ULSTER MEDICAL JOURNAL

Volume 95 Issue One 2026

- Annual Oration
- Artificial Intelligence
- Avoiding Prescribing Pitfalls

The Ulster Medical Journal

The journal of the Ulster Medical Society. First published in 1932.

Successor to the Transactions of the Ulster Medical Society (1862-1929), and the Transactions of the Belfast Clinical and Pathological Society (1854-1860)

Statement: The Ulster Medical Journal is an international general medical journal with contributions on all areas of medical and surgical specialties relevant to a general medical readership. It retains a focus on material relevant to the health of the Northern Ireland population.

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The journal is published in January, May and September, by the Ulster Medical Society, and typeset and printed in the UK by Dorman and Sons Ltd, Belfast. See inside back pages for institutional and personal subscriptions.

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Guest Editorial

Okay computer?

Michael Trimble

Embraced with enthusiasm by many, artificial intelligence (AI), it seems, is everywhere: on our computers, on our phones, and even in many domestic appliances. The chances are that when you use an internet search engine the first answer offered will be one generated by AI. But what are the implications of AI for the practice of medicine, education, and the wider society?

For someone to resist or even question such technological progress risks being labelled a Luddite. However, sociologist Neil Postman warns us of the impact it may have:

> New technologies alter the structure of our interests: the things we think about. They alter the character of our symbols: the things we think with. And they alter the nature of our community: the arena in which thoughts develop.[1]

Such effects can be seen to have occurred with other technologies that are now commonplace in our society. Whilst often viewed as an aid to efficiency, automation of process has been shown to change the dynamic and effectiveness of decision-making. The practitioner – in fields as diverse as finance [2] and aviation [3] – whilst in theory overseeing the automated process, becomes disengaged, out of practice, and less able to intervene when the technology fails. Use of the internet has been demonstrated to affect how individuals remember and process information with a loss of deep learning and comprehension,[4] and the smart phone along with development of messaging platforms has produced a level of connectivity that has radically changed the shape, not just of human interactions, but also adolescent psychological development – a situation described by psychologist Jonathan Haidt as "the great rewiring".[5]

It is to be admitted that there are many areas where artificial intelligence (AI) may offer significant benefits to medical practice, for example, the screening of pathology samples[6] and diagnostic radiology.[7] Generative AI, in the form of Large Language Models (LLM) such as ChatGPT, has demonstrated its impressive ability to summarise data, and even write prose and poetry at a level comparable to humans. However, it has also demonstrated a tendency to produce low quality "slop".[8] More concerningly, it has also proved that it can generate harmful falsehoods termed "hallucinations". A disturbing example is the case of a Norwegian man who asked ChatGPT a question about himself and was given the totally fictitious response that he had killed his two children.[9] An equally disturbing account is given by author Amanda Guinzburg who details a conversation with ChatGPT where it becomes apparent that the AI has been lying to her repeatedly from the outset.[10] For those hoping that AI may help them find appropriate references to support their research, one study found that "between 50% to 90% of LLM responses are not fully supported by the sources they provide".[11] Tellingly, even those behind AI systems, such as OpenAI's Sam Altman, do not advocate trusting them to be accurate.[12] The use of AI to support reasoning has been shown to diminish critical thinking skills in knowledge-based workers[13] , and a study of university students (undergraduate and postgraduate) demonstrated a "cognitive cost" associated with the use of AI for essay writing, with users less inclined to critically evaluate content. Interestingly, this was associated with a decrease in brain connectivity as demonstrated by EEG compared to the control group and was felt to be consistent with a lack of deep learning in the LLM users.[14] All this should raise concerns for those involved in education and knowledge-based professions such as medicine. Microsoft reckon that their *MAI Diagnostic Orchestrator* (MAI-DxO) outperforms human physicians in complex cases.[15] Whilst AI may be a useful adjunct for the experienced clinician, it may prevent the novice from gaining those skills. AI in higher education may have some benefits, such as personalised learning, overuse is associated with diminished interpersonal skills and emotional intelligence leading to social isolation.[16] As programmers improve their AI interfaces, making them seem more human, it can be easy for users to personify the technology. Indeed, some manufacturers even describe their products as having a persona. However, as Zimmerman et al. note:

> AI sifts through data; it does not have an emotional investment in a relationship with a human. It can execute the tasks that seem like caring for you, providing what you might perceive as companionship, social interaction, friendship, or romantic partnership.[17]

Users may even perceive their AI to be a sentient entity, as did Blake Lemoine, an engineer working on Google's LaMDA.[18] Before you scoff, have you ever thanked Alexa? AI can be programmed to pick up on conversational cues and simulate interest and empathy with the user. Regarding the use of AI in healthcare settings, one study has shown that patients viewed responses from ChatGPT as demonstrating greater empathy than those given by clinicians.[19] The bond that individuals develop with AI chatbots may be extremely strong and may displace normal human relationships. This can be seen in the popularity of AI romantic companions whose avatars may be crafted to suit their users' preferences and who will never be critical or condemning.[20] Morrin et al. raise concerns about "ChatGPT psychosis" where the AI "may mirror, validate or amplify delusional or grandiose content, particularly in

users already vulnerable to psychosis."[21] (Without irony, the authors note that the paper was written with the aid of LLMs).

In summary, whilst AI has potential in targeted areas, it is not without risk. We have already mentioned Haidt's description of the "great rewiring" and the unforeseen impact of the smart phone and social media on children's neurodevelopment and socialisation. The wider societal effects of AI, both in terms of cognitive processes and interpersonal interaction, have yet to be seen.

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Ulster Med J 2026;**95(1):**3-10

Clinical Paper

Thrombosis and Survival after Prothrombin Complex Concentrate Use to treat Oral Anticoagulant Associated Haemorrhage

A O'Kane[1], R Cullen[1], P Toner[1,2], G Benson[3]

Background

Recent trials for treatments of direct oral anticoagulant (DOAC) related acute haemorrhage have highlighted incidences of post treatment thrombosis. Prothrombin complex concentrate (PCC) is widely used for reversal of anticoagulant associated bleeding, yet thrombotic risks following PCC administration, particularly for DOACs, remain incompletely characterised in real-world settings.

Methods

This retrospective observational study analysed thrombotic and survival outcomes in 682 patients that received PCC for OAC associated haemorrhage in the Belfast Health and Social Care Trust between 2015-2021. Patients were categorised by OAC type (warfarin, rivaroxaban, apixaban and edoxaban). Primary outcome was thrombotic event rate at 30 days, while secondary outcomes included 30- and 90-day mortality and anticoagulation resumption rates.

Results

The cohort comprised 393 warfarin patients, 55 rivaroxaban, 221 apixaban and 13 edoxaban patients. Intracranial haemorrhage predominated (47-69% across DOAC groups vs. 49% warfarin). Thrombotic event rates were significantly higher in DOAC patients (rivaroxaban 13%, apixaban 8%, overall DOAC 8.7%) compared to warfarin (5%). Thirty-day mortality rates ranged from 13-23% across oral anticoagulant groups. Anticoagulation was resumed in only 29-47% of patients.

Conclusions

The findings suggest that PCC may be as effective as specific antidotes for DOAC reversal. In the absence of universal access to specific reversal agents, PCC continues to serve an important role in managing life threatening anticoagulant associated haemorrhage. Systematic pathways for post reversal anticoagulation resumption should be implemented to optimise patient outcomes.

Key words: Prothrombin complex concentrate, oral anticoagulant, warfarin, thrombosis, DOAC and andexanet alfa

PLAIN LANGUAGE SUMMARY (AI-GENERATED)

Reversing Blood Thinners Safely After Serious Bleeding

What was the purpose of the study?

Some people take medicines called blood thinners to stop dangerous blood clots. Examples include warfarin and newer ones called DOACs (like apixaban and rivaroxaban). But these medicines can sometimes cause serious bleeding, including bleeding in the brain.

Doctors have developed a specific treatment to stop the bleeding and help the blood clot again (Andexanet alfa), but it caused a lot of extra clots and is expensive. Previously doctors used a treatment called prothrombin complex concentrate (PCC) to help the blood clot again and stop the bleeding.

The purpose of this study is to review those given PCC after bleeding and assess what happened after.

What did the researchers do?

The researchers looked back at hospital records from the **Belfast Health and Social Care Trust**. They studied **682 patients** who were given PCC for serious bleeding between **2015 and 2021**.

They grouped patients by which blood thinner they were taking:

- Warfarin
- Rivaroxaban
- Apixaban
- Edoxaban

They mainly checked:

- How many patients had a **blood clot within 30 days**
- How many patients died within **30 days and 90 days**

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- How many patients restarted their blood thinner after treatment

What were the findings of the study?

The largest group of patients were taking warfarin. Many others were taking apixaban.

The most common type of bleeding was bleeding inside the skull, which can be very dangerous.

Blood clots happened more often in people who had been taking DOACs:

- 13% in rivaroxaban patients
- 8% in apixaban patients
- 8.7% in all DOAC patients combined
- 5% in warfarin patients

Death within 30 days happened in about 13% to 23% of patients, depending on the group.

Only 29% to 47% of patients restarted their blood thinner after the bleeding was treated.

What does this mean?

This study suggests PCC may work as well as the specific antidote to reverse DOAC blood thinners in emergencies.

But the results also show that blood clots after PCC may be more common in DOAC patients than in warfarin patients. So doctors need to watch patients carefully after treatment.

The study also suggests hospitals should have clearer plans for when to restart blood thinners. Restarting them at the right time may help stop future clots and improve patient safety.

Introduction

Direct oral anticoagulants (DOACs) have become the preferred antithrombotic therapy for the prevention of thromboembolic complications in patients living with atrial fibrillation or venous thromboembolism, offering equal or superior efficacy compared to traditional vitamin K antagonists [1-3].

However, major bleeding remains the most concerning adverse event associated with DOAC therapy, and the clinical challenge of rapidly reversing anticoagulation in life threatening haemorrhage has led to the development of multiple reversal strategies [4].

The management of DOAC associated bleeding historically relied upon non-specific reversal agents, particularly prothrombin complex concentrates (PCCs), which contain high concentrations of vitamin K-dependent clotting factors (II, VII, IX, and X). PCCs have demonstrated efficacy in reversing anticoagulant effects and restoring haemostasis together with an acceptable thrombotic safety profile compared to fresh frozen plasma [5]. The mechanism of action of PCC involves the provision of excess clotting factors to overcome drug-mediated anticoagulant effects, potentially resulting in a prothrombotic state [6-7] (figure 1).

The thrombotic risk associated with anticoagulation reversal is multifactorial, stemming from the rapid reinstitution of the thrombotic disorder requiring anticoagulation initially, the underlying haemorrhagic disease state necessitating reversal and the pharmacological consequences of each reversal strategy. Abrupt cessation of anticoagulation combined with administration of procoagulant agents creates a heightened

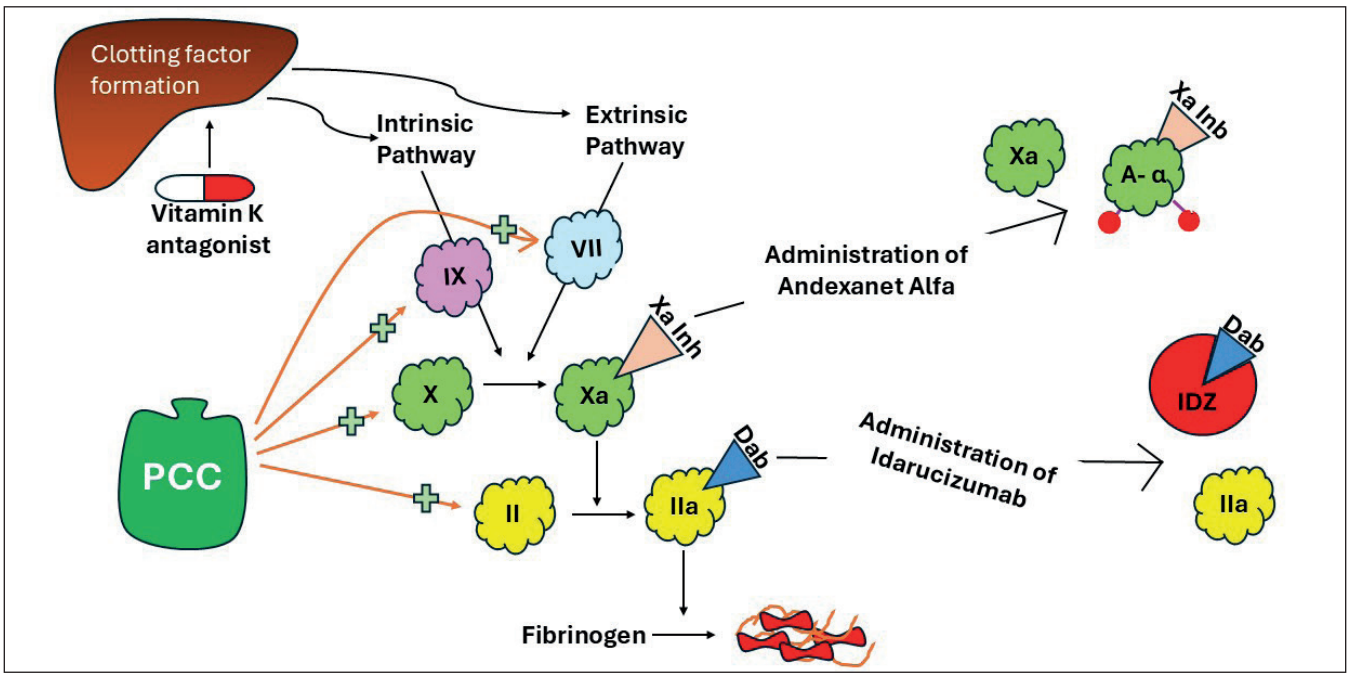

Figure 1: Simplified diagrammatic representation of coagulation pathway indicating where the oral anticoagulants interact and how the antidotes work.

Key PCC- prothrombin complex concentrate, Xa Inh- Factor Xa inhibitors, DAB- dabigatran, IDZ- Idarucizumab, A- a - Andexanet alfa.

thrombotic risk, particularly in patients with recent thromboembolic events.

The landscape of DOAC reversal has evolved substantially with the introduction of specific reversal agents targeted to individual drugs (figure 1). Idarucizumab, a monoclonal antibody fragment achieves complete and immediate reversal of dabigatran with only 6% thromboembolic complication rate at 90 days [8]. Similarly, andexanet alfa, a factor Xa decoy protein, offers targeted reversal of factor Xa inhibitors with anticoagulation reversal rates of 82% and thromboembolic rates reported at approximately 10% in patients with major bleeding on factor Xa inhibitors [9].

