Despite this, it is important in the interpretation of these data to recognise that measurements of stress and performance are distinctly separate, and measurement of one should not act as a substitute for the other. To illustrate, stress is commonly measured using biochemical (e.g., salivary cortisol) and physiological (e.g., heart rate variability) markers, as well as psychological questionnaires (e.g., perceived stress scale), whilst performance can be evaluated using a number of task-centric tools (e.g., objective structured assessment of technical skills).

Impaired Performance

Common themes regarding stress and impaired performance are immersion within environments of high psychosocial stress comprised of tasks characterised by a heightened sense of anxiety, increased cognitive load, and/or requiring fine motor skills. Of the 11 studies showing impaired performance, nine (82 %) involved healthcare students and/or junior medical residents; highlighting the deleterious effects of overstimulating those populations for whom learning is the gateway to proficiency. In 10 (91 %) studies, increasing levels of perceived anxiety, cognitive load and/or stress were associated with poorer performance. This finding alone is a stark example of how an individual's growing anxieties can predispose them to reduced learning outcomes.

Biomarkers, such as cortisol level and heart rate, serve as lenses through which the human response to stress can be observed. Five of 11 (45 %) studies reporting performance impairment used either salivary cortisol and/or heart rate as markers for stress; with all five studies displaying an increase in both markers from baseline to high-stress conditions. The remaining studies used a form of the State-Trait Anxiety Index (STAI) as a metric for perceived stress, the dominant theme being a negative correlation between perceived anxiety/stress and performance.

Effective pre-scenario briefing, and post-scenario debriefing are associated with improved instructional and learning outcomes[29,30]. Of the eleven studies reporting impaired performance, only two (18.1 %) mentioned structured briefing and debriefing processes. Three (27.3 %) performed a debrief with no pre-scenario brief. Three performed a brief with no post-scenario debrief, and three performed neither brief nor debrief. Therefore, these processes, or lack thereof, may also be a contributing factor to impaired performance.

Unaltered Performance

The category 'unaltered performance' details studies in which no statistical difference could be found between stress and control, or high- and low-stress groups. Common themes regarding stress and unaltered performance were similar to impaired performance in terms of stressors used; cardiac arrest, polytrauma cases, and high-/low-stress simulations involving varying degrees of psychosocial stress. However, of the eight studies in this category, only four (50 %) involved healthcare students and/or junior medical residents, with the remaining being composed of intensive care unit residents, surgeons, neurosurgical residents, and nurses; findings suggesting that increased participant experience may be a contributing factor to performance under stress. This is an intuitive suggestion, endorsing the adage that there is no substitute for experience.

Bakhsh *et al* (2019) [26] evaluated the effect of stress between surgeons, residents, nurses and medical students during a team thoracic endovascular aneurysm repair, reporting that surgeons did not experience the same level of perceived or physiological stress as their less experienced counterparts.

However, whilst a negative correlation was observed between stress and performance, it was not statistically significant. Of note, the mean number of participants for studies in the unaltered category is 35 compared with 49 in the impaired category; small sample size and associated under-powering may be a possible explanation for studies in this category failing to achieve statistical significance.

In terms of biomarker analysis, six studies reporting unaltered performance utilised salivary cortisol and/or heart rate; all displayed negative correlations between these markers and performance. All eight studies included a form of the STAI as a metric for perceived stress and, again, the dominant theme was a negative correlation between perceived anxiety/stress and performance. Specifically, Hunziker *et al* (2012) [13] went as far as stating that self-reported anxiety was the only predictor for low cardiopulmonary resuscitation performance.

Enhanced Performance

The only study showing enhanced performance involved medical students. Pottier *et al* (2015) [18] used a simulated ambulatory consultation, where the scenarios contained either an intrinsic (the case involved pulmonary embolism) or extrinsic (aggressive patient) stressor. The authors concluded that both intrinsic and extrinsic stressors had positive effects on performance. However, as perceived participant anxiety (measured by the STAI) showed a decline throughout the scenarios, these factors may have been ineffective at inducing sufficient stress. As this was the only study showing enhanced performance, common themes cannot be extracted. It could also be extrapolated that what educationalists feel should be stressful for a learner may, in fact, not be.

Risk of Bias

Only 7 (35 %) included studies were randomised control trials. Of these, 2 (29 %) were assessed as having a high risk of bias. No randomised control trials were assessed to have a low risk of bias (Table 3). The primary issue encountered when assessing studies for bias, was the tendency for researchers directly involved in the coordination of studies to have acted as raters for participant performance. Investigators acting as raters introduces potential bias, as these individuals are not blinded to study hypotheses.

Limitations

All studies contained quantitative data; however, heterogeneity was too great to allow for a reliable meta-analysis. Causes include differences in participant demographics (LeBlanc *et al*., 2005[14] – paramedics; Mills *et al*., 2016[20] – medical students), and scenario variation (Hunziker *et al*., 2011[11] – cardiac arrest; Moawad *et al*., 2017[25] – laparoscopic exercises). Nonetheless, 11 (55 %) studies with a quantitative element found that stress in simulation impaired performance and, as such, there is a general tendency toward this negative association. A further potential limitation is publication bias, where smaller studies with non-significant results are not published and thus not included in this review.

Implications for Practice and Future Research

Although simulation is widely used in healthcare education, the findings in this review highlight that as a learning method, particularly stressful simulations may not enhance performance, as previously thought. We have shown that simulation scenarios, as sole learning tools, are often ineffective and potentially detrimental, thus adjunctive measures such as effective briefing and debriefing should be strongly considered in course design. Given the wide variety of study designs, participant experience and specialties across healthcare simulation research, we suggest that additional investigation using studies with consistent and comparable methodologies is required. Furthermore, future research opportunities lie in exploring the effect of stress-reduction interventions on learning in simulation. Although there has been some research in this area[31-33], large scale studies would be beneficial to the simulation community in identifying effective interventions to enhance the learning of both healthcare students and professionals.

Conclusion

In conclusion, this systematic review has shown that inducing a high-stress environment during simulation in healthcare education is generally associated with impaired performance. There is a paucity of evidence of improved performance, thus the use of extensively stressful content in simulation scenarios may not be as beneficial as previously thought. The absence of structured briefing and debriefing may be contributing factors to the predominantly impaired/unaltered performance. We recognise, however, that there is substantial heterogeneity between studies and as such recommend that further investigation of this area using similar populations, scenarios and project design, along with structured brief/debrief, is warranted.

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Medical Ethics

Ethics – A matter of principle?
Part 2: Rationality, ends, and the levels of moral discourse

Michael Trimble

Abstract

Discussion of bioethical issues using four principles approach proposed by Beauchamp and Childress is now standard practice in the UK. An earlier paper documented the history of principlism before considering its impact and reviewing some criticisms of the approach. This paper will examine some of the philosophical difficulties in greater depth. A particular concern is that principlism leads to *thin* debate with consideration of means without due concern regarding their intended ends.

Rationality

As in the previous paper, we will use some of the themes developed by sociologist John H Evans in his analysis of bioethical debate. In common parlance *rational* appears as 'the opposite of *crazy*'.[1] In the social sciences rational may be used in a more formal sense. A rational belief is one that can be held legitimately. Rationality can be explored further. *Instrumental rationality* accords most closely with the common usage of the word *rational*. For example, for a student hoping to go on to study medicine, selecting biology is an *instrumentally rational* choice of subject. Whereas, if she hoped to become a musician, this would be less rational. For the purposes of this discussion, the terms that we need to understand are *substantive* and *formal rationality*. A pattern of action is to be considered *substantively rational* if it utilises the criteria of 'ultimate ends' or 'ultimate values' to the acts or means involved, i.e., are the means consistent with ultimate ends or values. This contrasts with *formal rationality*. Here ends and means are debated together, and a pattern of action may be considered *formally rational* if it is reckoned to be most efficacious means for achieving *predetermined* or *assumed ends*.[1] In evaluating an argument there are five components to be considered. These are: the link between means and ends, the extent to which the ends are debated, the number of ends considered legitimate in the debate, the commensurability of ends, and the universality of ends.[1] Let us unpack this last statement further as it has great relevance to the overall narrative.

The link between means and ends.

In considering the link between means and ends, it is noted that formal rationality tends towards a consequentialist view – essentially the ends may justify the means. Substantive rationality may see that some means are inherently wrong because they conflict with other ends or values.[1]

The extent to which the ends are debated.

In substantively rational debate the ends must be defined and argued for. 'Put simply, a substantively rational debate is about ends.'[1] This contrasts with a formally rational debate where the ends are assumed, either explicitly or implicitly. Including ends in the debate makes the outcome less easily calculable as it is difficult to weight competing ends against each other, for example beneficence versus respect for an individual's autonomy, without an appeal to a higher-level end.[1]

The number of ends considered legitimate in the debate.

Formal rationality requires that the number of ends be limited. Evans cites the 'scientific method' as the most extreme example of formal rationality, as it concerns facts about nature that allow for calculation of predicted consequences of an action without consideration of the ultimate ends to which such knowledge may be applied.[1] In substantive debate any number of ends may be considered. Evans notes the progression of bioethical debate over time and how the acceptance of the four pre-determined ends of principlism – autonomy, beneficence, non-maleficence, and justice – facilitated a move from substantive to more formal debate.

The commensurability of ends.

Commensuration describes the process of combining different ends into a common metric, examples being utility and cost. 'Commensuration transforms qualities into quantities, difference into magnitude. It is a way to reduce and simplify disparate information into numbers that can easily be compared.' It is just as important– if not more so – to consider what the process of commensuration of ends omits. Some things are incommensurable, a trivial example being whether chocolate ice-cream can be considered better than strawberry. More serious examples include questions of core values and absolute moral standards. So, whilst commensuration may be useful in determining a common metric to evaluate a proposed plan of action, it may also be driven 'by a wish to hide behind numbers, impose order, or shore up weak authority… Commensuration can provide a robust defence for controversial decisions, expand a group's organizational or professional turf.'[2] Thus whilst the utilitarian "greatest good to the greatest number" provides a metric that seems almost quantifiable, and so calculable,

"fidelity to God" does not. "Authors assuming substantive rationality resist commensurable scales because their ends cannot be commensurated with other ends without distorting their meaning."[1]

The universality of ends.

In a point related to the previous, one Evans describes two senses of universality, the first being a commensurable generality that is unlikely to cause disagreement. He gives the example "it is better to do good than to do harm". Ends such as these are assumed to be universal and so do not require debate. The sense in which an end may be considered universal is where the end can be considered to be applicable across a range of means. Here he gives the example of autonomy. If autonomy is paramount in one situation, then autonomy can be assumed to be paramount when considering various means. The assumption of universality makes decision-making more calculable. Universalism in both senses is unacceptable to those who favour substantively rational arguments.[1]

In describing the history of bioethical debate, Evans notes the progressive shift from substantive to formal debate with an increasing focus on commensurable ends. This is of great importance because 'following substantive rationality means are right or wrong for *a priori* reasons – for their consistency with certain ends – not because of their consequences.'[1] The implication being that some means should never be developed. However, from the perspective of formal rationality, there are no means which are inherently wrong, rather they may be considered wrong if they do not maximise their intended end. Hence, any means may be brought to the point where its consequences can be calculated. Pellegrino and Thomasma also notice this difficulty with the approach to medical ethics that arises from the Presidential Commission's report. They frame it as a move from *substance* to *procedure*. In order to avoid the irreconcilability of moral conflicts, ethical discussion focuses instead on the process of decision making. Another way of describing this situation is to consider whether a debate is *thick* or *thin.* Thick debates are substantive. Reliance on formal rationality results in thin debate.

Levels of moral discourse

Principles are undoubted important in ethical debate. Aiken describes ethical responses as occurring on four levels. First, and most simple, is the expressive-evocative level. At this level no reasons are given for the moral judgement and the judgement applies only to the particular case in view. The second level is that of rules. Rules apply not just to one case but to all similar cases. Rules tell us directly what to do or not to do. Underpinning the rules are principles. Principles may support rules or criticise them. A principle is more general than a rule and does not provide specific guidance or instruction. Finally, underpinning all of the above, are the individual's basic convictions, their core personal beliefs. Aiken's scheme is summarised in table 1.

Level	Characteristics	Example
Expressive-evocative	a) No reasons are given for the moral judgement. b) The moral judgement applies to one particular case	Simple decisions / gut feeling
Rules	a) The rule applies not just to one immediate case but to all similar cases b) The rule tells us directly what to do or not to do	The law The GMC also NICE, SIGN, etc.
Principles	a) A principle supports rules – or criticises them b) A principle is more general than a rule; it does not tell us directly and concretely what to do.	Autonomy, beneficence, non-maleficence, justice Duty Inviolability of life
Post-ethical / basic convictions	a) A basic conviction is the basis for our principles, rules and overall ethical reasoning b) You can't go deeper than basic convictions	Personal core beliefs World view Identity

Table 1.
Levels of moral discourse. Adapted from Aiken

It can be seen that keeping to the more superficial levels of discourse, i.e., the expressive-evocative and rules-based discussion, means that the quality of the debate will be thin. (see table 2)

Also, when discussing ethical questions in this manner, the ubiquitous presence of principlism can leave students confused when they are asked to consider other principles than Beachamp and Childress' four. We have already mentioned the self-evident principles of WD Ross. Reviewing the topic Veatch, notes systems of bioethics based on as many as ten principles or simply on one, e.g. utility. Beyond Beachamp and Childress' core principles he notes others such as veracity, fidelity, gratitude, reparation, and the avoidance of killing.

Richard Huxtable notes that the four principles can be

Level	Characteristics
Expressive-evocative	a) No reasons are given for the moral judgement. b) The moral judgement applies to one particular case
Rules	a) The rule applies not just to one immediate case but to all similar cases b) The rule tells us directly what to do or not to do
Principles	a) A principle supports rules – or criticises them b) A principle is more general than a rule; it does not tell us directly and concretely what to do.
Post-ethical / basic convictions	a) A basic conviction is the basis for our principles, rules and overall ethical reasoning b) You can't go deeper than basic convictions

Table 2.
Levels of moral discourse versus think and thin debate.

seen to set forth a position that is not simply Western but in fact Anglo-American. The four principles of Beauchamp and Childress are contrasted with those identified by the European BIOMED II project regarding "Basic Ethical Principles in European Bioethics and Biolaw" – these being autonomy, dignity, integrity and vulnerability. Of note, *dignity* here includes the 'inviolability of life' and restrictions on 'interventions in human beings in taboo situations'. [8] The group also did not claim to that these basic ethical principles should be 'understood as universal everlasting ideas or transcendental truths but they rather function reflective guidelines and important values in European culture'.[8]

Matthew Shea reckons that what principlism lacks is an adequate treatment of axiological phenomena, that is, a theory of the good. Shea suggests consequentialism, eudaimonistic virtue ethics, or natural law ethics as potential sources for such a theory but does not argue for one over the others.

Tom Walker also questions the sufficiency of the four principles. He notes that there are areas which they cannot provide moral guidance. He cites the examples of desecration of memorials to the dead and the moral repugnance towards instances of bestiality. It Is clear that people find themselves bound by moral norms beyond those articulated by the four principles. Walker suggests the development of 'culturally specific forms of principlism'.

However, this simply relocates the question regarding where we derive our principles and how to we determine which principle takes priority in any given situation. What accounts for such cultural differences? Moral psychologist Jonathan Haidt notes that the cultural aspects of morality may be explained by the specific focus of individuals from Western, educated, industrialised, rich, and democratic (WEIRD) cultures have on certain aspects of morality. People from WEIRD cultures tend to value autonomy and individualism extremely highly and may downplay or even ignore other factors. This may help explain why the four principles approach has taken root so strongly in the West. Similarly, both utilitarian and deontological favour forms of reasoning with a strong tendency to systematic thought but low levels of empathy.[11] Other, non-WEIRD, cultures exhibit a more sociocentric morality, where relationships whether within the family or wider community, have greater moral significance.[11] Haidt also notes that other cultures often have an 'ethic of divinity'[11] which impacts how they view the body and gives rise to ideas of cleanliness and purity. Haidt proposes that humans have a 'moral palate' composed of five 'taste receptors': care for others, fairness, loyalty, respect for authority, and sanctity.[11] WEIRD morality – which includes principlism – focuses on a limited number of receptors. Our culture and upbring play a role in determining how both personal and societal views of moral issues develop. In the West, the legacy of Christian morality looms large, as the source of our most strongly cherished beliefs – even if many forget their roots. French philosopher Luc Ferry, himself a secular humanist, writes

"There are in Christian thought, above all in the realm of ethics, ideas which are of great significance even today, and even for non-believers; ideas which, once detached from their purely religious origins, acquired an autonomy that came to be assimilated into modern philosophy. For example, the idea that the moral worth of a person does not lie in his inherited gifts or natural talents, but in the free use he makes of them, is a notion which Christianity gave to the world, and which many modern ethical systems would adopt for their purposes."

Whilst Christians 'tend to understand themselves as thinking out of a historical tradition' and 'especially accountable to the witness of the Bible', others will have a different perspective. We must remember the influence of each individual's background on the moulding of their moral landscape. In the words of philosopher Alasdair MacIntyre, "I can only answer the question 'What am I to do?' if I can answer the prior question 'Of what story do I find myself a part?[14]

What does this mean in practice?