Despite the advent of specific reversal agents, PCCs continue to be employed as an alternative or adjunctive strategy in clinical practice, particularly in resource-limited settings or when specific agents are unavailable or unlicenced. Comparative safety data reveal important differences in thrombotic risk profiles. A recent meta-analysis suggests thromboembolic event rates of 8% for PCC, 14% for andexanet alfa and 5% for Idarucizumab when used for DOAC reversal in intracranial haemorrhage [10]. This raises important questions regarding the relative prothrombotic potential of PCCs compared to specific reversal agents, and whether routine use of PCC is as justified as specific agents.

Current NICE recommendations emphasise the targeted use of specific reversal agents, especially andexanet alfa only for gastrointestinal bleeding in patients on apixaban and rivaroxaban. Andexanet alfa is, at present, unlicensed for reversal of edoxaban due to concerns over efficacy [11].

In Northern Ireland, political, geographical and economic factors impact health care delivery, so understanding the comparative thrombotic effects of PCCs versus a specific reversal agent is essential to provide evidence-based clinical decision making to optimise patient.

Methods

A retrospective observational analysis was conducted, including all patients across Belfast Health and Social Care (BHSCT) who received PCC in the setting of acute haemorrhage while taking an OAC between 2015 and 2021. Administrative approvals and permissions were obtained prior to data retrieval from BHSCT Blood Bank. All patient data were anonymised and collated by two trained medical doctors and subsequently analysed by a third trained medical doctor. A standardised approach was agreed prior to data collection and analysis to ensure validity and reproducibility.

Inclusion criteria specified patients who received PCC specifically for the reversal of an anticoagulant in the setting of an acute haemorrhage. Patients were excluded if PCC was administered in the absence of anticoagulant therapy. For eligible cases, demographic information, anticoagulant type, clinical indication, bleeding site, and severity of bleeding were recorded. Severity of bleeding was classified according to the definitions established by the Standardisation Committee of the International Society on Thrombosis and Haemostasis as fatal; non-fatal bleeding in a critical area; fall in Hb >20g/l; or non-severe bleeding [12].

Clinical outcomes included the incidence and classification of thrombotic events, all-cause mortality at 30 and 90 days and re-initiation of anticoagulant therapy.

Results

A total of 1166 prescriptions for PCC were recorded across BHSCT by the Blood Bank between 2015 and 2021. We excluded prescriptions for patients not actively taking OAC, patients not acutely bleeding and duplicate prescriptions for the same patient for the same haemorrhagic event. This resulted in a total of 682 eligible patients with 393 on warfarin and 289 on an alternative anticoagulant – apixaban (n= 221), rivaroxaban (n= 55) and edoxaban (n= 13).

The DOAC groups were largely comparable with regards to age. The edoxaban group, though small, had more females compared to the other groups (Table 1).

Atrial fibrillation was the main indication across all groups, with warfarin having a higher percentage of other indications, for example metallic cardiac valve replacement. The groups were largely similar with respect to comorbidities (Table 2).

Intracranial haemorrhage was the most common site of bleeding requiring reversal for all oral anticoagulants, especially the apixaban group (64%) and edoxaban group (69%). Gastrointestinal bleeding was the second most common area with other areas including genitourinary bleeding (Table 3).

The highest proportion of fatal bleeding occurred in the edoxaban (31%) group, however it is important to note the smaller number in this group (Figure 2). The lowest proportion of fatal bleeding requiring reversal occurred in the warfarin group (17%). Non-fatal bleeding in a critical area was the most common group overall (Table 4).

The thrombotic event rate was 5% for the warfarin group, 13% for rivaroxaban and 8% for apixaban, with overall DOAC thrombotic event rate at 8.7%. Using Fisher Test analysis there is a significant difference between the thrombotic rates (p= 0.0377), however this is an unpowered retrospective analysis. The 90-day mortality and number

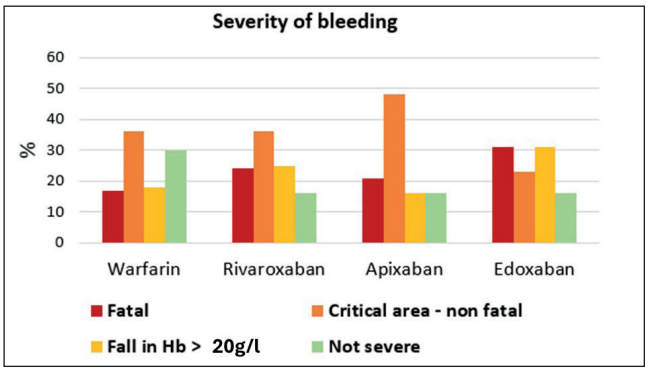

Figure 2: Percentage at each classification of severity for the bleed divided by each oral anticoagulant.

Table 1: Basic demographics of OAC groups.

	Warfarin	Rivaroxaban	Apixaban	Edoxaban
Number- no.	393	55	221	13
Age- years (SD)	76 (16)	81 (8)	80 (9)	81 (7)
Male sex- no. (%)	175 (45)	27 (49)	119 (54)	5 (38)

Table 2: Primary indication for OAC and past medical history of patients.

	Warfarin	F Xa Inhibitor
Total- no.	393	289
Primary indication for anticoagulation		
Atrial fibrillation - no. (%)	288 (73)	251 (85)
Venous thromboembolisation- short term- no. (%)	9 (2)	15 (5)
Venous thromboembolisation- long term- no. (%)	55 (14)	17 (6)
Other- no. (%)	41 (10)	13 (4)
Medical history		
Myocardial infarction- no. (%)	52 (13)	37 (12)
Cerebrovascular accident - no. (%)	64 (16)	43 (15)
Deep venous thrombosis- no. (%)	33 (8)	20 (7)
Pulmonary embolism- no. (%)	31 (8)	12 (4)
Diabetes mellitus- no. (%)	60 (15)	58 (20)
Atrial fibrillation - no. (%)	288 (73)	251 (85)
Heart failure- no. (%)	64 (16)	36 (12)

*Note some patient shave multiple indications and comorbidities.

Table 3: Site of bleeding at time of presentation requiring reversal with PCC.

	Warfarin	Rivaroxaban	Apixaban	Edoxaban
Gastrointestinal no. (%)	66 (17)	15 (27)	38 (17)	4 (31)
Intracranial no. (%)	191 (49)	26 (47)	141 (64)	9 (69)
Genitourinary no. (%)	18 (5)	0	3 (1)	0
Other no. (%)	118 (30)	14 (26)	39 (18)	0

Table 4: Severity of bleeding for patients at time of presentation requiring reversal with PCC.

	Warfarin	Rivaroxaban	Apixaban	Edoxaban
Fatal- no. (%)	65 (17)	13 (24)	47 (21)	4 (31)
Critical area- non fatal- no. (%)	142 (36)	20 (36)	105 (48)	3 (23)
Fall in Hb > 20g/l- no. (%)	69 (18)	14 (25)	35 (16)	4 (31)
Not severe- no. (%)	117 (30)	8 (16)	34 (16)	2 (16)

Table 5: Thrombotic events and mortality

	Warfarin	Rivaroxaban	Apixaban	Edoxaban
Thrombotic event; within 30 days- no. (%)	18 (5)	7 (13)	18 (8)	0
Total thrombotic event within 30 days- no. (%)	18 (5)*	25(8.7%)*		
Death within 30 days- no. (%)	53 (13)	9 (16)	47 (21)	3 (23)
Death within 90 days- no. (%)	82 (21)	13 (24)	55 (25)	5 (38)
Restart of anticoagulation- no. (%)	110 (29)	26 (47)	84 (38)	5 (38)

*Using FET p= 0.0377 difference between thrombotic rate (unpowered retrospective analysis)

Table 6: Thrombotic events

Type of thrombotic event	Warfarin	Rivaroxaban	Apixaban	Edoxaban
Myocardial infarction- no.	4	0	1	0
Pulmonary embolism- no.	4	2	3	0
Thrombotic stroke- no.	5	4	7	0
Deep venous thrombosis- no.	1	0	0	0
Ischaemic bowel- no.	2	0	5	0
Hepatic vein thrombosis- no.	1	0	0	0
Other- no.	1	1	2	0

restarting anticoagulant post event was largely comparable between the DOAC groups (Table 5).

The most common thrombotic event was ischaemic stroke (16 events), followed by pulmonary embolism (9 events) then ischaemic bowel (7 events) (Table 6).

Discussion

The introduction of drug-specific reversal agents for DOACs was anticipated to represent a major advance in the management of anticoagulant associated acute haemorrhage. Their clinical uptake, however, has been constrained by concerns regarding post treatment thrombotic risk and substantial economic burden. In this six-year retrospective observational study, 682 patients presenting with OAC related acute haemorrhage and managed with PCC were evaluated, yielding several potentially clinically important observations.

The incidence of thrombotic events after PCC administration was 5% among warfarin treated patients, compared with higher rates in those receiving DOACs (13% for rivaroxaban and 8% for apixaban and 8.7% overall). Ninety-day mortality was high across all oral anticoagulant cohorts (21–38%), although broadly similar between groups. Intracranial haemorrhage constituted the predominant bleeding site, particularly among DOAC treated patients (47–69% across groups). Collectively, this study suggests that PCC provides a broadly applicable and clinically acceptable reversal strategy in the context of DOAC associated bleeding.

Thrombotic Risk: Comparison with Existing Literature

The observed thrombotic event rate of 8.7% across all DOAC patients treated with PCC aligns with previously reported rates. A recent meta-analysis by Chaudhary et al. examining DOAC reversal in intracranial haemorrhage reported thromboembolic rates of 8% for PCC, 14% for andexanet alfa, and 5% for idarucizumab [10]. Our findings of 8% for apixaban and 13% for rivaroxaban are consistent with these findings. Our rivaroxaban cohort demonstrates a higher rate compared to this analysis, however the overall number was low.

The lower thrombotic rate observed in the warfarin cohort (5%) likely reflects PCC's specific action as a targeted reversal agent for vitamin K antagonists. This contrasts with the non-specific mechanism when PCC is used for DOACs. PCC has been shown to have variable impact on reversal of Xa inhibitors in laboratory tests [13]. Several mechanisms may account for the elevated thrombotic risk in DOAC patients receiving PCC. First, the provision of excess clotting factors to overcome Xa inhibition creates a prothrombotic state. In the setting of warfarin, the PCC is replacing deficient factors, whereas in DOAC administration the PCC is providing excess amounts of additional factors [14].

Furthermore, the abrupt cessation of anticoagulation combined with procoagulant factor administration occurring in patients with pre-existing thrombotic risk factors needs to be considered. Also considering the pharmacokinetics and half-life of PCC, warfarin and DOACs, there will be variation in post treatment outcomes. This may all be further compounded by the low rate of anticoagulant reinstatement in this study.

Comparison with Specific Reversal Agents

The clinical guidelines have evolved substantially since the introduction of mechanism directed reversal agents. Idarucizumab achieves complete dabigatran reversal with a thrombotic complication rate of approximately 5-6%, while andexanet alfa demonstrates anticoagulation reversal rates of 75-82% with reported thromboembolic rates of 10-14%. [8,11]

When comparing our PCC data with specific reversal agents, several considerations emerge. First, the thrombotic risk profile of PCC for DOAC reversal (8.7% overall in our cohort) lies between that of idarucizumab (5%) and andexanet alfa (14%), though direct comparison is limited by differences in patient populations, bleeding severity, and study methodologies. Second, the mortality rates in our study (21-25% at 90 days for oral anticoagulants) are comparable to meta-analytic estimates for both PCC (26%) and andexanet alfa (24%) in intracranial haemorrhage. This possibly suggests that reversal strategy may have less impact on mortality than baseline patient characteristics, bleeding severity and impact of the bleed itself [9].

Mortality and Bleeding Severity

The 30-day mortality rates observed in this study (13-23% across OAC groups) reflect the life-threatening nature of anticoagulant associated haemorrhage. These rates are consistent with previous literature mortality in DOAC associated bleeding managed with PCC [10]. The highest mortality was observed in the edoxaban (23% at 30 days, 38% at 90 days) group, though this cohort is small and likely represent selection bias toward more critically ill patients.

Intracranial haemorrhage accounted for 47-69% of bleeding events across DOAC groups, substantially higher than the 49% observed in warfarin patients. This distribution has potential prognostic implications, as ICH carries mortality rates of 23-33% in anticoagulated patients [15]. The predominance of critical-area bleeding (36-48% across groups) and fatal bleeding (17-31%) underscores the severity of the patient population and the challenging clinical scenarios in which reversal decisions occur.

Resource and Health System Implications for Northern Ireland

This study provides crucial real-world evidence from BHSCT, where political, geographical and economic factors impact healthcare delivery. The continued reliance on PCC for DOAC reversal reflects the practical reality that specific reversal agents are not universally available or are restricted by cost and licensing considerations.

Current NICE guidance restricts andexanet alfa to gastrointestinal bleeding in patients on apixaban or rivaroxaban, yet our data demonstrate that 47-69% of

DOAC related bleeding requiring reversal was intracranial haemorrhage. This creates a significant treatment gap whereby the most common and severe bleeding presentation has no access to specific reversal therapy.

The health economic implications are substantial. PCC may be a more cost effective first line agent, given its comparable to andexanet alfa with respect to mortality data and thrombotic risk. Future health economic analyses should incorporate real world thrombotic rates, mortality outcomes, and quality-adjusted life years to inform formulary and clinical pathway decisions.

Clinical Implications and Decision-Making

The findings of this study have several potential implications for clinical practice. First, while reversal agents are available, mortality form the bleed itself remains high.

Secondly, clinicians should exercise heightened vigilance for thrombotic complications when reversing anticoagulation, particularly in patients with recent thromboembolic events or strong thrombotic indications.

Third, the differential thrombotic rates between warfarin (5%) and DOACs (8.7%) suggest that the safety profile of PCC varies substantially depending on the anticoagulant being reversed. This information should inform consent discussions and post-reversal monitoring protocols.

Finally, multidisciplinary decision-making regarding anticoagulation resumption after major bleeding should be standard practice. Our data suggest that anticoagulation is resumed in less than half of patients.

Strengths and Limitations

The principal strength of this study is its comprehensive population-based design capturing all PCC administrations across BHSCT over 6 years, providing robust real-world evidence free from the selection biases inherent in randomised trials. The large sample size (682 patients) and inclusion of multiple DOAC types enhances generalisability.

However, several limitations warrant acknowledgment. First, the retrospective observational design precludes definitive causal inference regarding the relationship between PCC administration and thrombotic events, hence results were largely descriptive of our cohort. Thrombotic events may reflect the underlying prothrombotic state of patients requiring anticoagulation rather than the reversal strategy.