So far, we have covered a lot of theory in some depth but what might it mean for policy makers, clinical ethics committees, or an individual practitioner? Using the worked example of a woman requesting a late-term abortion to highlight the difficulties with principlism as a methodology, Brock and

Wyatt describe how the form of the debate can determine the outcome of deliberations. In brief, because principlism does not make allowance for what Brock and Wyatt term 'unconsidered variables', it makes an assumption of moral consensus where none exists. In particular, this methodology is seen to exclude "particularist" belief systems such as Christianity. This, in effect, marginalises the 'actual moral narratives which have grounded the ethical lives of social groups for all of human history.' Legal ambivalence toward late-term abortion places the moral weight of the decision on the physician. Principlism leaves little room for the conscience of the physician as society demands the 'separation of the doctor's personal 'prejudices' from his or her practice.' We can envisage similar challenges in the contemporary debate surrounding the matter of euthanasia and physician-assisted suicide. If we begin deliberation with autonomy as the starting point and without an accepted consensus surrounding the question of beneficence or ultimate good, the discussion soon becomes one of rights and process, of relevant groups and equity of access; a discussion of means to achieve the outcome rather than the rightness of the outcome in itself. The morality of the individual doctor gets lost amidst the question of whether conscience clauses should provide an option for individuals to decline to provide the service.

Conclusion

Should the four principles approach be abandoned? Not necessarily. But they do need to be set in a wider and deeper moral context. To appreciate autonomy, we must know why each person matters. To comment on beneficence, we must know what we mean by good. To pursue non-maleficence, we must acknowledge evil. To act justly, we must know what it means to be just. We can use the principles as useful pegs upon which to hang our thoughts, but we need to be able to exercise the full range of our 'moral taste receptors' and to be able to delve down into the deeper levels of moral discourse, both to understand our own moral foundations and to appreciate the concerns of others as we consider difficult cases.

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Letters

Seasonal variations regarding incidence of CTPA confirmed pulmonary embolism in Belfast, Northern Ireland, from 2014 to 2022.

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C Neil, RL Lavery, GM Benson

BACKGROUND: Studies[1,2] have reported seasonal variations regarding the incidence of pulmonary embolism (PE). The aim of this study was to identify differences in seasonal patterns regarding the diagnoses of PE patients via CTPA in the Belfast Health and Social Care Trust.

Pulmonary embolisms can result in acute cardiopulmonary collapse and death, and when not fatal can lead to chronic conditions such as pulmonary hypertension[3]. They can reduce the quality of life of patients and caretakers due to the social and economic costs associated with them[3]. Therefore it is crucial that we improve knowledge of the chronobiology contributing to increased VTE incidence to improve monitoring, prevention and treatment[3]. A German nationwide inpatient sample analysed 885806 PE hospitalisations[1].The quarterly annual incidence (25.5 versus 23.7 of 100,000 citizens per year, p=0.021) and in-hospital mortality (17.0% versus 16.7%, p=0.008) were higher in the winter months than in summer, but not primarily explained by age, sex or comorbidities[1]. A study conducted in the Emilia Romagna region in Italy at the Centre for Health Statistics between January 1998 and December 2005 analysed a sample of 19,245 patients[2]. PEs occurred least frequently in spring (n=4,442 or 23.1%) and most frequent in winter (n=5236 or 27.2%, chi(2)=75.5, p<0.001)[2].

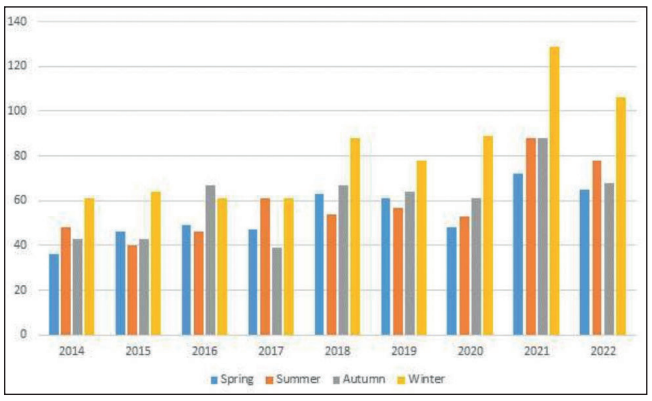

Figure 1

A study conducted in the Spanish NHS between the period 2001-2010, reviewing 162032 PE events concluded that PEs have been increasing linearly over the years with a peak in winter and a drop in summer and a difference between February and June of 29% [4]. VTE incidence varies seasonally, with cases peaking during the winter (January and February) and the lowest incidence occurring in the summer months (August and September) [3]. This was still the case after adjusting for sex, age, type of VTE and combined cancer diagnosis, concluding that winter is a significant independent factor in VTE incidence[3].

METHODS: We collated all CTPAs performed in the Trust over the eight-year period, noting those positive. Initially analysed by weekly variations before collating them by seasons. We analysed the impact of seasons on incidence of PE patients in Belfast, diagnosed using CTPA, (2014–2022). Seasonal PE variations by year are depicted in *Figure 1*.

RESULTS: The Belfast cohort comprised a total of 24 353 CTPAs performed over the eight-year period with 2719 (13% positive rate). Seasonal variations in incidence was of significance as higher in winter (December to February) than in summer (June to August).

DISCUSSION: There are various factors that are thought to lead to these seasonal variations. Vasoconstriction induced by the cold and reduced physical activity may lead to reduced blood flow to the lower limbs[4]. Hypercoagulability may be induced by winter respiratory tract infections[4]. The lower temperatures in winter cause hypercoagulability leading to decreased fibrinolytic activity and increased fibrinogen[4]. A number of studies have concluded that risk factors for VTE such as cardiovascular and respiratory diseases are more prevalent in the winter months and therefore this could be contributing to the PE seasonal variations[5]. It is also important to note that we had also undertaken the assessment of the total number of scans performed weekly over the years but there was no evidence to suggest a greater number of scans performed in winter months compared to the other seasons.

CONCLUSION: Incidence of PE patients showed a significant seasonal variation as per previous published regional data e.g. Germany and Italy. Although it has to be hypothesised that the seasonal variation of PE is multifactorially dependent. This finding could be considered when designing future research on the pathogenesis of the disease, and can guide decision making for the prevention or suspected diagnosis in selected patients at high risk.

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Curiositas - No Time To Die

QUIZ 1

Photo from Wikipedia (https://en.wikipedia.org/)

a) What is this and why is it famous?
b) How many people die per second worldwide?

Dr Amy Jones (ST4 in Palliative Medicine), Dr Sarah Cousins (Palliative Medicine Consultant SHSCT), Dr Sinead Hutcheson (Palliative Medicine Consultant BHSCT)

QUIZ 2

Photo by Ramsey Cardy for Sportsfile, The Times

a) Prior to the Paris Olympics 2024, 300 water fountains were installed around the city in an effort to prevent spectator dehydration due to an anticipated heatwave throughout the competition.[1]

What is the most reliable and accurate clinical measure of dehydration from the following:
i. Thirst
ii. Reduced skin turgor
iii. Postural hypotension, >/= 20mmHg?

b) What percentage of patients in the terminal phase of advanced cancer are likely to receive clinically assisted hydration (CAH)? Are there specific evidence-based guidance to guide for its use in patients in their last days?

Dr Amy Jones (ST4 in Palliative Medicine), Dr Sarah Cousins (Palliative Medicine Consultant SHSCT), Dr Sinead Hutcheson (Palliative Medicine Consultant BHSCT)

QUIZ 3

Photo from Shutterstock.com 2156716329

a) Why might a hospice inpatient complain of pain while combing their hair?
b) What would you do to manage this?

Dr Amy Jones (ST4 in Palliative Medicine), Dr Sarah Cousins (Palliative Medicine Consultant SHSCT), Dr Sinead Hutcheson (Palliative Medicine Consultant BHSCT)

QUIZ 4

Photo: Ó ehopisce 2024

a) Who is the lady standing behind the late Queen Elizabeth II?
b) Why was 1990 a significant year for both her and the wider palliative care community?

Dr Amy Jones (ST4 in Palliative Medicine), Dr Sarah Cousins (Palliative Medicine Consultant SHSCT), Dr Sinead Hutcheson (Palliative Medicine Consultant BHSCT)

CONSIDER CONTRIBUTING TO CURIOSITAS?

Please refer to *'Curiositas: Guidelines for contributors'* http://www.ums.ac.uk/curiositas.html and email curiositas@ums.ac.uk with your ideas and submissions.

Curiositas: Answers

QUIZ 1

a) Although it looks like a crowded city, according to the Guinness World Records, this is the largest burial ground is the world. It is an Islamic cemetery called Wadi al-Salam - translated as 'Valley of Peace' - and it is located in the city of Najaf, Iraq.[1] Iraq estimates the graveyard to cover an area of 9.17 km2 (3.54 sq mi) – or more than 1,700 football fields and is thought to contain around 6 million sets of human remains.[1] Burial at the Wadi al-Salam usually means being interred in one of the tens of thousands of communal crypts, mausoleums or catacombs, some of which can hold as many as 50 sets of remains.[1] The cemetery is also considered one of the oldest in the world, as it has been in continuous use for more than 1400 years.[2]

b) In 2024, approximately 1.98 people die worldwide every second.[3] Or about 119 people worldwide every minute.[1] Or about 7,116 worldwide deaths an hour.[3] Or 170,791 worldwide deaths a day.[3] Based on 2022 annual data, an average of 47 people die in Northern Ireland every day.[4] This mortality rate is predicted to grow, and with it, the need for palliative care services. The inevitability of death often causes us to mentally look away – 'staring at the sun' or contemplating death can be an overwhelming task for our patients and for ourselves. There are many concepts looking at coping with death anxiety – including the idea of 'middle knowledge'.[5] 'Middle knowledge' suggests we can both simultaneously deny death, and at the same time make practical plans for death – perhaps allowing us a little breathing room to accommodate the inevitable at a manageable pace.[5]

[1]*Guinness World Records Largest Cemetery (Online). Available: https://www.guinnessworldrecords.com/world-records/69153-largest-cemetery. (Accessed 26/09/2024)*
[2] *UNESCO World Heritage Centre Wadi Al-Salam (Online). Available https://whc.unesco.org/en/tentativelists/5578/ (Accessed 26/09/2024).*
[3]*World Population Review. (Accessed 26/09/2024). https://worldpopulationreview.com/countries/deaths-per-day*
[4]*Registrar General Annual Report 2022 Deaths. Northern Ireland Statistics and Research Agency. 2023. https://www.nisra.gov.uk/publications/registrar-general-annual-report-2022-deaths (Accessed 26/09/2024)*
[5]*Breitbart W. On the inevitability of death. Palliat Support Care. 2017 Jun;15(3):276-278*

QUIZ 2

a) iii: postural hypotension, >/= 20mmHg.
There are currently no universally accepted diagnostic criteria for dehydration in palliative medicine, although a number of laboratory investigations are deemed more accurate and reliable than most symptoms/clinical findings.[2] Postural hypotension has a medium to high reliability and accuracy, with thirst having medium and reduced skin turgor low.[2]

b) Clinically assisted hydration (CAH) can be hugely emotive in a patient's last days. The use of CAH in the terminal phase is extremely variable within clinical practice, with it suggested that anywhere between 12-88% of cancer patients in the last week of life may receive CAH.[3] In some cases, the decision is relatively straightforward depending on the indication or contraindication (e.g. malignant hypercalcaemia or decompensated heart failure respectively), however in many cases the decision is much more subjective. With this variability in mind, there has been updated guidance published in March 2024 on the use of CAH in patients with advanced cancer by the Palliative Care Study Group of the Multinational Association of Supportive Care in Cancer (MASCC).[4] Due to the paucity of evidence, they were unable to develop a specific guideline and so a collection of 12 "expert opinion statements" have been collated, plus a helpful algorithm to aid decision making (https://link.springer.com/article/10.1007/s00520-024-08421-6). They acknowledge that the provision of CAH in the terminal phase is one of the most contentious issues in medicine, but give a framework from which we can guide our decision-making in this often emotive situation.

1 - All patients with advanced cancer should be regularly assessed regarding hydration/dehydration
2 - Patients should be practically supported to maintain oral intake
3 - Reversible causes of decreased fluid intake, or increased fluid loss, should be treated
4 - Decisions relating to clinically assisted hydration should be made by an appropriately constituted multidisciplinary healthcare team together with the patient and their family
5 - Clinically assisted hydration should be considered in patients at risk of dying from dehydration before dying from their cancer
6 - Protocols/processes should exist to deal with conflicts over the initiation (or withdrawal) of clinically assisted hydration
7 - Patients receiving clinically assisted hydration should have a hydration care plan which defines the agreed objectives of treatment and the agreed conditions for withdrawal of treatment
8 - Patients should be given fluids via the most appropriate route (for that patient)
9 - Patients who are dehydrated should be given sufficient fluids to reverse the dehydration
10 - Patients who are not dehydrated should be given sufficient fluids to maintain hydration/prevent dehydration
11 - Clinically assisted hydration should be available in all settings, including the home setting
12 - All patients receiving clinically assisted hydration should be regularly reassessed.
As with much of our decision-making in palliative medicine, this requires an individualised approach.

[1]*Rings of Fire II: report published by BASIS, Front Runners and Climate Central (Accessed 27/09/2024) (https://basis.org.uk/resource/rings-of-fire-2/)*
[2]*Armstrong LE, Kavouras SA, Walsh NP, Roberts WO (2016) Diagnosing dehydration? Blend evidence with clinical observations. Curr Opin Clin Nutr Metab Care 19:434–438*
[3]*Raijmakers NJ, van Zuylen L, Costantini M, Caraceni A, Clark J, Lundquist G et al (2011) Artifcial nutrition and hydration in the last week of life in cancer patients. A systematic literature review*

of practices and efects. Ann Oncol 22:1478–1486
[4]Hayes J, Bruera E, Crawford G, Fleury M, Santos M, Thompson J, Davies A (2024) Multinational Association of Supportive Care in Cancer (MASCC) expert opinion/guidance on the use of clinically assisted hydration in patients with advanced cancer. Supportive Care in Cancer 32:228

QUIZ 3

a) If they are taking opioids, they may be suffering from opioid-induced hyperalgesia (OIH). OIH is an increased response to a painful stimulus, associated with exposure to opioids.[1] It has been shown in both acute and chronic pain and appears to result from sustained sensitization of the nervous system, in which excitatory neurotransmitters and the NMDA-receptor–channel complex play important roles.[2] Clinical features include increased sensitivity to pain stimulus (hyperalgesia), worsening pain despite increasing doses of opioids or pain which becomes more diffuse, extending beyond the distribution of the pre-existing pain. It can occur with any dose of any opioid, but particularly with high-dose morphine or hydromorphone, and in renal impairment. On examination you may elicit pain from ordinary non-painful stimuli, e.g. stroking skin with cotton or combing hair (allodynia). There may also be the presence of other manifestations of opioid-induced neural hyperexcitability, e.g. myoclonus, seizures, delirium.[3] A diagnosis of OIH **is** generally made on the basis of a high level of clinical suspicion, probability, and pattern recognition.

b) Treatment options include reducing the opioid dose, switching opioid and using a multimodal approach to analgesia with adjuvants such as **paracetamol**, NSAIDs, **pregabalin or ketamine**, an NMDA-receptor–channel blocker. If these steps do not lead to a resolution of the OIH, consider spinal, regional or local analgesia, and tail off systemic opioids completely. Remember to check for hypomagnesaemia because this can aggravate OIH. [4,5]

[1]Higgins C et al. ***(2019) Evidence of opioid-induced hyperalgesia in clinical populations after chronic exposure: a systematic review and meta-analysis.*** *British Journal of Anaesthesia. 122: e114–e126.*
[2]Edwards DA and Chen L (2014) The evidence for opioid-induced hyperalgesia today. Austin Journal of Anesthesia and Analgesia. 2: 12.
[3]Zylicz Z and Twycross R (2008) Opioid-induced hyperalgesia may be more frequent than previously thought. Journal of Clinical Oncology. 26: 1564.
[4]Walker SM and Cousins MJ (1997) Reduction in hyperalgesia and intrathecal morphine requirements by low-dose ketamine infusion. Journal of Pain and Symptom Management. 14: 129–133.
[5]Charlesworth, S. (Ed.). (2020). *Palliative Care Formulary* (7th ed.). Pharmaceutical Press.

QUIZ 4

a) Dame Cicely Saunders (1918-2005), considered the founder of the modern hospice movement, opening St Christopher's Hospice in 1967.[1] She originally trained as a nurse, then a social worker and, finally, a physician. While working in hospital, she was known to reject the concept of the term "nothing more can be done" and instead, adopted the approach of "there is so much more to be done".[1] This attitude is part of what drove her to establish the modern hospice movement and the concept of "holistic" care of patients with terminal illness, including their physical, practical, spiritual and emotional needs.[1]

b) 1990 was the year that Palliative Medicine as a specialty was born. Although practiced as a sub-specialty prior to this, the World Health Organisation recognised palliative medicine as a distinct specialty in its own right in 1990, dedicated to relieving suffering and improving quality of life for patients with life-limiting illnesses; still only a young thing!

[1] St Christopher's (accessed 27/09/2024) https://www.stchristophers.org.uk/about/damecicelysaunders/

Book Reviews

Medical Presentations:
A Prescription for Success
Terry Irwin, Julie Terberg, Echo Swinford
CRC Press, Taylor and Swift Group 2024
ISBN 9781032263526

This 200 page book[1] from Terry Irwin and colleagues is actually undersold by the title 'Medical Presentations'. It is a comprehensive and completely up to date guide on all forms of medical communication, from submitting an e-poster to controlling an online teaching session, plus of course the basics of improving your powerpoint design skills which one might expect from the title and which takes up a fairly large section of the book.