Second, data on PCC dosing, timing of administration relative to bleeding onset, and haemostatic effectiveness were not uniformly available, precluding dose response analyses or assessment of reversal efficacy. Third, the classification of thrombotic events relied on clinical documentation, which may underestimate asymptomatic events or events occurring after hospital discharge. Fourth, the small sample sizes in the edoxaban (n=13) group limit the reliability of estimates for this cohort.

Conclusions

This large retrospective cohort study from BHSCT demonstrates that thrombotic event rates following PCC administration for DOAC associated bleeding (8.7% overall) are higher than those observed with warfarin reversal (5%) and lower than rates reported for andexanet alfa. The findings suggest that PCC may be as effective as specific antidotes for DOAC reversal. In the absence of universal access to specific reversal agents, PCC continues to serve an important role in managing life threatening anticoagulant associated haemorrhage. However, clinicians should maintain heightened awareness of thrombotic complications, particularly in patients receiving PCC for DOAC reversal, and should implement systematic approaches to anticoagulation resumption decision-making to optimise patient safety.

Key recommendations for clinical practice:

- Consider some form of anticoagulation resumption within 7-14 days for most patients after major bleeding, based on individualised assessment of thrombotic versus bleeding risk
- Maintain high clinical suspicion for thrombotic events in the 30 days following PCC administration for DOAC reversal.

Disclosures & Statements

Conflicts of interest

The authors have no financial or ethical conflicts of interest regarding the contents of this manuscript.

Author's contributions

All authors have made a substantial contribution, including data collection, analysis of data and compiling the paper. All authors have read and approved the manuscript

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Ulster Med J 2026;**95(1):**11-17

Clinical Paper

Investigating Iron Deficiency Anaemia in the Elderly

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ABSTRACT

Introduction: Iron deficiency anaemia (IDA) is often attributed to gastrointestinal (GI) blood loss and warrants thorough investigation. In elderly, endoscopy carries increased risk, especially in those with multiple comorbidities and poor functional status. This study aimed to evaluate the outcomes of elderly patients with IDA, identify underlying causes, and assess one-year mortality.

Methodology: Patients ≥75 years referred to gastroenterology for investigation of IDA were recruited. Demographics, comorbidities, antiplatelet/antithrombotic use, investigations performed, and one-year mortality were recorded.

Results: 92 patients were recruited. Mean patient age was 81.2 years (SD: +/- 4.02) with a female preponderance (70.7%). Mean Charlson Comorbidity Index (CCI) was 5.96 (SD +/- 1.93). Frailty precluded any investigation in 13% of patients. 26% underwent upper and lower GI assessment (14% had bidirectional endoscopy and 12% had oesophagogastroduodenoscopy (OGD) + computed tomography (CT) colonography). Malignancy was diagnosed in 6.5%. Overall, one-year mortality rate was 28% (CCI mean score: 6.7). Mortality was statistically significantly higher for patients living in care homes (p=0.03). Higher CCI was associated with increased risk of one-year mortality, and each additional CCI point increased odds of dying within one year by 40% (OR = 1.40, 95% CI: 1.10–1.79, p=0.007).

Conclusion: Elderly patients referred for investigation of IDA frequently have a high CCI score, making endoscopy a high-risk procedure. A high CCI score and living in a care home are independent risk factors for one-year mortality. Alternative strategies including trans-nasal endoscopy and CT colonography, should be considered as first-line tests to balance diagnostic yield, prognosis and procedural safety.

Keywords: elderly, iron deficiency anaemia, Charlson Comorbidity Index, CT colonography, mortality

Introduction

Iron deficiency is the most prevalent nutritional deficiency worldwide[1], typically resulting from a sustained imbalance in which iron loss exceeds dietary intake or absorption. It is particularly common amongst older adults and individuals with chronic conditions, often leading to anaemia and its associated complications, including reduced quality of life and shortened overall survival[1-3]. According to the World Health Organization (WHO) criteria, anaemia is defined as a haemoglobin (Hb) concentration below 13 g/dL in men and below 12 g/dL in women[1].

Current diagnostic guidelines, including those from the British Society of Gastroenterology (BSG), recommend excluding gastrointestinal (GI) and urinary sources of blood loss in the evaluation iron deficiency anaemia (IDA)[4]. The criteria to diagnose IDA vary in literature. However, a serum ferritin (SF) ≤45 µg/L is often used as a cut-off to trigger further investigations. Other blood tests, such as transferrin saturation (TSAT) and total iron-binding capacity (TIBC), may be used when anaemia of chronic disease is suspected[4].

Investigating IDA often necessitates invasive bidirectional endoscopy, which at times requires anaesthesia and thus carries an increased risk for older individuals, especially patients with a high Charlson Comorbidity Index (CCI) score. Clinical decision-making should be guided by careful patient selection and thorough assessment of the risk-benefit ratio, to minimise potential harm and avoid unnecessary use of healthcare resources[5].

The CCI is a validated clinical tool used to assess comorbidity and mortality. It has been shown to stratify outcomes effectively in elderly cohorts, by triaging acutely hospitalised elderly adults. A prospective cohort study supported the CCI as being a useful tool for early risk stratification in the elderly hospitalised population, with an age & sex-adjusted mortality risk at various time intervals such as one year and five years[6].

In the recent British Society of Gastroenterology & Association of Coloproctology of Great Britian and Ireland guidance on the management of colorectal polyps in patients with a limited life expectancy, the risk and role of undergoing colonoscopy and polypectomy depending on the CCI and risk of procedure, is outlined[7]. It provided estimates of significant complication (hospitalisation) risk per 1000 elderly patients. This included both the colonoscopy risk and the polypectomy-specific risk and varied from 10 if a <5mm polyp is removed, increased to 30 if on antithrombotic medication and if the polyp size was ≥20mm, the risk increased to 45 and further to 135 if on antithrombotic medication[7].

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Demographic	Category	Number of Patients (n)	Percentage %	Mean Age (+/- SD)
Gender	Male	27	29.3	80.7 (+/-3.8)
	Female	65	70.7	81.4 (+/- 4.12)
Residence	Care Home	22	23.9	81.9 (+/- 4.2)
	Own Home	70	76.1	80.9 (+/- 4.94)
Overall Mean Age	n/a	n/a	n/a	81.2 (+/-4.02)

Table 1: Patient demographics
n/a: not applicable

Studies classified elderly adults between the ages of 65 and 74 years as youngest-old, those between ages 75 and 84 years as middle-old, and those aged over 85 years as oldest-old[8]. A study demonstrated that patients aged 75 and older undergoing colonoscopy have a statistically significant risk of complications, including 30-day mortality, than those <75 years[9].

The aim of our study was to evaluate the outcome of patients, in middle and oldest-old elderly (≥75 years), who required admission to hospital and were diagnosed with IDA and referred for GI assessment.

Methodology

Patients ≥75 years referred to the Department of Gastroenterology for investigation of IDA between January 2021 and December 2023 were identified. All the patients were in-patients and referred from the Department of Internal Medicine.

IDA was defined as a haemoglobin level <13 g/dL in men and <12 g/dL in women, with a SF ≤45 µg/L. Data was retrieved through the hospital electronic medical records which include clinical notes, radiological, endoscopic and histological results.

Data collected included patient demographics, comorbidities, CCI, use of anticoagulants or antiplatelets and investigations performed. Patients with an eGFR <59mL/min/1.73m^2 were classified as having chronic kidney disease (CKD). Endoscopic and radiological findings were recorded. Additionally, any documented history of malignancy, overt bleeding or relevant procedures/surgery prior to IDA onset was noted. Place of residence, death, and cause of death were also documented.

Patient comorbidity was quantified using the CCI. The primary outcome was one-year mortality (alive = 0, deceased = 1). A binary logistic regression model was fitted to assess the association between CCI score and the risk of one-year mortality. Results are expressed as regression coefficient (β), odds ratio (OR) with 95% confidence intervals (CI), and associated p-values. Statistical significance was set at $p<0.05$. Model fit was evaluated using the likelihood ratio test. All analyses were conducted using Python (statsmodels v0.14).

This study was approved by the research committee, data protection officer and legal department of the hospital.

Results

A total of 92 patients met the inclusion criteria. The mean patient age was 81.2 years, (SD: +/- 4.02) with a female predominance (70.7%). The majority of patients (76.1%) resided in their own home. The demographic profile of the study population is shown in Table 1. Anticoagulants were used by 43.5% of patients. The majority of patients did not have any GI symptoms (76.1%). The rest complained of weight loss and loss of appetite (15.2%), while 8.7% had documented fresh rectal bleeding and/or melena.

Table 2 denotes the various medical comorbidities. A history of malignancy was present in 17.4% of patients (Table 3).

Approximately a third of patients (30%) had a history of surgical interventions, these being cardiothoracic procedures (29%), orthopaedic interventions (25%), general surgical procedures (18%), vascular procedures secondary to peripheral vascular disease (18%) and gynaecological interventions (total abdominal hysterectomy and oophorectomy: 14%). The remaining 29% included urological, otorhinolaryngeal and ophthalmic interventions. With regards to cardiothoracic procedures, coronary arterial bypass grafting was the most common intervention (87.5%) followed by mitral valve replacement (12.5%).

Figure 1 compares the diagnostic investigations performed in the assessment of IDA. Most of the patients (62%) underwent computed tomography thorax, abdomen and pelvis (CT TAP), 47% underwent oesophagogastroduodenoscopy (OGD), and 18% had a colonoscopy. A computed tomography colonography (CTC) was performed in 17% of cases. Bidirectional endoscopy (OGD and colonoscopy) was performed in 14% of patients while 12% underwent OGD and CTC. 13% of patients were deemed unfit for endoscopy and cross-sectional imaging due to frailty.

Almost half of the patient cohort that underwent CT TAP

Comorbidity	N	Percentage %
Hypertension	61	66.3
Congestive Heart Failure	45	48.9
Diabetes Mellitus	38	41.3
Atrial Fibrillation	28	30.4
Hyperlipidemia	25	27.2
Chronic Kidney Disease	20	21.7
Ischemic Heart Disease	18	19.6
History of Malignancy	16	17.4
Hypothyroidism	14	15.2
Aortic Stenosis	11	11.9
Asthma	8	8.7
Transient Ischemic Attack/Cerebrovascular Accident	6	6.5
Peripheral Vascular Disease	2	2.2
Chronic Obstructive Pulmonary Disease	2	2.2
Von Willebrand	1	1.1

Table 2: Underlying comorbidities of the patient cohort

Malignancy	N (total = 16)	Percentage %
Breast	5	31.3
Prostate	3	18.8
Bladder	1	6.3
Thyroid	1	6.3
Lung	1	6.3
Endometrial	1	6.3
Laryngeal	1	6.3
Hepatocellular carcinoma	1	6.3
Cholangiocarcinoma	1	6.3
Melanoma	1	6.3

Table 3: Primary tumour site among the study population

Cause of death	N (total = 25)	Percentage %
Metastatic disease	4	16
Congestive heart failure	17	68
Pneumonia	3	12
Urinary tract infection	1	4

Table 4: Causes of death in relation to one-year mortality of the study population

Charlson Comorbidity Index Score	N (Total =92)	Percentage %
3	6	6.5
4	16	17.4
5	21	22.8
6	18	19.6
7	12	13.0
8	11	12.0
≥ 9	8	8.7

Table 5: Distribution of Charlson Comorbidity Index score among the patient cohort

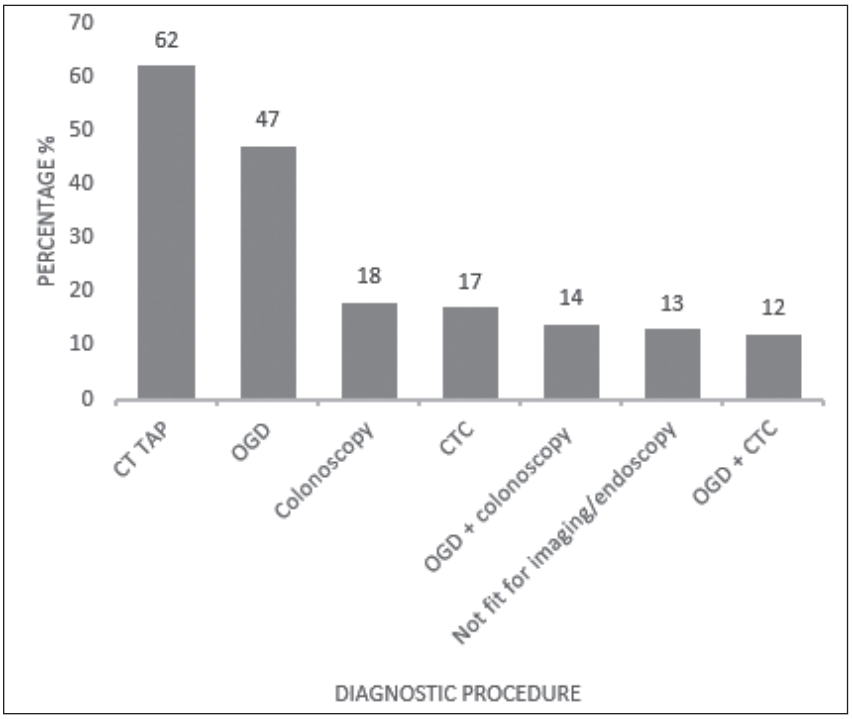

Figure 1: Bar chart comparing the different diagnostic procedures undertaken

(51%), did not have an OGD or colonoscopy to further evaluate the cause of their IDA due to frailty.

Malignancy was present in 6.5% of the referred patient cohort, all of which were colonic tumours. All malignancies were present on imaging.

Within the patient group who were diagnosed with malignancy, 33% had alarm symptoms, these being weight loss and rectal bleeding. Three patients underwent hemicolectomy with a curative intent; one underwent hemicolectomy as a palliative measure. The others had palliative management due to metastases.

Four of the patients with a diagnosed malignancy died within one year due to disease-related complications. There were no recorded urological malignancies as a cause of IDA in our patient cohort.

Charlson Comorbidty Index and One-Year Mortality

The one-year mortality rate of the referred cohort was 28%. The one-year mortality rate of patients without an underlying malignancy was 24%. The causes of death among the patient cohort are presented in Table 4.

The mean CCI of the patients referred was 5.96 (SD+/-1.93), whereas those who died within a year of referral had a mean score of 6.7. Table 5 outlines the CCI score across the patient cohort. The majority of patients (60%) were living in their own home. There was no significant difference in the CCI score between patients living in a care home (Mean CCI score = 6.43) and those living in their own home (Mean CCI score = 7) (p=0.83).