The book starts not with powerpoint but with a chapter on Educational Theory. The reader should not be tempted to skip this, as it contains a host of important observation and research about how we learn. Did you know if you read out word for word information which is also included as text on a slide, you *reduce* the retention rate? Redundancy, Cognitive Load, One Big Idea – if you are not familiar with these concepts and are involved in any sort of medical presentations, then you should be. Don't write down a case history in point after point on a slide (how often Have I done that?) – report the history verbally the way we do in real life. Use a strong image and one or two words instead.

The bulk of the book is, as you would expect, comprehensive and clearly presented on how to do all the things on powerpoint presentations which we were never taught, and often have to go to find someone else to show us. How to insert a video (how to record the video in the first place), how to align pictures, how to use and not use animations, what does it mean to embed a font (and why you might avoid doing it) – the list goes on. But this is not just technical 'how to do it' advice, it is 'how to do it well' advice, which is the key to the usefulness of this book. It's not a manual, it's a guide. Not just how to format and insert an image, but how to choose the right image, where to get stock images, which ones work and which don't. I learned for the first time the difference between a JPEG a PNG and a BMP. More than 5 slices in your pie chart? Use a treemap instead.

The final section on Presenting is, as admitted in the introduction, set in the era of the COIVD-19 pandemic and leans heavily into the pitfalls and possibilities of online presenting. How many of us would have benefited from reading this section in 2020? Again there is both basic information on how to practically set up and run an online presentation, coupled with advice on how to do it well. How to pre-record a talk is included, as well as how to inset QR codes and many other 'things I'd wish I'd known in 2020'.

Is this book aimed at medics born before 1995 (or 1965)? I had considered that as a possible critical observation, but on speaking to medical students as well as Emeritus Professors, the lack of formal teaching on how to do presentations well runs throughout the generations. There may be some redundancy for younger readers on how to do some of the more simple things – copying and pasting text – but medical students seem to be just as much in need of instruction on how to get your video to run properly on the last slide as those of us who started teaching drawing on curling acetates with an overheating overhead projector.

A recommended read.

David J Armstrong

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55 cases in Neurology.
Case Histories and Patient Perspectives
Publisher: Cambridge University Press (£29.99)

55 cases in Neurology[1], written by Consultant Neurologist Mark McCarron provides the reader with an engaging display of cases encountered during the practice of clinical Neurology in a District General Hospital. The action occurs at a site located one degree of latitude above the equator for each case presented (Altnagelvin Hospital). Although written for an audience of medical trainees interested in Neurology, the contents provide an entertaining, informative read for a wider range.

Cases begin with an alluring title (e.g. "A raspberry causing trouble") before a concise presentation of a clinical history, giving the reader some suggestion of where the case is headed. We are then informed of the clinical examination findings, summarising relevant positives and negatives from the bedside. Each case reads in the way one would wish to present on the post-take a ward round, using crisp and clear language. Necessarily, investigations come only after history and examination, culminating in an opportunity for the reader to pause and challenge oneself; what next? What could this diagnosis be? What would I do here?

Diagnosis and management plans are then laid out, each with thorough explanation and reasoning. Some conditions are primary neurological disorders (Parkinson's disease, CJD), but many are neurological manifestations of systemic disease (e.g. eosinophilic granulomatosis, Hyperglycaemic chorea) requiring input from different areas like Dermatology, Respiratory, Genetics, Ophthalmology, Radiology and Surgery. The case collection demonstrates that working

in any branch clinical medicine means you will encounter Neurological disorders. Nomenclature and historical aspects of diseases, recent advances and opportunities for future study are weaved together in a learning section for each case. This section succeeds in providing interesting facts on how our knowledge in medicine has steadily evolved, from how a trade embargo caused blindness in 1800s-era Cuba to how a cup of coffee can fix an alarm-clock headache.

Information on how diagnostic tests perform, how sensitivity, specificity and predictive value are influenced by population prevalence and pre-test probability provide crucial reminders to those practising medicine that test results are not binary outcomes of disease being present/absent, but are probabilistic and require interpretation in the setting of this patients' case history (e.g. false negative antibody testing in optic neuritis, PCR testing in Herpes simplex encephalitis). Anyone who regularly requests tests will welcome explanations on how test characteristics and population prevalence are both related, meaning clinicians are required to think carefully when requesting tests and acting on results.

A patient perspective rounds off each case. The unfiltered feedback from patient /carer often contrasts with the medical view of the case beforehand. Requests for better and earlier treatments are unsurprising, but first-hand description of patient experience, the impact of disability and a perceived lack of support are a stark reminder of that living with neurological illness is a challenging and sometimes lonely experience. One patient's ability to contrast the good support she received after breast cancer with the absence of support after encephalitis serves as an example of inequity facing patients with less common, yet important medical conditions. The perspective from a patient with Functional Neurological Disorder should be essential reading for all medical students and any healthcare professional with a patient-facing role.

There are abundant examples of literature inspired by Neurology for the general reader (Oliver Sacks, Suzanne O'Sullivan) while there are many reference books available to learn about diagnosis and treatment in Neurology. 55 cases functions both as a source of learning and reference on the numerous manifestations of neurological disease but also as a sobering insight into the experience of patients and families dealing with symptoms, disability and uncertainty. The target audience is medical trainees but the book deserves a wider audience and is recommended to anyone with an interest in how the human body works, and sometimes doesn't work.

Ferghal McVerry

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Medical History

'A Night with Venus' in Late Georgian Dublin

Alun Evans

Introduction

The old saying 'A night with Venus, a lifetime with Mercury' reflected the fact that until early in the twentieth century, Mercury was the standard treatment for Syphilis. Its use had a long history and was widely deployed in Dublin in the 1830s.

Syphilis

Gonorrhoea had long been prevalent in Europe, but European expansion, resulting in the 'Columbian Exchange', may have produced a highly unequal trade-off in which Columbus helped import Syphilis from the Americas.[1] In return, the Americas acquired Smallpox and Measles. Syphilis erupted in 1693-4 during a war between France and Spain, which was fought in Italy. After the French celebrated their victory at Naples in the traditional debauched fashion, and their army disbanded, a terrible epidemic ensued across Europe: genital sores heralded a generalised rash which proceeded to ulceration and revolting bone-destroying abscesses, affecting the nose, lips and genitals, and often proved fatal. There is another theory that the disease is more ancient, but the Columbian Exchange origin remains the frontrunner.[2]

Its name evolved too: initially it was the 'disease of Naples', then 'The French Pox', and so on, with countries usually naming the disease after other countries. It also became known as 'The Great Pox', in contrast to Smallpox. The name Syphilis derives from Fracastoro who, in a poem, tells of a mythical shepherd named 'Syphilus' who kept the flocks of King Alcithous.[2]

Syphilis in Late Georgian Dublin

In the eighteenth century, Dublin was the second city of the British Empire. Economic expansion resulted, as did population growth, but "was coloured by riches for a few and poverty for the many".[3] The 1798 Rebellion culminated in the Act of Union in 1801 when 100 Irish MPs took their seats at Westminster. This was followed by recession while the population burgeoned. Morton quotes Curwen who made a tour some years after the Act of Union was passed: "Poverty, disease and wretchedness exist in every town but in Dublin the misery is indescribable", adding, "Typhus, long endemic, sprouted into epidemics".

Attempts to live off the land were frustrated by the high rents being exacted by absentee landlords. By 1815 the economic plight was dire and by 1821 the population density of Ireland was the highest in Europe.[3]

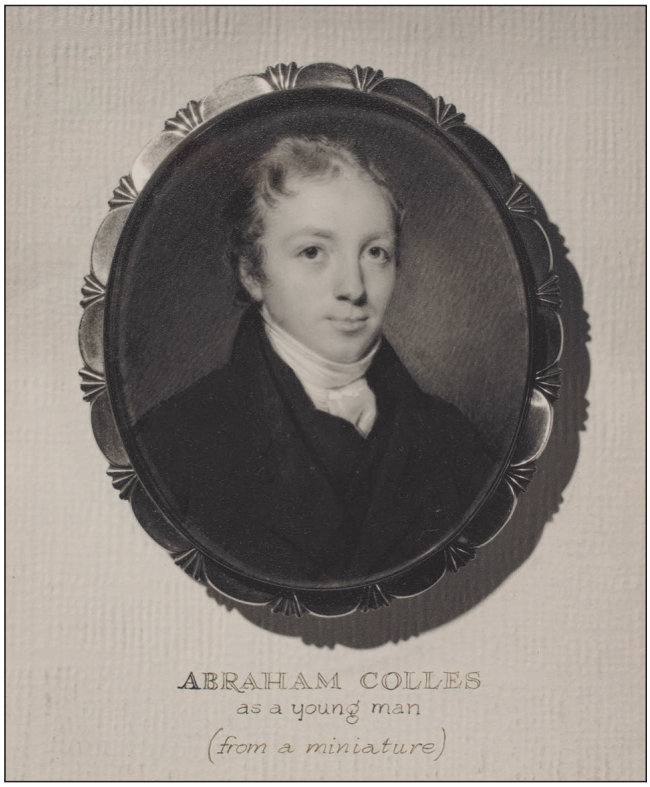

Figure 1: Abraham Colles (1773-1843) as a young man (Courtesy of RCSI).

Despite Francis Bacon's maxim that, 'Prosperity doth best discover vice, but adversity doth best discover virtue',[4] the incidence of Syphilis in Dublin was high with "an enormous number of cases".[3]

Abraham Colles (1773-1843 - see Figure 1), the pre-eminent Surgeon of his day, was famous for his fracture, ligament and fascia, and his Law.[5] The latter stated that when a child with congenital Syphilis was breastfed by a wetnurse, which was common at the time, the wetnurse would develop a chancre (ulcer) on her breast, but the child was:[6]

> …never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lips and tongue.

The only trouble was that another Dublin-based doctor,

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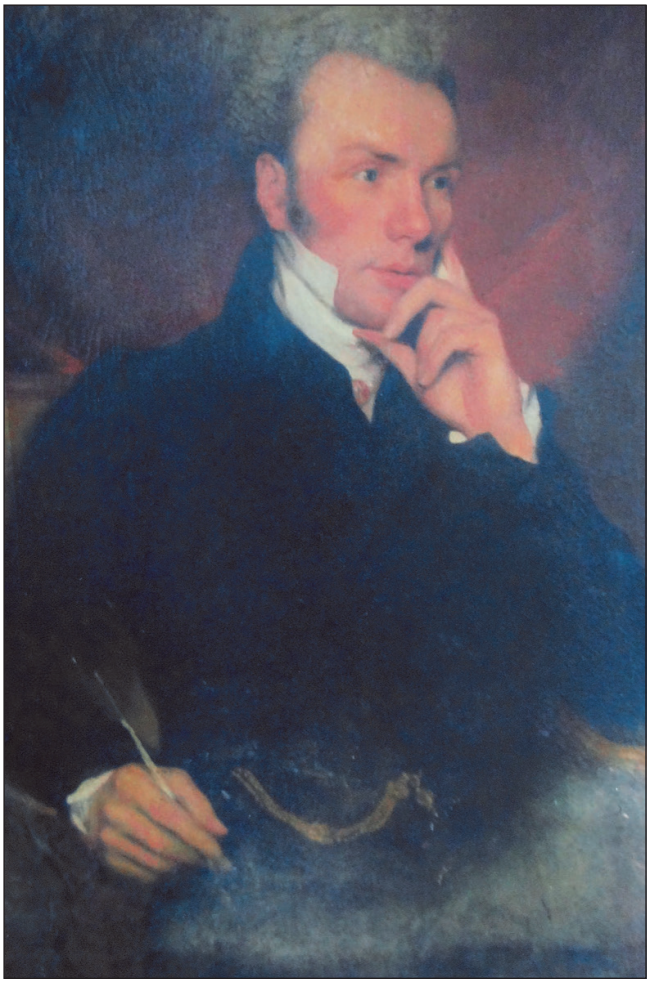

Figure 2: William Wallace (1791-1837) (Courtesy of RCSI).

William Wallace (1791-1837 - see Figure 2), who wrote extensively on the disease, had already described the Law,[3] as was pointed out by a Dr Shaw-Mackenzie in a *Lancet* paper in 1899.[7] This is by no means the only example of a misattributed eponym: for example, Cheyne-Stokes breathing had originally been described by Hippocrates.[8]

The Treatment of Syphilis in Late Georgian Dublin

Although no new treatments were introduced in Dublin over the period, significant advances were made in refining the dosage of the existing ones. Fracastoro had introduced Mercury as a treatment in 1530,[2] and he coined the term gumma (*resin L*) for the scabs that form later in the course of the disease. Mercury treatment had awful side effects such as neuropathies, kidney failure, severe mouth ulcers and loss of teeth, and countless patients died of mercurial poisoning rather than the disease itself. The treatment would typically go on for years, so gave rise to the saying quoted in the Introduction. It was taken by mouth, applied to the skin and even vapourised.[9]

Colles was born in Kilkenny in 1773, entered Trinity College Dublin in 1790, and then undertook apprenticeships in Dublin.[10] He subsequently qualified MD in Edinburgh in 1797, and later worked with Astley Cooper in London, before returning to Dublin. Colles believed that the best results of Mercury treatment were obtained at low doses. His great contribution was to carefully delineate the dose of Mercury so that its efficacy was maintained while the minimum side effects resulted.[11] Since Mercury was a sialagogue, he achieved this by carefully adjusting the dose so that the minimum quantity of saliva was produced while the benefits were preserved.

According to Coakley:[11]

> Large pewter mugs were kept in Dr Steevens' Hospital for the patients to spit into, and the dose of mercury was adjusted depending on the number of mugs filled during the day.

Another treatment for secondary Syphilis was Potassium Iodide.[12] Its dosage was refined by Dr William Wallace, who was born in Downpatrick in 1791. He undertook apprenticeships in Dublin, obtaining his Diploma in 1813. Like Colles, he afterwards spent time with Astley Cooper in London. In 1818, at his own expense, he opened the Dublin Infirmary for diseases of the Skin, at 20 Moore Street, which accepted male patients with venereal disease. He was "probably the first true dermatologist in Dublin".[13]

Between 1819 and his death in 1837, Wallace published no less than five books, three being revised for a second edition, and nearly thirty papers;[3] his Treatise on the Venereal Disease and its Varieties appeared in 1833.[14] In 1835-6, he published a series of 142 patients taking Potassium Iodide in the *Lancet*.[15] Iodine as a treatment had been introduced by Martini of Lubeck in 1821.[16] Wallace showed by experimenting on dogs that Potassium Iodide was better tolerated than Iodine, which was converted to Hydroiodic Acid and irritated the gastric mucosa.[15] He controlled the dosage by testing the urine for Iodine, which was liberated by the addition of dilute solutions of Sulphuric Acid and Chlorine; starch was then used as an indicator. The Iodide was given until the urine when tested became as black as ink.[17]

The Contagious Nature of Syphilis

In experiments, which Cameron described as 'indefensible', Wallace was first to show that secondary Syphilis was contagious. He published his series of three male patients, whom he had inoculated with infected material, in the *Lancet* in 1837.[18] He claimed that he had cured all three by administering Mercury. The only snag was that none of the subjects had been told the nature of the experiment, although the results were of considerable scientific value.

Wallace's approach followed that of the great Scottish anatomist John Hunter, who in 1767, set out to prove that Gonorrhoea and Syphilis were the same disease. With greater ethical probity than Wallace, however, Hunter infected himself with the former and developed Gonorrhoea. Sure enough, within ten days, he also developed Syphilis.

The unfortunate Hunter's source of Gonorrhoea was also infected with Syphilis.[19]

Wallace's experiment was to be echoed almost a century later, only on a vastly greater scale, when the 'Tuskagee Study of Untreated Syphilis in the Negro Male' at Alabama, in America's 'Deep South', ran from 1932-72.[20] It involved 399 men with Syphilis and 201 without. The men were told that they were being treated for 'bad blood', but the shocking aspect was that they were not offered Penicillin when it became available in the 1940s. By the Study's end, many deaths had occurred and many family members had been infected. It became a powerful symbol of racism in Medicine, leading to a Presidential apology in 1997.[21] Strangely, as part of his study of human dermatology, with foretastes of the Tuskagee Study, Wallace kept a person of African ethnicity in his house so that he could make observations on his skin![12] He was to apply the results to the treatment of skin naevi.

In the Oslo Study of the natural history of Syphilis,[22] which ran from 1891 to 1910, Boeck also withheld treatment from approximately 2,000 patients with primary and secondary Syphilis. Although it was forerunner of Tuskagee, and on a far greater scale, the treatment withheld was nowhere near as effective as Penicillin, and there was no racial dimension. The study demonstrated that hospitalisation reduced community spread, but unlike the approach adopted in the WLH (see Figure 3 below), patients of both sexes were included.

In 1838 Philippe Ricord had indubitably established[2] that Syphilis and Gonorrhoea were separate diseases, something which Hunter could have claimed, had he been aware of it. Ricord differentiated Syphilis' three stages, and he adopted Wallace's regime of Potassium Iodide which soon became used throughout Europe[3].

Figure 3: The Westmoreland Lock Hospital (Courtesy of Archiseek).

The causative organism of Syphilis, *Treponema pallidum*, was not identified until 1906, when an accurate serum test was also introduced by Wassermann,[2] and the disease remained a huge problem until the introduction of Penicillin in 1943. Similarly, there was no effective treatment for Gonorrhoea until sulfonamides were introduced in the1930s.[1]

Figure 4: Skin Lesions of Secondary Syphilis: Jane Sutherland – possibly 'the victim of her husband's profligacy'? (Courtesy of RCSI).