Statistical Analysis

There was no significant association between one-year mortality and the use of anticoagulants (chi-square, p=0.46) but this was statistically higher for patients living in a care home (chi-sqaure: p=0.03).

Logistic regression demonstrated that higher CCI scores were significantly associated with increased risk of one-year mortality. Each additional CCI point increased the odds of dying within one year by 40% (OR = 1.40, 95% CI: 1.10–1.79, p=0.007). Mortality risk was minimal at scores below 4 and increased sharply at scores above 8. The area under the ROC curve (AUC) was 0.69, indicating moderate discriminatory performance in CCI in predicting one-year mortality.

Though there was no statistically significant correlation between the investigations performed and CCI, the mean scores were highest in patients who did not have any investigations performed (mean 6.42; 95% CI ±1.05), followed by those who only had radiological tests (5.94; 95% CI ± 0.62) and the lowest mean score was in those patients who had any form of endoscopy (5.68; 95% CI ± 0.54).

Discussion

In this retrospective cohort study, we evaluated the diagnostic approach, identified underlying causes and assessed the one-year mortality of patients ≥ 75 years of age who were referred to the GI department for assessment of IDA. The proportion of malignancies diagnosed within our cohort (6.5%) is consistent with previously published literature, in which the reported prevalence of colorectal cancer (CRC) in symptomatic elderly individuals has ranged between 3.7% to 14.2% [10].

Notably, all malignancies were detected on cross-sectional imaging. These findings prompt a reconsideration of the diagnostic value of imaging modalities and raise questions about the need and risk for endoscopic evaluation, particularly in frail, elderly patients with a high CCI and increased risk for adverse events.

The role of CTC as an alternative to colonoscopy to detect CRC is supported by both the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) [11]. The accuracy for the detection of CRC and suspicious polyps has been proven to be similar to that of optical colonoscopy in both symptomatic and asymptomatic patients[11]. A meta-analysis demonstrated that CTC had a sensitivity of 96.1% in detecting CRC, with an interstudy heterogeneity of 0% [12,13].

Indeed, the BSG recommends taking into consideration the risks and benefits of endoscopy in the elderly cohort, especially those with multiple comorbidities and poor performance status[4]. Although anaemia affects more than 20% of those over the age of 85[4], there is a higher risk of cumulative adverse events as documented in a meta-analysis (3.49% risk in individuals >80 years (95% CI, 3.19-3.80%) vs 2.60% risk in individuals >65 years (95% CI, 2.50-2.70%), including GI bleeding and perforation[10,14].

A study demonstrated that the rate of adverse events in the very elderly was significantly higher compared to the younger group (6.3% vs. 1.1%; p<0.01). Independent risk factors of adverse events were very elderly patients (OR 3.30), inpatients (OR 3.22), and use of pethidine hydrochloride (OR 3.44)[15].

OGD is a high-yield procedure in symptomatic elderly patients, with no significant increase in adverse events when comparing to the younger population[16], but when considering colonoscopy, a meta-analysis demonstrated a mean completion rate of 84% in patients >65 years and 84.7% in patients > 80 years, with studies showing higher completion rates in younger individuals[10]. Most common factors amongst elderly leading to incomplete colonoscopy are inadequate bowel preparation and poor tolerance to sedation[10]. In our study, 13% of patients were deemed unfit for investigations due to frailty. Only 26% underwent both upper and lower GI assessment (14% had bidirectional endoscopy and 12%

had an OGD+CTC), which can be considered as complete GI assessment for IDA. The rest underwent a variety of tests, including CT TAP, which though important, is still not as accurate as the combination of the above tests.

Our study demonstrated that higher CCI scores were significantly associated with increased risk of one-year mortality. Each additional CCI point increased the odds of dying within one year by 40% (OR=1.40) with a sharp increase at scores above 8.

In this study cohort, congestive heart failure contributed to more than two thirds of one-year mortality. Metastatic disease was attributed to 16%, and the remaining was due to underlying infective processes resulting in sepsis. This shows that short-term mortality was driven by underlying comorbidities, mainly cardiovascular compromise, rather than occult GI pathology.

These findings are relevant when considering investigation of IDA in the elderly, as the potential benefit of identifying a curable GI cause must be weighed against underlying comorbidities contributing to a high CCI score and procedural risks, especially cardiovascular events. This is even more important when considering that the main cause for one-year mortality was related to cardiovascular events.

Nonetheless, metastatic disease as a cause of death in 16% of patients implies that malignancy remains a clinically important consideration, emphasising the need for an individualised decision-making approach rather than one standardised approach.

One-year mortality was significantly higher among patients residing in care homes compared with those living in their own homes (chi squared test, $p = 0.03$). This difference occurred despite no statistically significant difference in comorbidity burden as measured by the CCI between care home residents (mean CCI 6.43) and community-dwelling patients (mean CCI 7.00; $p = 0.83$).

This suggests that the CCI may inadequately capture important determinants of mortality in this population. Indeed, it does not account for obesity, functional status (including frailty and mobility), cognitive impairment (excluding dementia), or mental health disorders, all of which can adversely affect medication adherence and self-care. Several clinically relevant conditions not included in the CCI such as smoking, alcohol or substance use and poor nutritional status, may also contribute to increased mortality risk. Additionally, age is incorporated into the CCI as a simple linear increment (example +1 point per decade over 50 years), which may fail to reflect the nonlinear and condition-specific effects of aging on outcomes.

These results thus imply that residence in a care home is an important marker of mortality risk despite not being incorporated in conventional comorbidity indices, supporting the study's aim to identify factors associated with one-year mortality.

In our study there was no significant association between the use of anticoagulants and one year mortality ($p=0.46$). Antiplatelets and/or anticoagulants were prescribed in 43.5% of patients. These medications have been known to "unmask" underlying malignancy, resulting in earlier recognition of IDA[12]. Malignancy rates in patients on anticoagulation therapy have been reported to be equivalent to those not on such treatment, meaning that IDA should not be solely attributed to these medications without investigation[12].

Apart from GI pathology, IDA may be explained by other causes. Anemia in CKD is primarily a result of erythropoietin deficiency or iron deficiency and is considerably overlooked, especially in non-dialysis-dependent individuals[17]. In our cohort, 21.7% had CKD. The association of severe aortic stenosis and anaemia is multifactorial and may be due to concurrent antiplatelet and/or antithrombotic use and Heyde's syndrome[18]. This was present in 11.9% of our patients.

Limitations

The study's findings are limited by its retrospective design and reliance on medical records. However, considering the potential unfavorable outcomes in this group, patient documentation should have been thorough. More than half of patients referred were deemed unfit for endoscopy due to high CCI, which might have led to underdiagnosis of GI pathology. However, this is very often a realistic aspect in daily medical care and decision making. Instead, the majority of patients underwent imaging as the primary diagnostic modality as all malignancies were detected on imaging rather than endoscopy. Nutritional factors as a cause were also not assessed. These factors collectively highlight the challenges of evaluating IDA in the elderly, comorbid population. A proposed algorithm would be the combination of trans-nasal endoscopy using an ultraslim scope[19] and CTC, thus alleviating the need and risks associated with sedation. In patients with CKD, there is no need for intravenous contrast as the colon will still be adequately assessed.

Conclusion

This study highlights several important matters relating to frailty and complication risk and the need to investigate IDA as to determine the cause and thus be able to give a prognosis. Considering the findings of our study, especially the one-year mortality rate, there will always be those patients who cannot undergo bi-directional endoscopy safely. A high CCI score and living in a care home are independent risk factors. However, making use of the appropriate investigations immediately may enable the clinician to both manage the patient and provide a realistic prognosis.

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Abstracts

Winning Abstracts from the Ulster Society of Gastroenterology Biannual Research and Educational Meetings, 2024

The Ulster Society of Gastroenterology (USG) comprises a group of healthcare professionals from the fields of medicine, surgery, nursing and allied health. The aim of the USG is "To promote and maintain high standards of patient care, education, research and training in GI disease in Northern Ireland". The Society arranges biannual research and educational meetings in spring and autumn, and invites abstracts for presentation.

The prize winners are listed below, together with the winning abstracts.

Spring Meeting

C. McColgan & J. Addley	1st Place
L. McAleese, A. McConway & K.L. Diong	2nd Place

Autumn Meeting

C.M. Kumar & D. Mark	1st Place
S. McIlwaine, I. Mainie & P.S.J. Hall	2nd Place

Getting To The Gut Of The Problem - The Impact Of Dietetics In A Gastroenterology Ambulatory Hub

Mrs C. McColgan., Gastroenterology Dietitian
Co Author: Dr J Addley. Consultant, Department of Gastroenterology, Ulster Hospital, South Eastern Health & Social Care Trust, Belfast, Co. Antrim.

Introduction: Within the South Eastern Trust, speciality specific rapid access hubs were introduced to provide same day/same week specialty care. The Gastroenterology hub have access to a Dietitian as an essential component of the team, providing patients with immediate specialist nutritional advice as well as oral and enteral nutrition support.

Aim: Assess the impact of dietetic services within an ambulatory setting over 2 years.

Method: Dietetics offered a 5 day service parallel to the rapid access medical/nurse led clinics. Impact was assessed via quantitative and qualitative methods; patient feedback questionnaires and dietetic outcome measures to evaluate patient outcomes and service outcomes.

Results: In 2021/22 25-30% of all new referrals to the hub required dietetic input. Dietetics assessed; 221 new and 477 reviews in 2020/21. The following patient outcomes were achieved;
In 2021/22;

- 100% of patients required condition related diet advice.
- 63% required nutritional support.
- 70% required advice on bowel function.

In 2022/23 similar results to 2021/22 were found as well as;

- 75% of patients reported an improved ability to manage their diet.
- 94% of patient found a benefit from a multi-disciplinary (MDT) approach.

Overall 100% of users (n= 245) would recommend this service.

In addition between October 2021-Sept 2022; 6 enterally fed patients were in the hub which avoided admissions, saved 207 bed days and an estimated cost saving of £72,450.

Conclusions: These results demonstrate the value a Dietitian can add to a rapid access service as part of the MDT. This can in turn save bed days and associated costs.

Use of Fibroscan Results To Predict Liver Steatosis On Ultrasound

L.McAleese, A.McConway, KL.Diong
(Northern Health & Social Care Trust)
Queen's University Belfast

Introduction: A Fibroscan uses transient elastography to calculate the Liver Stiffness Measurement (LSM) score and fat content with the Controlled Attenuation Parameter (CAP) score.

Aim: The purpose of this study was to investigate the optimal CAP score on Fibroscan to predict the presence of steatosis on ultrasound and if LSM and CAP scores correlate.

Method: Data was collected on 168 patients who were identified from Fibroscan. Data including their CAP, LSM, Body Mass Index (BMI), and presence of diabetes, hypertension, liver cirrhosis and steatosis on ultrasound were recorded. After exclusions due to lack of data, 158 patients were analysed.

Results: There were 110 patients with steatosis and 48 without on ultrasound. Using the CAP of 238dB/m, correlating with Steatosis Grade 1 as a cut off, had a sensitivity of 80% and specificity of 50% for predicting steatosis. To achieve a higher sensitivity, we modified our score to 199dB/m with a sensitivity of 96.4% and specificity of 25% and successfully predicted ultrasound steatosis in 106 of 110 patients. LSM and CAP showed no correlation in all patients, however, when separated by presence of cirrhosis there was a positive correlation in patients with no cirrhosis and negative correlation in patients with cirrhosis, consistent in obese and diabetic subgroups.

Conclusions: The role of Fibroscan in steatosis is promising. Further investigation should assess its ability to track disease progression to cirrhosis using LSM and CAP correlation and the benefit of earlier intervention for patients with a CAP above the cut score prior to ultrasound.

Assessing the Efficacy of Lower GI Red Flag Referrals

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Introduction: The red flag referral system for lower gastrointestinal malignancies is currently under significant stress due to high volumes of referrals. Effective referral pathways are essential to reduce the burden on waiting lists.

Aim: To evaluate the efficacy of the current Red Flag referral pathway for Lower GI malignancies over a seven month period, assessing malignancy detection rates as a metric of efficacy of referrals.

Method: A retrospective review was conducted on 2,622 patients referred under the lower GI red flag pathway between December, 2023 and June, 2024. Following triage, 2,540 referrals proceeded to investigation. Confirmed cases of colorectal and anal cancers were recorded. Detection rates were calculated and compared to previous studies using chi-square tests for proportions, with a significance level set at $p < 0.05$.

Results: Seventy-eight cancers were diagnosed from 2,540 referrals—87 Lower GI Malignancies— resulting in a detection rate of 3.07%. This rate is significantly higher than the less than 1.5% reported in previous studies (chi-square = 25.89, $p < 0.0001$). Additionally, the high referral volume, averaging approximately 375 per month, indicates substantial pressure on the healthcare system, potentially due to inappropriate referrals.

Conclusions: The current red flag referral pathway demonstrates a significant improvement in the quality of red flag referrals for lower GI malignancies compared to previous reports, suggesting that the NICaN 2023 guidelines may be more effective compared to prior guidelines. Further analysis is required to optimize referral criteria, enhance the efficiency of the referral system, and ensure sustainable resource utilization.

Endoscopic Submucosal Dissection for Rectal Lesions: Initial Belfast Experience

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Belfast Health and Social Care Trust

Introduction: Endoscopic submucosal dissection (ESD) is well established internationally in the management of complex rectal polyps and early neoplasia. It offers superior en-bloc resection rates compared with endoscopic mucosal resection (EMR) but its uptake is limited by technical difficulty, training, service constraints and higher rate of complications.

Aim: To report on initial experience following introduction of an ESD service in Belfast.

Methods: Retrospective analysis of ESD database.

Results: 15 cases of rectal ESD were performed between 2020-2024 with annual progression of case numbers. Mean age was 70 (43-89). The mean size of lesion was 44mm (20-78mm). One case was performed under general anaesthesia, the remainder under light or no sedation. All lesions were completely removed endoscopically. En-bloc resection rate was 66%, whilst 33% of cases were completed using hybrid ESD/EMR. Risk factors for conversion to hybrid technique were age of patient and more advanced lesions, with conversion rates being higher in the initial cases. One patient was admitted for observation and had minor post-procedural bleeding, whilst all others were discharged on the same day with no other complications noted. 21% of lesions removed were shown to harbour high grade dysplasia, 71% low grade dysplasia and 7% adenocarcinoma. All available follow up scopes have shown no residual neoplasia.

Conclusions: ESD offers en-bloc resection for even large rectal lesions with low complication rates, same day discharge and without general anaesthesia. Training and mentorship, along with careful initial case selection is vital. ESD offers superior en-bloc resection compared to EMR, a less invasive approach than TAMIS, and should be an available option when deciding on management of complex rectal lesions.