The Wallace Collection

Wallace encouraged his two young daughters to draw pictures of the structure of the skin and the diseases affecting it. The elder died in her seventeenth year from scarlet fever.[12] He also commissioned several professional artists, including William Burke Kirwan and James Connolly, for a medical atlas that was never published (personal communication). [23] After Wallace's death from Typhus in 1837, his widow sold a large portfolio of coloured drawings to the RCSI for £50.[3] The RCSI has made the Wallace Collection of 372 images and 13 casebooks available online.[24] The site is searchable, and many images depicting advanced syphilitic lesions are not for the fainthearted: for two of the less disturbing images of patients during the 1830s, see Figures 3 & 4.

The Westmoreland Lock Hospital (WLH)

The WLH was established in Townsend Street, Dublin in 1792, bearing the name of the then Lord lieutenant, the Earl of Westmoreland.[25] At the time of its charter, it was the only Irish hospital dedicated to venereal diseases, especially Syphilis, until 1955, when it closed and was demolished (see Figure 5). The name derives from earlier *Lazars*, or hospitals for treating Leprosy, which used 'locks' (derived from the French '*loque*', meaning 'rag') to cover the leprous lesions.[26] It replaced an earlier Lock hospital in south Dublin which was founded in 1755[27]. It became the largest institution for treating venereal disease in the British Dominions.[3]

Abraham Colles was President of the Royal College of

Figure 5: Skin Lesions of Secondary Syphilis: Rosella Keenan (Courtesy of RCSI).

Surgeons of Ireland (RCSI) in 1802 and 1830.[12] He became a Governor of WLH in 1802, demonstrating the increasingly close links which grew up between the RCSI and WLH.[27] It is worth noting in passing that Frances Ray served as Matron in the WLH from 1835 until 1861. She was the widow and former accomplice of Wilson Ray,[25] a surgeon who organised the export trade in cadavers from Dublin in the 1820s. Ray seems to have used the RCSI as 'a kind of warehouse',[28] so perhaps the RCSI had been more complicit in the trade than it cared to admit?

A Memorial sent to the Earl of Mulgrave,[29] the Lord Lieutenant, by the WLH's Governors on 3rd February 1838, gave much of the WLH's early history. It originally had beds for 128 male and female patients, but by 1796 these had swelled to 250. Unfortunately, "several evils" arose, and a Report of 1820 concluded that the failure of the Institution was to be especially attributed:

> 1st to the evils consequent on the intercourse between Male and Female patients which had never been guarded against - 2nd To a deficiency of moral and religious instruction and employment…and 5th To the abuse of the design of the Institution in the adoption of the erroneous principle of extending it to Male Patients…

Subsequently the WLH only admitted females.

Similar problems must have arisen with the presence of Medical Students, who were all male, in the WLH, because it admitted them until 1820 when they were excluded, and "medical students became the crux of many disputes".[30] The Governors urged the admission of students under restrictions necessary to ensure "propriety and morality".[31] They were finally readmitted in 1858,[32] as a need to teach Medical Students about the venereal disease in women was recognised, but it was not a success. The antipathy to Medical Students on the premises can be appreciated because:[33]

> Some twenty-three years ago, Dr. M'Dowell of happy memory, was resident medical officer in the Lock Hospital, and he kept a class of young men in his own room, where he ground them. When leaving after his lecture, they would endeavour to force open the door to one of the wards to get amongst the inmates. And it often took the doctor, two porters, the matron, and nurse to prevent them; this took place when they had no access.

The Memorial continued by asserting that a new regime had effectively stamped out drunkenness in the staff, had improved therapy and outcomes, and from 1821 had established a laundry which catered for the WLH's needs, and employed 13 former patients, a strategy akin to the Magdalene Institutions "for unfortunate females abandoned by their seducers".[3]

The Memorial asserted that thanks to carefully classifying patients, it had been possible to:[29]

> … separate the novice in crime from the hardened offender, and the married woman, who is the victim of her husband's profligacy, from those where disease has proceeded from choice and personal misconduct.

Indeed, there is some evidence[34] that the 'Domestic Goddess' Mrs Beeton died of Syphilis - a gift which her husband may have brought to the marriage bed.

One might be forgiven for detecting a strong undercurrent of moralism in all this, particularly in view of the rationale later given for segregating women in a Lock Hospital:[35]

> Two distinct classes of cases come into the Lock Hospital; first, those who have fallen but once, and enter our walls but once; and secondly, the hardened sinners, women who have for years been making a livelihood by prostitution; we try to reform girls of the former class, and if we left the hardened sinners free to roam through the hospital, they would taint these beyond the hope of reclamation.

What precisely underlay all the strong undercurrent of moralism in the Memorial? The Lords of the Treasury had written[36] to the Lord Lieutenant querying the need for the complete financial support of a 'Charitable Institution', which surely should be supported by charitable subscription. In reply, the Memorial stated:[29]

> - great prejudices exist (however lamentably and unjust) against the support of persons of profligate character, as tending to diminish the funds applicable to other charities, and as holding out an encouragement to vice,…

This was sufficiently convincing to ensure that the costs of the WLH continued to be borne by the State and although, intermittently, financial threats recurred, the WLH survived. As we shall see, the real reason for the WLH Governors' reluctance to seek truly charitable status was tied to a desire for total secrecy.

In an 1842 Report, the Chairman saw one of the WLH's main roles as:[37]

> …preventing the extension of a disease of which every infected woman is the centre, and the unhappy instrument of diffusing it around;…

Thanks to the WLH's strict discipline, after discharge many former patients had a disinclination to return to a "life of infamy", and "preferred the paths of industry rather than the wages of prostitution". He went on to justify the full parliamentary support, describing the possibility of any truly charitable support of the WLH as "utterly hopeless". He added that the WLH was for patients from all over Ireland, so it was unfair to try to raise charitable support locally.

It is not until a Parliamentary Report of 1854 that the true *raison d'etre* of the WLH was divulged:[31]

> The importance of such an institution in a town like Dublin can hardly be over-rated. It appears that in large garrison towns the establishment of a Lock hospital for females is the best mode of preventing venereal disease among the soldiery. On the mere grounds of economy its support by Parliament can be justified, as venereal disease constantly incapacitates and even cause the discharge of the soldier at the very age that he is most serviceable to his country.

Here the question is left moot as to which country is meant, but it certainly is not Ireland. The British Garrison in Dublin around 1850 averaged about 6,000 men, with nearly 9% of them suffering from venereal disease at any one time.[38] There were "great objections" to treating female venereal disease patients in general and workhouse hospitals; in Dublin they had been almost totally excluded from the former and "serious evils" had arisen when they were treated in the latter.[31]

According to the Surgeon of Dublin's military prison, soldiers did not see prostitution "as any immoral act".[39] Indeed, "Prostitution is absolutely necessary" and if it was discouraged in soldiers, their "moral character" would be reduced.[40] He highlighted the problem of young soldiers being discharged from the army because of venereal disease, "just as they are fit to be sent to the colonies":[41]

> A great many are discharged under three years of service, because a soldier discharged under three years of service is entitled to no pension whatever; consequently when he shows this disposition he is got rid of; but then if it is argued that the country is no loser by it, it is wrong, because that man has been kept and trained for three years; it is like buying horses at three years old, and selling them at five, and getting the same price for them.

This statement, made at the time of the Crimean War, makes it abundantly clear how young soldiers were regarded as 'Cannon Fodder'.

In 1849 Thomas Byrne estimated that around half the females admitted to the WLH were "victims of the British soldiery".[42] Moreover, this very soldiery may have been responsible for importing many of the female cases to the WLH from Britain, deserting them when the 'soldiery' was posted elsewhere.