Ulster Med J 2026;**95(1):**20-22

Opinion

The Ethics of Authorship

Lauren Venning[1], Emma Keelan[2]

In modern postgraduate medical training, academic authorship has evolved from a desirable addition to a 'must-have' credential. Somewhat concerningly, in several UK specialty training application processes, the strength of an academic CV now outweighs direct evidence of a doctor's clinical skills or knowledge. As a result, for resident doctors seeking to progress into specialty training, posters and publications have become the necessary currency for success.

While the development of academic writing and presentation skills offers genuine educational value, the current emphasis on publication accumulation "for points" has generated significant tensions. Residents may feel conflicted between rapidly producing low-impact outputs to satisfy application requirements and pursuing meaningful research that contributes substantively to medical knowledge. This pressure is further compounded by the financial burden of conference attendance and publication fees, often incurred at the expense of investment in essential clinical examinations. Such examinations not only enhance patient safety but also play a critical role in the development of competent future clinicians. Navigating the already complex and opaque landscape of medical authorship presents an additional challenge for resident doctors, a difficulty that has been further intensified by the rapid advancement of artificial intelligence (AI).

This commentary examines the prioritisation of academic competence within the medical specialty application process, focusing on three intersecting issues: (1) the privileging of publication quantity over academic quality and clinical competence; (2) the persistence of gift authorship and consultant pressure; and (3) the emerging ethical and practical challenges of AI-assisted authorship.

Publishing for Points

The current UK Physician Higher Specialty Training Recruitment (PHST) process allocates interview selection based on a self-assessed score across clinical, academic, and leadership domains. Overseen by the Royal College of Physicians through the Physician Specialty Recruitment Office (PSRO), this system is intended to standardise selection into Internal Medicine Training (IMT).

In practice, however, publication records exert a disproportionate influence on shortlisting. A first-authored original research paper in a peer-reviewed journal attracts the highest academic score, yet applicants may accrue equivalent (or greater) points through multiple case reports, abstracts, or letters. While such outputs have educational value, they may carry substantially less scientific weight than sustained academic training, such as higher research degrees or long-term projects.

The consequences of this system are twofold. First, resident doctors are acutely aware that without publications, progression may be unlikely regardless of clinical excellence, with many capable clinicians being excluded from interviews solely on the basis of portfolio scoring. Second, the structure actively incentivises a "publish for points" culture, in which scholarly activity becomes instrumental rather than intrinsically academic.

As Stehlik et al. observed in their analysis of mandatory research requirements in Australia and New Zealand, such systems can lead to "unintended consequences", including low-quality research or poorly planned and executed projects."[1] Time spent producing minimally contributory manuscripts detracts from clinical training and may expose trainees to superficial collaborations, poor academic practice, and ethical vulnerabilities, all in service of portfolio optimisation rather than scientific or clinical value.

What Constitutes Authorship?

The International Committee of Medical Journal Editors (ICMJE) defines authorship as requiring substantial contribution across four domains: conception or design of the work; acquisition, analysis, or interpretation of data; drafting or critically revising the manuscript; and final approval of the published version.[2] Authorship also entails accountability for all aspects of the work.

However, under pressure to secure first-author publications, resident doctors often encounter ethically problematic situations. These may include being expected to produce manuscripts primarily for senior colleagues, sometimes with limited supervision or educational benefit. Such demands add to workload strain and increase burnout risk, as trainees

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attempt to balance clinical duties, examinations, and academic output.

Medicine's hierarchical culture further complicates matters. Gift authorship, the inclusion of individuals who do not meet recognised authorship criteria, remains widespread despite being unethical.[3] A 2020 analysis found that 41% of Cochrane reviews contained gift authorship, even though the practice constitutes intellectual corruption.[3,4] Alarmingly, 15% of first authors were unaware of ICMJE authorship criteria, highlighting the lack of formal education in this area.[4]

Gift authorship commonly occurs in an "upward" direction, where junior doctors feel compelled to include senior clinicians due to perceived obligation, implicit pressure, or fear of repercussions. In some cases, trainees may deliberately include senior figures to lend credibility and improve publication prospects. Lateral gift authorship between peers and "gift-down" authorship from seniors to juniors may also occur, often to inflate publication counts. While the prevalence of 'lateral' authorship is difficult to quantify, the allocation of application points for roles such as joint first author, corresponding author, or co-author may inadvertently facilitate this form of honorary authorship. This structure risks normalising reciprocal arrangements among resident doctors, whereby collaborative authorship is pursued primarily for mutual portfolio benefit rather than genuine scholarly contribution.

Regardless of intent, such practices undermine transparency, accountability, and fairness. They breach publication ethics, contravene the General Medical Council's principles of honesty, and distort responsibility for the scientific record.[5,6] Most concerningly, they disadvantage those most vulnerable; typically women, international doctors, non-substantive/ locum staff and junior colleagues, who undertake the majority of the scholarly labour while bearing the greatest professional risk.

To be clear, clinical involvement in patient care alone does not justify authorship.[2] Similarly, supervision without substantive intellectual contribution does not meet ICMJE criteria. Addressing this requires explicit education on authorship ethics and visible leadership from consultants, including declining authorship when criteria are not met and resisting institutional pressures that equate academic worth with publication count.

AI and Authorship

The rise of artificial intelligence introduces a further challenge to authorship integrity within an already strained academic system. Tools such as ChatGPT and GPT-4 can generate ideas, draft manuscripts, restructure text, and summarise existing literature.[7] When used transparently, such tools may help level the playing field for time-pressured clinicians, non-native English speakers, and those with additional caring responsibilities. However, undisclosed AI use represents another form of authorship without accountability.[8]

Detection of AI-generated content remains challenging. Dunn et al. demonstrated that manuscripts produced by ChatGPT were largely indistinguishable from human-written text.[9] This has direct implications for fairness in trainee selection, as applicants who rely heavily on AI may gain an artificial advantage over peers who invest significant time and effort in genuine research and writing. While leading journals such as *Nature* and *JAMA* now mandate disclosure of AI use, many trainee-led or lower-tier journals lack clear policies, creating ethical inconsistency across the academic landscape.[10]

Undisclosed AI involvement also weakens accountability. Large language models may fabricate references or propagate inaccuracies, which can then enter the scientific record under human authorship.[10,11] Given that a substantial proportion of trainee publications are already low impact, with 59% failing to receive any citations, the risk of further diluting research quality is considerable.[12] As per the International Committee of Medical Journal Editors, AI cannot be listed as an author because it cannot assume responsibility or accountability.[2] The unresolved question, therefore, is not whether AI can be used, but the extent to which its use is acceptable and how transparently it should be acknowledged across all levels of medical publishing.

Potential Solutions

Education is central to addressing many of the issues outlined above; however, it must be accompanied by a cultural shift driven from the top down. Formal training in authorship ethics should be embedded within both undergraduate and postgraduate medical curricula. Early and repeated education on ICMJE authorship criteria, gift authorship, and academic accountability would better equip trainees to navigate authorship decisions with confidence and ethical awareness.

Crucially, such training must also extend to consultants and supervisors. Explicitly addressing gift authorship as an ethical issue reinforces shared responsibility for academic integrity and encourages those in positions of authority to model appropriate behaviour. This would help trainees to challenge inappropriate practices without fear of reprisal. Recognising and rewarding supervisors for high-quality mentorship rather than publication volume alone may further help shift the culture away from performative authorship towards meaningful scholarly engagement.

In addition, the routine use of written authorship agreements at the outset of projects, including posters and written submissions, should be normalised. Early clarification of roles, expectations, and authorship criteria can reduce misunderstandings, mitigate hierarchical pressure, and protect junior researchers. While such agreements cannot eliminate power imbalances entirely, they do provide a framework for transparency and accountability that is

currently absent from many trainee-led projects.

That being said, addressing the role of artificial intelligence in authorship presents a more complex challenge, largely due to the absence of comprehensive guidance. Although the ICMJE states that AI use should be documented and that chatbots cannot be listed as authors, there is currently no mechanism to regulate or define acceptable levels of AI involvement in academic work.[2] As such, it is imperative that selection bodies, journals, and training programmes develop unified standards for AI disclosure and responsible use. Education on the capabilities and limitations of AI tools, including the risks of fabrication, bias, and over-reliance, should form a core component of academic skills training at undergraduate and postgraduate level. Used transparently and ethically, AI has the potential to enhance scholarly communication; used covertly, it risks further eroding trust in academic outputs.

Conclusion

Authorship disputes are not new in medicine; however, the growing emphasis on publication metrics and the integration of artificial intelligence have intensified longstanding ethical challenges. Whether credit is granted to a consultant who did not meaningfully contribute, or derived from reliance on an algorithm incapable of assuming responsibility, the underlying issue remains the same: authorship without accountability.

These concerns underscore the need to re-evaluate specialty recruitment systems that prioritise academic outputs over demonstrated clinical competence. Trainees who wish to engage in research should be supported through protected time, appropriate supervision, and structured training, rather than incentivised to produce minimal publications for application points. A shift in emphasis from publication quantity to research quality and integrity is urgently required.

As Douglas G. Altman cautioned, "We need less research, better research, and research done for the right reasons."[13] Reaffirming this principle within postgraduate training is essential if authorship is to remain a meaningful marker of merit rather than a hollow credential.

Disclosures & Statements

- All authors were involved in the conceptualisation and drafting of the piece. Reflecting workload and contribution to the review of the existing literature, Dr Lauren Venning is listed as the primary author.

- The authors acknowledge the use of an AI language model (ChatGPT) to assist with phrasing and refinement of certain sections of the text for the purposes of clarity, spelling, and grammar. All sections were reviewed and edited to ensure accuracy and accountability. All ideas, interpretations, and conclusions are the authors' own.

No conflict of interest is declared.

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Ulster Med J 2026;**95(1):**23-25

Pitfalls In Practice

Avoiding Prescribing Pitfalls to Tackle Problematic Polypharmacy and Adverse Drug Reactions in Northern Ireland

P. Toner

Polypharmacy is an escalating epidemic in modern medicine, yet current systems and training often fail in assisting clinicians tackle the problem. Across the UK, more than 876,000 patients are prescribed ten or more medicines, with older and frail populations disproportionately exposed to potentially toxic combinations and preventable adverse drug reactions (ADRs)[1-2]. In Northern Ireland (NI), where a regional Medicines Optimisation Framework and NI Formulary are already established, the challenge is no longer a lack of tools but lack of knowledge of these resources to help guide prescribing[3].

Differentiating appropriate from problematic polypharmacy is essential. Appropriate polypharmacy involves evidencebased prescribing with clear indications, monitoring and regular review, such as initiating the multiple therapeutic pillars following a diagnosis of heart failure. In contrast, problematic polypharmacy occurs when medicines accumulate without clear rationale, interactions are missed and treatment regimens become overly complex. The consequences are considerable, ADRs account for around one in five hospital admissions, and those taking ten or more medicines are significantly more likely to experience a drugrelated admission than those on fewer drugs[1-2,4].

This article outlines common prescribing pitfalls relevant to NI and proposes practical steps for prescribers to embed safer prescribing and deprescribing into routine care.

Common prescribing pitfalls

When admitting patients, reviewing medicines or initiating new drugs, prescribers should be aware of the following potential pitfalls:

- Prescribing cascades
- Anticholinergic burden
- Inappropriate prescriptions
- Drug–drug and drug–disease interactions
- Inadequate patient counselling
- Lack of documented indication or timeframe
- Failure to monitor appropriately

Prescribing cascades

The prescribing cascade describes the events when an ADR is misinterpreted as a new medical condition resulting in another medicine prescribed, instead of reviewing the original drugs. Examples include prescribing diuretics for amlodipine induced ankle swelling, antitussives for ACE inhibitor cough or adding potassium supplements to loop diuretic induced hypokalaemia. When new symptoms appear, the default response should be to diagnose and exclude ADRs rather than look for additional medications to treat.

Anticholinergic burden

Anticholinergic burden is an important and modifiable concern. Medicines with anticholinergic properties include tricyclic antidepressants, antipsychotics, antihistamines and urinary antispasmodics. Cumulative burden, commonly quantified using the Anticholinergic Cognitive Burden (ACB) scale, is associated with cognitive decline, delirium, falls, fractures, constipation, urinary retention, prolonged hospital stay and increased mortality. These are all common presenting complaints to both the general practitioner and emergency department. An ACB score of three or more is clinically significant[5-7].

In older people, particularly those with frailty or cognitive impairment, lowering an anticholinergic burden from an ACB score of 3 or more is linked to fewer falls, better cognitive function, less constipation and quicker resolution of delirium. However, stopping these medicines abruptly can trigger cholinergic rebound symptoms, so a gradual reduction in dose (around 25% every two weeks with careful monitoring) is generally a safer approach[8]. Routine calculation and reduction of anticholinergic burden should become as normal as checking renal function before initiating an ACE or DOAC.

Inappropriate prescriptions

NI has the highest rate of antimicrobial prescribing in the UK, a trend which is unfortunately increasing.[9,10] Unnecessary antibiotic use for self-limiting infections or prolonged broad-spectrum therapy increases medication burden, drives antimicrobial resistance and exposes patients to preventable harms.[11,12] For prescribers, antimicrobial stewardship therefore needs to sit alongside medication review by enforcing Trust or society guidelines, using narrow spectrum when possible, document durations and review daily..

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Drug interactions

Drug–drug and drug–disease interactions remain a significant source of avoidable harm despite electronic prescribing and decision support. Examples include coprescribing oral anticoagulants and low molecular weight heparin on admission or using gentamicin in patients living with myasthenia gravis. Manual medication reviews are insufficient in identifying all clinically important interactions, so prescribers should use validated tools such as the BNF app (free to NHS staff)[13-14]. Particular caution needs to be considered with acute illness or change in health which often results in variation of the normal pharmacokinetics and pharmacodynamics.

Inadequate patient counselling

A significant proportion of longterm medicines are preventive in nature and offer no immediately noticeable benefit to the patient, like statins or antihypertensives, resulting in poor compliance. Non- adherence to hypertensive medications is often misinterpreted as treatment resistance, leading to unnecessary escalation of therapy. Prescribers should explain the indication, expected benefits and key side effects for each medicine, provide written information where appropriate and check understanding. This is particularly important when discussing deprescribing, where shared decision making and agreed monitoring plans support adherence and acceptance.

Lack of documented indication or timeframe

Medications frequently continue long after the original indication has resolved often accidently or due to automatic processes. Common examples include pain relief, antihistamines and sleeping tablets. Every prescription should include a specific indication, intended duration and monitoring requirements. Recording this information within electronic prescribing systems supports safer handover between primary and secondary care, and ultimately less problematic polypharmacy.