In the 1860s, the Surgeon John Morgan was experimenting on

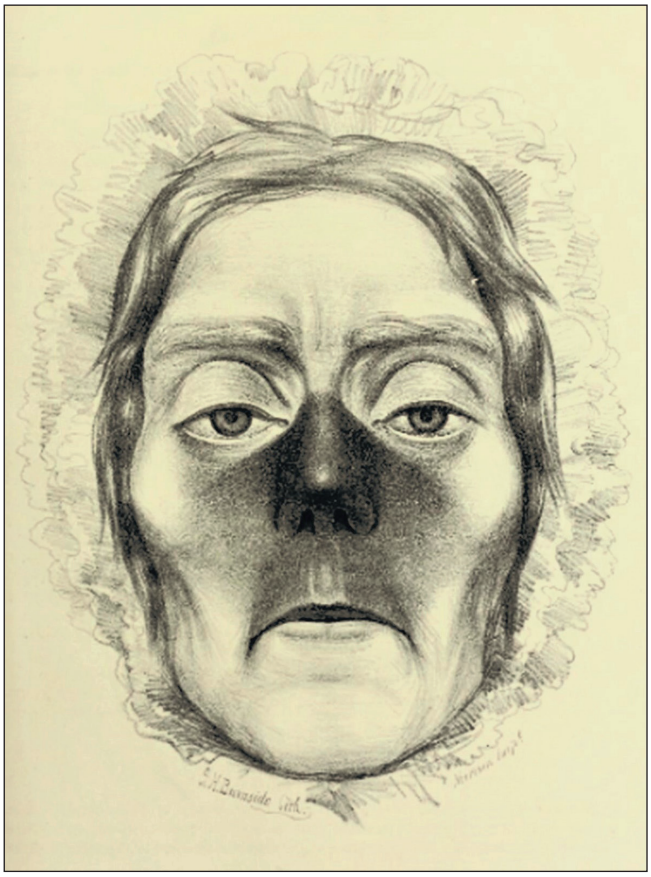

Figure 6: Gangrene of the face caused by Mercury therapy. Source: Morgan ?1869. (Courtesy of Wellcome Library).

two eight-year-old girls with Syphilis[43] by inoculating them with material from older patients with the same condition. He hoped to arrive at a cure, but his experiments were just as ethically flawed as those conducted by William Wallace, and the WLH's Governors ordered him to desist. He also wanted to take serial photographs of his patients, but, once again, his

ambitions were reined in by the Governors.[44]

Morgan also published a Report of cases under treatment in the WLH for the half-year ending 31st December 1868.[45] For each unmarried woman he records the period over which they had been 'unvirtuous', highlighting the moral opprobrium in which unmarried females with venereal disease were held at the time. George Bernard Shaw was later to describe virtue as 'the Trade Unionism of the married'.[46] The Report included[45] a haunting image of a woman with gangrene of the face caused by Mercury therapy (see Figure 6).

The Treatment of Females with Venereal Disease in the 19th Century

Between 1800 and 1940 thousands of women worked as prostitutes in Ireland,[47] and were looked upon as "carriers of disease and immorality". The official responses, however, were erratic and often the result of some crisis. The authorities obsessively attempted to classify 'immoral' women, and this resulted in the classification of unmarried females with venereal disease as 'fallen' and married sufferers as victims of their husbands' philandering.

The designation of unmarried female patients as 'fallen' seems grossly unfair, for, some at least, would have enjoyed steady relationships with their common law husbands, and became infected by them. Moreover, the classification of females with venereal disease into the two groups is reminiscent of the Victorian obsession with differentiating between the 'Deserving' and 'Undeserving' Poor in the 1834 Poor Law Amendment Act.[48]

Speaking from an Epidemiological perspective, if the 'immoral' women represented the disease reservoirs of venereal disease, men represented the vectors (transmitters), just as mosquitos spread Malaria. It has therefore been prudent to limit the spread of the disease by controlling the mosquito population. Thus, the adoption of a wholly female-orientated approach to controlling the disease by incarceration in the WLH was not only grossly unfair to females, but also irrational. In effect, "...it was the body of the prostitute that became identified as the source of venereal disease".[27]

The results of the Oslo Study demonstrated[22] that community control could be achieved by incarcerating men as well as women. Although the derivation of 'Lock' has been given above, another meaning of the word is a pretty accurate description of the punitive practices which were exercised at the WLH. This meant that the inmates were segregated by religion,[49] their heads were shorn,[50] they were not allowed to look out the windows,[51] and there was no "yard to walk about in".[52]

There is a poignant letter,[53] written in 1853, after a shocking incident, "in a house of bad repute" in French-street, which involved the shooting of a young woman and a man's suicide. The incident coincided with Queen Victoria's visit to Dublin. There was a letter in *Saunders's News-Letter* a few days later under the heading 'A Refuge for Outcasts' in which the writer, 'J. D. S.', suggested that the refuge should be for men.[54] A flurry of letters in the same newspaper a few days later were emphatic that the Refuge should cater for women.[55] One of these, from 'B', described the writer's experiences as a pupil in the WLH (the writer must have been a student before 1820). The writer had been a witness to:[55]

> …the mental sufferings which many abandoned females endured while patients in that institution; and I well remember the dreadful imprecations which they used in cursing the libertines by whom they had been seduced. I was induced to go round the wards and ask each individual whether she would, if restored to health, prefer the sanctuary of a penitentiary [a place of penitence] to reverting to a life of sin and shame, and all of them, with one or two exceptions, implored of me to get them into an asylum, as nothing but dire necessity would induce them to lead the lives of inconceivable sorrow and degradation which they had been leading;…

There is no doubt that prostitution was driven above all by poverty, and gainful employment for poor, young women, other than domestic service, was scarce in Victorian times. Hurren starkly illustrates[56] this by quoting individual histories. These cut through the rhetoric of much of what is popularly accepted. The reality was that once a girl had a baby, and they were abandoned by the biological father, prostitution sometimes represented the only means of supporting the child.[57] Shockingly, for most of the 19th century the age of consent for girls was just 13 years. The Criminal Law Amendment Act of 1885 raised it to 16 years.[58]

Some women became "comfortable mistresses," but others developed serious venereal disease, and if they died, their bodies, being unclaimed by disaffected family members, were sold and ended up on the dissecting table at St Bartholomew's Hospital.[57] Such dissections were carried out rapidly as students were wary of acquiring an infectious disease. One nick of the skin with the lancet would suffice, and this was before the days of latex gloves.

The treatment of women suspected of having venereal disease became even more draconian with the passing of the first of three Contagious Disease Acts in 1864.[59] They applied not only to England but also to the garrison camps of the Curragh, Cork and Queenstown (now Cobh) in Ireland, and extended to a five-mile radius of each camp. Women on the street were subjected to arbitrary and compulsory testing.

As usual, the spread of venereal disease was blamed on women, particularly prostitutes. Lamentably, supporters of the Acts argued:[60]

> ...while men would be degraded if subjected to physical examination, women who satisfied male sexual urges were already so degraded that further indignities scarcely mattered. Protection for males was supposed to be assured by inspection of females.

The Acts ordained that women could be arrested and ordered to be examined at a certified hospital, with a refusal punished by a month in jail. All 'common prostitutes' were registered. The soldiers in the camps:[59]

> …all seemed to agree to speak of these abandoned women as a kind of dreadful and scandalous necessity, and as beings beyond the pale of human sympathy or help.

Some vigorously defended the Acts,[59] such as Sir Charles Cameron; others were diametrically opposed to them, especially various women's groups. The Belfast branch of the Ladies' National Association saw them as an affront: "to the dignity and independence of every woman in the land". As ever there was religious split on this island with many denominations opposing the Acts: Catholic priests were an exception as they tended to support them.

The Acts were suspended in 1883 and withdrawn three years later.[59] Malcolm observed[60] that the repeal of the Acts in Ireland, while thwarting state public-health regulation, in the long run simply strengthened clerical moral control – as became all too obvious after 1922. Before that watershed, Nationalists had linked prostitution to the British garrison's presence in Ireland, but after independence, the levels of illegitimacy and venereal disease actually increased.[61]

Conclusions

Dublin Medicine's major contribution to the treatment of Syphilis in the late Georgian period was the downward adjustment of the doses of the Mercury and Potassium Iodide employed, while still maintaining their efficacy.

The vilification and subjugation of females with venereal disease in 19th century Ireland may have been 'of its time' but it seems abhorrent today. The simple fact is that the WLH was being used to maximise the 'Coercive Control' of the British garrison by ensuring that venereal disease was reduced in its soldiers.

Researchers have difficulty in establishing women's history before 1900, as women were largely 'invisible' then, being identified by their husbands' Christian names, and reduced to mere appendages. Things had begun to change in Ireland in the late 1800s with the advent of the Suffrage movement, which held its first public meeting in Dublin in 1870. In 1872, Isabella Tod in Belfast founded[62] the North of Ireland Suffrage Society, followed by Anna Haslam in Dublin, who in 1876 established[63] the Irish Suffrage Society. Ireland's Suffrage movement flourished in the early years of the last century, becoming increasingly militant. Key figures were the 'Sheehy-Skeffingtons'. The surname was famously adopted by Hanna Sheehy and Frank Skeffington when they married in 1903.[64] Like Willliam Wallace, Frank was reared in Downpatrick.[65] When the 1916 Easter Rebellion was in full swing, 'Skeffy' as he was known, went to the GPO to exhort the leaders to stop people looting. He was later arrested and summarily executed.[66] The efforts of the Suffragettes delivered limited suffrage to England and Ireland in 1918, probably in recognition partly of women's role in the war effort.[67] Full parity with men was achieved in Ireland in 1922 when the Irish Free State drew up a constitution which firmly placed women and men as equal citizens (Tiernan), six years ahead of England.[68]

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Roe Valley Hospital, Limavady, County Londonderry. Built in 1842 as the Newtown Limavady Union Workhouse, the impressive building served as the town hospital until its closure in 1997.

The structure was saved and restored by a local community initiative, and part of the building is still used for outpatient, radiography and physiotherapy services in the Western Health and Social Care Trust.