Failure to monitor appropriately

Prescribing without a clear monitoring plan is another common pitfall. Typical examples include ACEI/ARB therapy without renal function and potassium checks, flucloxacillin without liver function tests and diuretics or PPIs without periodic electrolyte review. For every prescription, clinicians should specify who will monitor, what parameters should be measured and at what intervals.

Using existing Northern Ireland tools

NI already has many of the components required for a systematic approach to deprescribing. The NI Formulary's deprescribing and polypharmacy guidance, together with PrescQIPP IMPACT tools, allows prescribers to identify highrisk cohorts (for example, age ≥75, ten or more medicines, recent falls or ACB ≥3) and to generate plans for medication reviews. In General Practice the PolyPrime pilot demonstrated that a relatively simple practicelevel intervention (education, recall clinics, weekly prioritisation meetings and a focus on highrisk medicine) can normalise polypharmacy review within routine chronic disease care[3, 13-17].

What NI prescribers can do differently

First, prioritise multi-disciplinary and structured medication reviews by incorporating tools such as STOPP/START and validated anticholinergic scales at every possible encounter.

Second, reframe conversations with patients. Public messaging in NI already challenges the expectation that all symptoms require a new medication or that all infections require antibiotics. In consultations, clinicians should explain the rationale for stopping as well as starting medicines and present deprescribing as a therapy.

Finally, strengthen prescribing education. A Northern Ireland specific educational focus on polypharmacy, prescribing cascades, anticholinergic burden and deprescribing could help embed safer habits early. Supervisors in hospital and primary care can reinforce this by modelling "start low and go slow then think stop" behaviour during ward rounds, clinics and medication reviews.

A practical call to action

Problematic polypharmacy is an inevitable consequence of population ageing but also reflects systems and culture, which can be changed. NI has already invested in frameworks, digital tools and pharmacist capacity. The next step is to use these assets appropriately so that deprescribing becomes a routine part of acute and primary care.

TAKE HOME MESSAGES

When you prescribe

- Document indication, duration and monitoring plan for every prescription
- Check for interactions or risks
- Before adding a new drug for a new symptom, consider whether this could represent an ADR or a prescribing cascade.

When you review

- Use a structured medication review template (NI deprescribing guidance, STOPP/START, and ACB).
- For each medication, consider: current indication, effectiveness, potential harm, patient suitability, and whether you would still start it today.

Useful resources

- NI Formulary (www.NIformulary.hscni.net)
- ACB Score- (www.acbcalc.com)
- STOPP/START (www.cgakit.com/stopp-start-v3)
- BNF (www.bnf.nice.org.uk)

DISCLOSURES & STATEMENTS

Philip Toner is Honorary Assistant Editor and Section Editor of the Ulster Medical Journal.

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Student Overseas Elective Reflections

Towards the end of their medical training, students at the Medical School, Queen's University Belfast are encouraged to undertake overseas medical electives, especially in areas of the world where experience of medical care may be very different from that in the United Kingdom. On return, they are invited to submit reflective essays on their experiences, and this essay has been chosen as the best submissions for the 2025 round of electives.

Beyond the Bones: Reflections on Paediatric Orthopaedics Past and Present: An Elective in The Royal Children's Hospital, Melbourne, Victoria, Australia.

Medha Sridhar Rao[1], Sandra Van Schaeybroeck[2]

To me, the term "Victorian child" once conjured images of frailty in Dickensian London, where most children lived amid soot and poverty and were employed in factories enduring long hours. Paediatric illnesses and disabilities were often hidden, stigmatised and misunderstood. Orthopaedic conditions such as talipes equinovarus, scoliosis and cerebral palsy invited societal prejudice, while osteogenesis imperfecta (OI) or developmental dysplasia of the hip could cause limb deformity, recurrent fractures, pain and disability. Its management would have been mostly non-surgical and specialist care was rare; many pillars of modern surgery like aseptic techniques, anaesthesia and microbial awareness were still in their infancy.

In contrast, paediatric orthopaedics in 2025 is an evolving specialty where the focus is on improving children's function and quality of life. However, the musculoskeletal diseases observed in paediatric orthopaedics and their management are still influenced by geographical factors (eg. location and its resources) and demographics across the world. During my 4 years undergraduate training in medicine, I developed a particular interest in orthopaedic surgery. Hence, for my medical elective, I decided to visit the Royal Children's Hospital (RCH), a leading paediatric tertiary centre in Victoria, Melbourne, with ongoing research areas in cerebral palsy and limb reconstruction. The elective exposed me to a breadth of complex conditions within paediatric orthopaedics and provided a valuable opportunity to compare experiences across settings, reflect on my contributions, and consider the specialty's role "beyond the bones."

Clinical scenarios:

Neuromuscular disorders: One memorable case during my time at the RCH was a 13-year-old boy with severe cerebral palsy and spasticity, not able to walk since birth. Despite previous custom orthoses, his feet remained in hyper-dorsiflexion, causing Achilles tendon pain and impaired bone development. He underwent bilateral gastrocnemius lengthening with botulinum toxin injections. I supported the team intra-operatively by holding the feet in position and retracting structures. This case deepened my understanding of calf anatomy and surgical approaches such as Strayer and Vulpius procedures, also called "gastrocnemius recession"[1]. More importantly, I reflected on how surgery aimed not at cure but at enabling comfort and participation in sport activities in school, which is a sharp contrast to the possible neglect of such a child in the nineteenth century.

Scoliosis: Scoliosis, both idiopathic and neuromuscular types, were common bone/joint conditions seen at the RCH. In one particularly complex case with cerebral palsy, the patient underwent correction of an S-shaped curve using a two-staged anterior-posterior fusion approach. In this approach, the 5th rib was removed to access the vertebrae from their anterior aspect and the laminae were removed from T4-T7. During the second stage of the procedure, the thoracic vertebrae were accessed using a posterior approach to perform spinal fusion. I assisted by passing instruments and retracting. Technology such as cell saver systems, neuro-monitoring and *Brain Lab* navigation[2] demonstrated the precision and safety of modern spinal surgery. From this, I recognised how multidisciplinary collaboration and innovation transform outcomes in cases that once carried huge morbidity and mortality rates. In the Victorian period, a child might have needed to wear harsh corsets for scoliosis. However, the present surgical technology and techniques have made it more likely that a child with severe scoliosis can undergo surgery to not only fix their spinal curvatures but also their posture, breathing, daily functioning and quality of life.

Limb reconstruction: Another striking experience for me was a child with OI who suffered a comminuted fracture of the tibia and who managed using an Ilizarov frame. The principle

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of distraction osteogenesis[3], the gradual manipulation of bone segments to stimulate growth, was demonstrated as I adjusted bolts and wires under supervision. The fragility of the limb required meticulous care from the whole team, and I felt trusted to contribute meaningfully. This case emphasized to me the balance between surgical ingenuity and careful handling in achieving long-term functional outcomes. Comparing contexts highlighted the influence of history, culture and geography on paediatric orthopaedics. In Victorian society, a child with cerebral palsy might have been hidden from view, a child with scoliosis labelled "deformed" and an infant with OI confined to a life of fractures and disability. Braces, splints or crude traction were often the only options, while social stigma limited opportunities for education or independence. By contrast, modern practice aims for inclusion, comfort and participation.

In my life, I have had the privilege of exploring three different healthcare systems across the world. The first one in a country with an emerging economy, India, and the two others in countries with established economies, the United Kingdom (UK) and Australia. During a rural health work experience camp in India, I encountered a child with rickets and genu varum. A multi-centre study in 2500 Indian children found that only 36.8% of subjects had sufficient vitamin D levels[4]: education of children and parents on aspects of nutrition and intake of calcium/vitamin D is a major focus in this healthcare system. In contrast, nutritional rickets is rare with incidences of 4.9 and 1.38 per 100,000 children in Australia and the UK respectively[5,6]. However, in these two countries paediatric orthopaedics has been affected by childhood obesity and this has become a major risk for increased incidence of fractures[7]. Therefore, approaches to improve a healthy diet and activity in children within these two healthcare settings has become a priority. Taken together, it is essential to tailor paediatric orthopaedics according to demographic and cultural needs[8].

My medical elective also emphasised the role of specialist centres such as RCH, which serve as providers of complex paediatric surgery but also deliver the next leaders who develop the national/international guidelines within paediatric orthopaedics (e.g. https://www.rch.org.au/clinicalguide/fractures). Compared with my previous experience in Belfast, where I had seen mainly trauma and fracture clinics, the RCH in Melbourne exposed me to subspeciality clinics in scoliosis, neuromuscular disorders and limb reconstruction. Personally, the elective encouraged me to reflect on my role as both learner and contributor. The magnitude of my learning was largely due to my immersion in the theatre sessions, clinics, treatment planning meetings and seminars (eg. seminar on paediatric knee conditions and surgeries). My practical contributions at the RCH theatres, including retracting, positioning and adjusting external fixator appliances, appeared relatively small but they made me feel like I was a part of the surgical team. Consequently, when arriving back in Belfast, I felt a personal responsibility to contribute more towards medical education to show what I had learned at the RCH. To accomplish this, I was able to translate my experiences back home by organising a *Stryker* scoliosis simulation workshop along with a *Synthes* fracture fixation simulation at the *QUB Scrubs Surgical Skills Conference* which was held on 29th March 2025 in Belfast, QUB. This provided Northern Irish medical students with exposure to rare complex procedures, echoing my own learning at the RCH and promoting practical surgical education taught by NI's leading orthopaedic surgeons and industry representatives. More broadly, the experience reshaped my understanding of paediatric orthopaedics as a discipline that extends beyond the bones. It requires sensitivity to children's growth, families' needs, and cultural perceptions of disability. It reminded me that surgery is not just about correcting deformities but about enabling lives.

Figure 1: the "12 Apostles" sea stacks on the Great Ocean Road, Victoria.

Figure 2: White Cockatoo at the Great Ocean Road, Victoria

In conclusion, my elective in Melbourne reframed my image of the "Victorian child." No longer frail and hidden, the children I met in modern state of Victoria, Australia were active, valued, and supported by highly specialised multidisciplinary teams whilst growing up amongst regional wildlife such as cockatoos, koalas and sceneries like the *Great Ocean Road* (Figures 1,2). Cases of cerebral palsy, scoliosis and OI showed me the technical demands and emotional dimensions of paediatric orthopaedics, while experiences in India and Belfast (UK) highlighted how geography and resources shape national clinical practice across the world. Ultimately, I learnt that paediatric orthopaedics is not solely about anatomical correction but about restoring function, independence and quality of life. The elective strengthened my commitment to surgery, taught me the importance of adaptability and cultural awareness, and showed me how reflections from the past can inform compassionate, adaptable care in the future.

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De Motu Cordis

Royal Victoria Hospital Annual Oration, 3rd October 2025

Pascal P McKeown*

Mr Chairman, distinguished guests, members of the Trust Board and Executive Team, students, colleagues, family and friends, I am delighted and humbled to be awarded the honour of delivering this year's Oration.

The tradition of the Oration dates to 1827, eight years before the founding of the Belfast medical school, when Dr James McDonnell delivered a welcome address to the new medical students at the Belfast Fever Hospital and General Dispensary.

So, this morning, I extend a particularly warm welcome to our medical and dental students.

My first attendance at an Oration was on the 4th October 1984, when Mr Derek Gordon was the Orator and his title was 'The Changing Face of Medicine'. During his presentation, Mr Gordon talked about the history of the Royal Victoria Hospital as well as his own speciality of neurosurgery.

As the orator is 'simply' invited to deliver a talk, I was initially faced with the dilemma: where does one start to build a story which may be of interest to the new medical and dental students as well as a wider audience?

I found some inspiration from the opening lines of Graham Greene's 1951 novel, The End of the Affair, where he had written:[1]

> *A story has no beginning or end: arbitrarily one chooses that moment of experience from which to look back or from which to look ahead.*

As such, having specialised in Cardiology, I have entitled this oration De Motu Cordis (On the Motion of the Heart), an abbreviation of the title of William Harvey's landmark book which was written in Latin and published in Germany in 1628.[2] However, for the purposes of this Oration, I have used a version in English, translated by Robert Willis, edited by Jarrett Carty, and published in 2016.[3]

Harvey's treatise was a radical publication, as it challenged the existing knowledge about the workings of the heart, as well as beliefs which had been in place for many centuries.

In this talk, I will look back at relevant scientific, historical, and cultural references to the heart over the past two millennia and will also look ahead to what the future may hold for healthcare. I may also take a few detours along the way.

Hippocrates, Aristotle, Galen and Avicenna

For many centuries, medical practice was greatly influenced by the writings of Hippocrates, Aristotle and Galen. Hippocrates (c. 460 – 370 BC) is credited with introducing the concept of the four humours, namely blood, phlegm, yellow bile and black bile. When the humours were balanced one had good health, whereas any imbalance resulted in disease (and that led to the development of treatments, such as bloodletting, to restore that balance). We still use the adjectives, sanguine, phlegmatic, choleric and melancholic to describe individual personality characteristics. As, at that time, human dissection was not permitted, Hippocrates believed that the heart was responsible for distributing 'pneuma' (variously translated as air or spirit) around the body.

Aristotle (c. 384 – 322 BC) promulgated the concept that the soul was located in the heart and he had a huge influence on the development of the humanities as well as Medicine.

Several centuries later, Galen (c. 129 – 216) challenged the Hippocratic perspective that the arteries contained only air. His view was that, having received the necessary nutrients from the gut, blood was made in the liver and then passed to the heart where it mixed with breath from the lungs. As he was unable to explain how the blood got from the right side to the left side of the heart, he postulated that there must be pores in the septum between the two ventricles, even though he had not identified them. Blood was then thought to simply 'ebb and flow' between the heart and the rest of the body.[4]

Almost a thousand years later, Ibn Sina (known in the West as Avicenna, c. 980 – 1037), one of the most important figures in the heritage of Islamic medicine, made significant contributions to the knowledge base around the function of the pulse but neither he nor Galen introduced any novel concepts around the circulation of blood.

St Thomas Aquinas

Of note, in 1273, St Thomas Aquinas (c. 1225 – 1274), who was greatly influenced by Aristotle, published a short text entitled De Motu Cordis, in which he discussed various themes about the motion of the heart, such as intrinsic principles, ebb and flow, heat, heavenly bodies, and emotions.[5] His publication opens with the words:

> *Since everything that is moved must have a mover, the problem arises: What moves the heart and exactly what kind of movement does it have?*

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He then writes:

Thus, the motion of the heart is a natural result of the soul….

And, several paragraphs later, he simply concludes:

And let this be enough said on the motion of the heart.

Leonardo da Vinci

In his many drawings, Leonardo da Vinci (1452 – 1519) beautifully illustrated the structure of the heart, including the valves and coronary arteries (Figure 1). Having studied

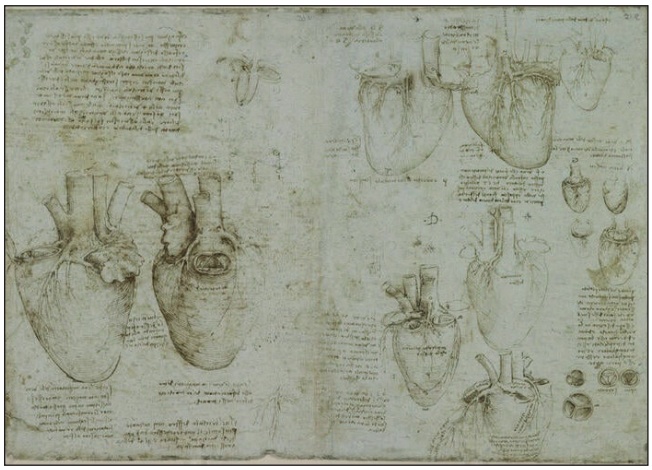

Figure 1: Leonardo da Vinci, Studies of the coronary vessels and valves of the heart © Royal Collection Enterprises Limited 2025 | Royal Collection Trust

the flow of water in rivers and canals, he then described the important effects of turbulent flow in relation to closure of the heart valves. However, following his death, and possibly because at that time he was not considered to be a scientist, many of his drawings lay undiscovered for several centuries.

William Harvey

And now I return to William Harvey (1578 – 1657, Figure 2): who was he and why is his work so important?

Figure 2: William Haravey, attributed to Daniel Mytens, oil on canvas, circa 1627, NPG 5115 © National Portrait Gallery, London. Licensed under CC-BY-NC-ND 3.0

He was born in Kent in 1578, and initially studied arts at Gonville and Caius College, Cambridge, at a time when the study of science alongside the humanities was much more integrated than it is today. Then, in 1600, he travelled to Italy to attend the medical school at the University of Padua, which was one of the pre-eminent medical schools of its day. One of his teachers was the famous anatomist Hieronymus Fabricius, who had commissioned the building of the Anatomical Theatre.

On his return to England, Harvey was elected a Fellow of the Royal College of Physicians in 1607, appointed as a physician to St Bartholomew's Hospital in 1609, and then in 1618 he obtained royal patronage, initially being appointed as physician to King James I until James's death in 1625, subsequently retaining this position with King Charles I.

In 1615, Harvey was appointed as the Lumleian Lecturer at the Royal College of Physicians, where he was required to give periodic lectures on anatomy. It was during this period that he undertook a significant amount of novel research and refined his theories on the circulation of blood.

In 1628, he published Exercitatio anatomica de motu cordis et sanguinis in animalibus (On the Motion of the Heart and Blood in Animals).[2] This book consists of an Introduction and 17 short chapters as well as a dedication to Dr Argent, the President of the Royal College and his colleagues. In addition, he includes a wonderful letter to King Charles I on pages 1 and 2:[3]

To the Most Illustrious and indomitable Prince Charles, King of Great Britain, France and Ireland, defender of the faith, most illustrious prince!

The heart of animals is the foundation of their life and the sovereign of everything within them; it is the sun of their microcosm, upon which all growth depends and from which all power proceeds.

Similarly, the king is the foundation of his kingdom, the sun of the world around him; he is the heart of the republic, the fountain from which all power and all grace flows.

I most humbly implore you, illustrious prince, to accept therefore, with your accustomed clemency, this my new treatise on the heart.

Indeed, I wonder if this type of approach would work well nowadays with modern journal editors.

There is clear evidence that Harvey undertook a lot of painstaking work before publishing his book. In Chapter 1 (pages 17-18),[3] he has written:

When I first turned my attention to... discovering the motions and function of the heart, and sought to discover these from actual inspection and not from the writings of others, I found the task so truly arduous, ... that I was

> *almost tempted to think ... that the motion of the heart was only to be comprehended by God.*
>
> *Finally, by using greater diligence and investigation every day, ... I thought that I had the truth that I had so much desired about the motion and function of the heart and arteries...*

Harvey was greatly influenced by the work of Fabricius, his teacher in Padua, who had clearly described the anatomical appearances of valves within the veins, although Fabricius had not delineated their exact function.

There are only four illustrations in Harvey's book (pages 73 and 74) and all of these are of arm veins, as Harvey needed to demonstrate visually the importance of those valves in controlling unidirectional flow in veins.

Then, in Chapter 14 (page 76), having summarised his observations and experiments, he writes:[3]

> *It is absolutely necessary to conclude that the blood in the animal body is impelled in a circle and is in a state of ceaseless motion.*

It is clear that Harvey had already experienced and was expecting to incur a lot of criticism of his work, as he was essentially challenging the conventional wisdom of his time. In Chapter 8 (page 47), Harvey notes:[3]

> *But what remains to be said about the quantity and source of this passing blood is of a character so novel and unheard of that I not only fear injury because of the envy of a few, but I fear that I could have all of mankind for my enemy, so much does habit and custom become a second nature.*

His concerns in this regard may provide, at least in part, a rationale for the letter to King Charles and the Dedication to the President of the Royal College at the start of his book, as he needed the support of the King and the President in the face of significant criticism of his work.

In his excellent book 'The Beating Heart' published in 2024,[6] Robin Choudhury, Professor of Cardiovascular Medicine at Oxford University, has provided a history of what he calls 'our most vital organ' and has written these comments about William Harvey (page 104):

> *his remarkable accomplishment was born from rigour, rational analysis and a willingness to take considerable professional risks in challenging the prevailing view.*

I will return to this theme later in the talk.

Of note, one of the missing pieces of the jigsaw for Harvey was that he did not elucidate how the blood travelled back to the veins from the arteries. It was only in 1661, just a few years after Harvey's death, that Marcello Malpighi, the Italian physician and founder of microscopical anatomy, identified capillaries as the missing link.

Laennec, Einthoven and Noble

In the 19th and 20th centuries, many additional advances occurred. For example, in the early 1800's, Rene Laennec invented the stethoscope and, using this new instrument, he investigated the sounds made by the heart and lungs. Then, in 1902, Willem Einthoven published a seminal paper on the development of the electrocardiogram.

At this point, in terms of a local context, it is interesting to review the following entry from Dr Robert Marshall's book Fifty Years on the Grosvenor Road.[7] Dr Marshall was one of the Royal Victoria Hospital's physicians and he records the following (pages 19 and 24):

> *In 1913 the new Electrocardiograph was installed and was naturally a source of great pride, not only to the Staff but to the Board of Management. In the Annual Report it states that "this instrument has already more than justified its purchase and promises to revolutionise the diagnosis and treatment of heart affections".*

He also notes with some pride:

> *Ours was one of the first "provincial" hospitals to have this valuable new instrument.*

In the earlier part of this talk, I had noted that William Harvey's work was subject to significant criticism, as he had challenged Galen's work. Whilst he had demonstrated the circular motion of blood, individuals such as Rene Descartes highlighted that he had not explained how and why the heart had a spontaneous rhythm. It was over three hundred years later, in the 1940's and 50's, that Alan Hodgkin and Andrew Huxley explored the origin of action potentials in the nervous system and, for their pioneering work using the squid giant axon, they were later awarded the Nobel prize in 1963. Inspired by their work, Denis Noble, who in 1960 was a young PhD student in London, managed to develop a computational model of the cardiac action potential, publishing a letter to Nature as a single author, and that revolutionised the field of cardiac electrophysiology.[8]

Cardiac Research in Belfast over the past Sixty Years

I would now like to provide a brief summary of cardiac research in Northern Ireland over the past sixty years. In 1987, when I first arrived on wards 5 / 6 on the old Main Corridor as a Senior House Officer in Cardiology, I was aware of the very significant research activity which had been undertaken by the Royal Victoria Hospital Cardiologists, in collaboration with the cardiac surgeons and cardiac anaesthetists. The pioneering work undertaken by Professor Pantridge and colleagues in the 1960's and 70's delineated the autonomic sequelae associated with myocardial infarction and led to the development of pre-hospital coronary care, alongside the development of portable defibrillators – all of this work had very significant national and global impact. In the 1980's, thrombolytic therapy for myocardial infarction

was in its infancy and many of the early clinical trials in thrombolytic therapy were led by Professor Adgey. At that same time Doctors Khan, Patterson and Webb pioneered interventional cardiology, initially with the introduction of balloon angioplasty and then coronary stents. Dr Campbell was instrumental in developing echocardiography and nuclear cardiology services. Likewise, Professor Alun Evans and other colleagues at Queen's University were involved in many population-based epidemiological studies on heart disease, such as the World Health Organisation's MONICA project. In recent years, my Cardiology colleagues have greatly expanded the range of coronary and structural interventions, alongside services for patients with heart failure, congenital heart disease, and cardio-oncology. Advances in cardiac electrophysiology and the introduction of implantable devices have significantly enhanced the care of patients with cardiac arrhythmias.

I would also like to explain how my personal interest in cardiac genetics was stimulated by a very memorable patient. It was in 1988 and I was the Senior House Officer on call. The young male patient had presented to the Emergency Department with chest pain and had a very abnormal ECG. Following admission, it became clear that the patient had not had a myocardial infarction, but had a condition called hypertrophic cardiomyopathy, which was thought then to be a rare condition, and I was asked to present the case at our weekly teaching meeting. Around that time, the first gene causing hypertrophic cardiomyopathy had been identified by teams working in Boston, London and Germany.[9,10] Having obtained funding support from Queen's University, the Alexander von Humboldt Foundation, and Dr Jack McCluggage, the Postgraduate Dean, I had the opportunity to spend two years gaining specific research and clinical experience with two of these authors, namely Professor Hans-Peter Vosberg in Bad Nauheim, Germany and Professor Bill McKenna in London, as they were spearheading research in this area.

On my return to Belfast, and working with clinicians and scientists in this hospital, Italy, Netherlands, Canada, and other centres in the UK, we managed to develop services for patients with inherited heart muscle and electrical disorders. I am delighted that the area of Inherited Cardiac Conditions has greatly expanded and, aligned with the best evidence and international guidelines, it is now supported by a wonderful multi-disciplinary team of adult and paediatric cardiologists, specialist nurses, clinical geneticists, cardiac physiologists, laboratory scientists and administrative staff. I am very grateful that many of these colleagues are in the audience today.

Cultural References and the Heart

Before I move on to the next part of my talk, I thought that it would be useful to consider how central the heart has been in relation to our language and cultural references. In ancient Egypt, the Book of the Dead was designed to guide a person to the afterlife, as the Egyptians believed that a final judgement took place during the 'weighing of the heart' ceremony - the heart was weighed against the goddess Maat's feather, and a determination was then made as to whether or not the life of the deceased was virtuous. In terms of a local context, the Takabuti Mummy resides in the Ulster Museum. It is thought that she died in Egypt ~660BC. Whilst I recognise that there are complex consent and ethical issues around retention of human remains in museums, recently published research does confirm that, whilst Takabuti's heart was initially removed, it was subsequently wrapped and returned to her body.[11]

There are many references to the heart in religious texts, including the Bible and the Quran. Examples include:

> *I will give you a new heart and put a new spirit in you; I will remove from you your heart of stone and give you a heart of flesh.* Ezekiel 36:26

> *They show that the requirements of the law are written on their hearts.* Romans 2.15

> *Then, after that, your hearts were hardened and became as stones or even worse in hardness.* Quran 2:74

Indeed, several English words are derived from cor – the Latin word for heart. These include the word 'record' which is derived from the Latin recordari (remembering). We still talk about learning by heart. Likewise, the word courage is derived from the French 'corage'.

In Rachel Clarke's amazing book 'The Story of a Heart' about a child receiving a heart transplant,[12] she states:

> *No other part of the human body comes close to matching the metaphorical richness of the human heart. Hearts sing, soar, race, burn, break, bleed, swell, hammer and melt.*

We are also familiar with many examples of the heart being used in art, literature, jewellery, advertising, emojis, and in the food we eat. Indeed, we know that every year, our shops are filled with similar heart-shaped merchandise for St Valentine's Day.

Takotsubo (Broken Heart) Syndrome

For centuries, people have talked about individuals dying of a broken heart and, in recent years, Takotsubo (or broken heart) syndrome has been described. It generally results from severe emotional or physical stress and is thought to result from a sudden increase in sympathetic nervous system-related activity in the heart, resulting in a marked reduction in LV contraction in a pattern which looks like a takotsubo, that is a Japanese octopus pot. Most people will recover fully from the condition, but a small number of individuals may die of a 'broken heart' during the acute attack.[13]

Cardiovascular Disease in Europe

However, despite all the advances which I have noted to-date, it is important to recognise that cardiovascular disease still remains the number one cause of death in Europe, accounting for almost 1.7 million of the 4.9 million deaths per year across the European Union. And it is the number one cause of death in women accounting for just under 40% of those deaths, a much higher number than those caused by all cancers. I anticipate that this information may come as a surprise to many in this audience. It is estimated that, each year, cardiovascular disease costs the European Union at least €282 billion.[14] Of note, in Budapest in December 2024, the 27 Ministers of Health in the European Union announced the development of a new European Cardiovascular Health Plan. This was largely driven by the work of the European Society of Cardiology Advocacy Committee, which was until recently co-chaired by Professor Donna Fitzsimons, who had previously worked in Belfast Trust and is currently one of my colleagues at Queen's University in the School of Nursing and Midwifery. [15]

Social Determinants of Health

In 1919, Dr Charles H Mayo, one of the founders of the Mayo Clinic, stated:[16]

> *It is a poor government that does not realize that the prolonged life, health and happiness of its people are its greatest asset.*

Unfortunately, in our society we still have very significant differences in life expectancy as well as quality of life depending on where one is born. This is evident in the NI Health Inequalities Annual Report, which was published a few weeks ago.[17] There is currently a 5 to 7-year difference in life expectancy depending on where one lives. For example, in the 2021-23 period, the mean life expectancy for men living in the most deprived areas was 74.5 years as compared to 81.8 years for men in the least deprived areas, for females it was 79.3 years as compared to 84.5 years. And, of particular concern, there has been no improvement in the last decade (Figure 3).

Professor Sir Michael Marmot, who is the Professor of Epidemiology and Public Health at University College London, has published widely on the epidemiology of heart disease and has also been one of the key global advocates highlighting the social determinants of health. There is indeed a link between Professor Marmot and William Harvey as Michael Marmot gave the Harveian Oration at the Royal College of Physicians in London in 2006. The Harveian Oration was established in 1656 by William Harvey, when he left a bequest to the College:

> *with an exhortation to the Fellows and Members to search and study out the secrets of Nature by way of experiment'.*[18]

Prof Marmot's talk was entitled 'Health in an unequal world'.[19] From his work with government agencies over many years we now have the Marmot Principles, which

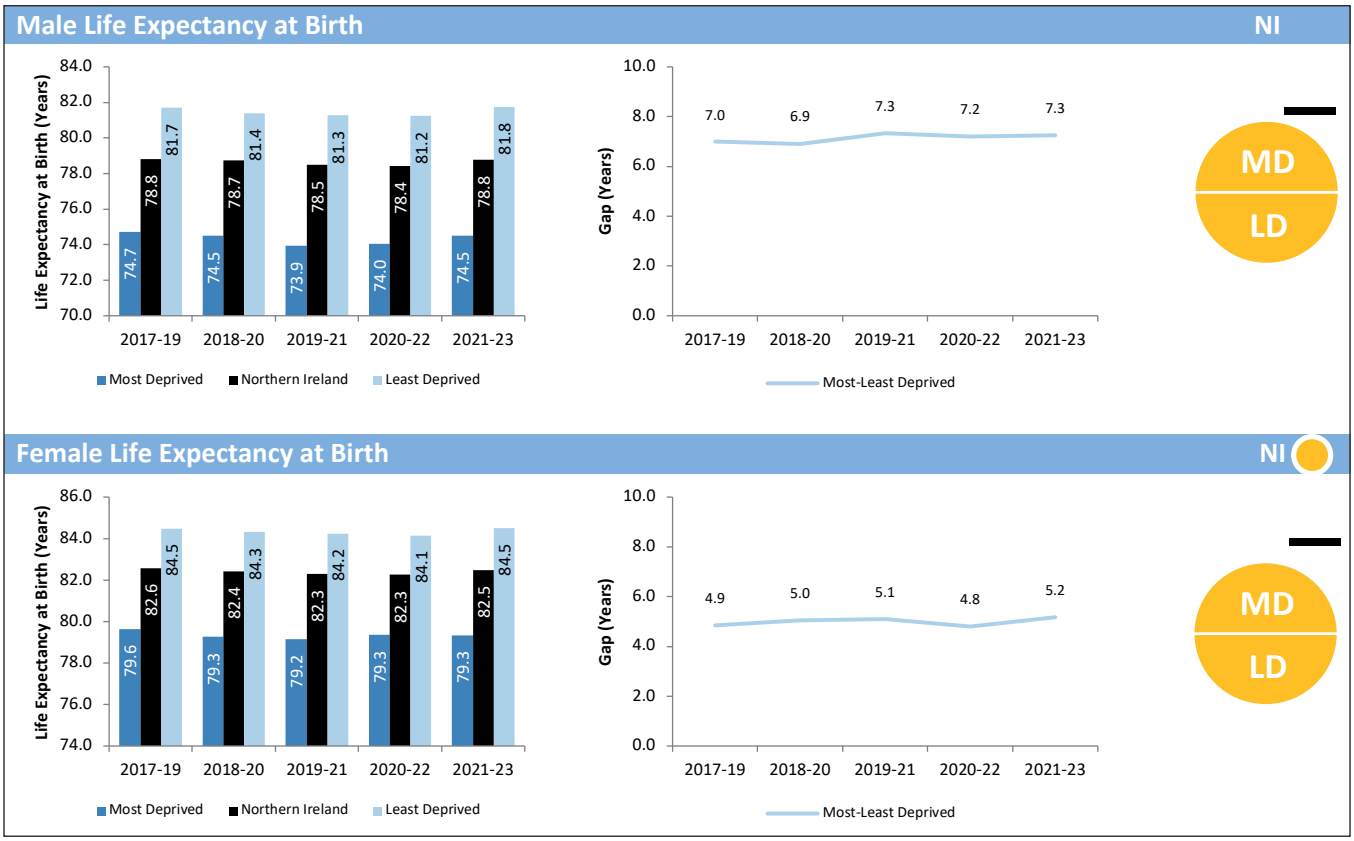

Figure 3: Male and Female Life Expectancy, courtesy of the Department of Health (Northern Ireland)

Figure 4: 'Millie', with the permission of Seosamh Mac Coille / extramuralactivity.com

help to direct and focus efforts to address these social determinants.[20]

For many years, I have walked between Queen's University and the Royal Victoria Hospital. I have been impressed by the images on the Donegall Road Railway bridge concerning the history of the Belfast linen mills and, in particular, by this poem, entitled Millie, by Eliza Hamilton (Figure 4).

> *I started work when I was eight, my childhood lost at the factory gate.*
> *The flight of shuttle, noise and dust, the wage of labour not good enough.*
> *My life was weaved outside my dreams, days always longer than they seemed.*
> *I vowed the day that I was wed, my child would have a childhood.*

Even though this describes life in Belfast over 130 years ago, it reminds us to reflect on the first of the Marmot principles, which is entitled 'Give every child the best start in life'. I am very aware that millions of children across the globe still do not have 'the best start in life'.

I am cognizant that it is virtually impossible not to be aware of the many negative and distressing messages on the media, such as global unrest and economic issues. There is much discussion about the challenges facing healthcare, including the significant workload and long waiting lists.

Personal Anecdote

I am now going to digress slightly – it is a personal anecdote. My parents kept all our old schoolbooks in the attic and we re-discovered these in the past couple of years. I thought that you may be interested in an extract from one of my primary 3 notebooks. I appreciate that you may not be able to read it on the screen, as it is written in pencil. The date is Tuesday 19 September 1967 (when I was 6 years old) and it is entitled: My News (Figure 5). There is a painting on the same page - well I exaggerate – it's not exactly a painting so you can see why I didn't pursue a career as an artist! As background context, John is my brother and I quote:

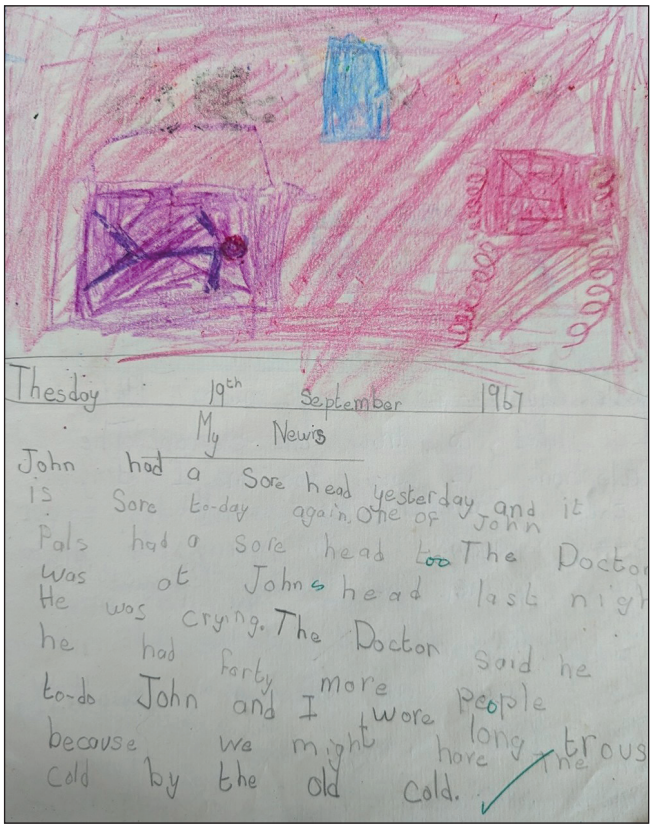

Figure 5: 'My News', courtesy of the author

John had a sore head yesterday and it is sore today again. One of John's pals had a sore head too. The doctor was at John's head last night. He was crying.

The syntax is not entirely clear here but I think that it was my brother and not the doctor who was crying. However, the most salient line for me is:

The doctor said that he had forty more people to do.

GPs in the 1960's often ran single-handed practices and were indeed very busy. However, I am pretty sure that our family GP used the old Lloyd George note system. It is likely that the entire note taking for this consultation with John was very brief and I speculate that it may have read something like: Complaining of Headache – nil on examination. No treatment needed.

Looking Ahead

In the opening lines of Graham Greene's novel,[1] which I mentioned at the start of my talk, he also refers to looking ahead. So, what will healthcare look like in the next few years? The Danish theoretical physicist, Neils Bohr, has stated:

Prediction is very difficult, especially if it's about the future.

Mark Twain has noted and I paraphrase–

plan for the future because that's where you're going to spend the rest of your life.

What will the healthcare ecosystem look like in the coming years? How do we best educate our students and trainees as well as our current workforce to work in multidisciplinary teams?

In 2019, Professor Eric Topol was commissioned to undertake a piece of work for the Department of Health in England and he published a review entitled: Preparing the healthcare workforce to deliver the digital future.[21] Key themes identified by Professor Topol included Data Science, Artificial Intelligence, and Genomics.

In recent weeks, there has been a lot of media interest in trade discussions between the US and the UK which have highlighted significant investment in Artificial Intelligence. There are many potential roles for AI in Cardiology, including: ECG interpretation, Analysis of cardiac images, Recording of consultations, and Clinical decision support. Indeed, at the European Society of Cardiology's annual congress in Madrid in August 2025, the results of an AI trial were presented and the authors concluded that an AI-enabled stethoscope (which also records an ECG) can help doctors detect heart failure, valve disease and abnormal heart rhythms in just 15 seconds.[22]

And, just for clarification, I wish to confirm that I didn't use Artificial Intelligence to produce this talk!

Clinical Academia

What exciting opportunities are available for our medical and dental students as well as our dental trainees and resident doctors?

From my earlier description of Harvey's work, it is clear that Harvey was what we might call today a clinical academic, that is someone whose job includes significant contributions to research and education, alongside their clinical work. Indeed, Sir William Osler, in his Harveian Oration in 1906, stated that Harvey's work was the beginning of what we now call 'experimental medicine'.

However, we are currently facing real challenges, with very small numbers of clinical academics. Whilst there has been significant growth in the numbers of hospital consultants and general practitioners over the past decade, the number of clinical academics has remained very low (Figure 6).[23] As a clinical academic myself, I recognise that partnership with the health service is vital to ensure that research and education are truly embedded as core elements of the health service. Without this, how are we going to innovate, transform, discover new treatments, and reorganise health services?

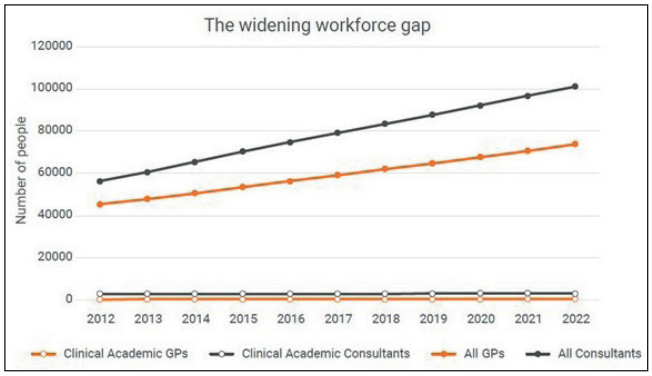

Figure 6: The Widening Workforce Gap, Medical Research Council. Licensed under a Creative Commons Attribution 4.0 International (CCBY 4.0) License Deed - Attribution 4.0 International - Creative Commons.

This is really important as we know that patients who are managed in research-active hospitals have better outcomes – not specifically because of any individual research project but because of the culture of enquiry which exists in those units, thereby driving better quality of care.

The NI Department of Health has recently published its Health and Social Care Reset Plan and it is particularly reassuring to note that 'exploiting opportunities for research' is listed as one of the seven priorities.[24]

There has also been significant investment of around £1billion in NI to deliver what are known as Regional City deals. In particular, I would like to highlight iREACH Health as part of the Belfast Region City Deal. This joint venture between Belfast Trust and the universities will open on the Lisburn Road site in 2027 and it has the potential to truly transform

clinical research but its success is predicated on collaborative working across the clinical / academic interface.

The environment in which we work is also critical. Dr Chris Turner's recent work entitled Civility Saves Lives reminds us of the importance of civility and kindness in optimising healthcare delivery.[25]

Sir Ken Robinson

A person I greatly admire is Sir Ken Robinson who has written extensively about education and has also created several amazing Technology, Entertainment, Design i.e. TED talks. Sir Ken states:

> *human life is inherently creative….. and one of the roles of education is to awaken and develop these powers of creativity.*

He also tells a story about Death Valley National Park in California.[26] Death Valley is one of the hottest and driest places in America. In the winter of 2004 it rained and, in the spring of 2005, the valley was carpeted in flowers. This phenomenon happens about once every decade. He notes:

> *Right beneath the surface are these seeds of possibility waiting for the right conditions to come about and …. if the conditions are right, life is inevitable.*
>
> *The real role of leadership…. is not …command and control. The real role of leadership is climate control, creating a climate of possibilities.*

I am delighted to note that, on Wednesday of this week, Jennifer Welsh commenced her role as Belfast Trust Chief Executive. Cognizant that she has an extremely busy diary, I am particularly delighted to see Jennifer at today's Oration. She returns to this hospital at a time of opportunity to make a huge difference and I note that, in her first message to all staff (personal communication), she has stated:

> *There is much work to do, but I am confident that we can do so together and with purpose, keeping our values at the heart of how we go about this.*

I am also delighted to note her metaphorical use of the heart in this statement to the staff.

When One Day Becomes Today

One of my favourite parts of the week is to read the humanities-related sections of the major journals. I recently read this personal report entitled 'When One Day Becomes Today' by Joseph Pettus, a US urologist who had been born with a bicuspid aortic valve and had recently needed an aortic valve replacement.[27] He describes his in-patient stay and I quote:

> *I am a surgeon, accustomed to being in control and accountable. I trained in an era that rewarded doctors who pushed through pain, sleep deprivation, hunger, and sickness... Thus, by the fifth day of being helpless, unable to care for myself, struggling to breathe without pain, …and answering asinine questions to suit a computer algorithm, I broke.*
>
> *I had my first full-blown panic attack. I showed my ugliest side: crying, lashing out, and raging against the medical-industrial complex.*
>
> *When the nurse came in the following morning, I apologized. She was not the one who had witnessed and endured my outburst. That nurse had gone home already, but my new nurse had gotten news of my meltdown during report…*
>
> *Her absolution was so kind, so unexpectedly humane; words fail to describe the lift it gave me.*

And he concludes:

> *In medicine, we physicians get so caught up trying to streamline care and optimize outcomes that it is easy to forget that our patients are human, and the hospital is a scary place where one's dignity is checked at the door. In the end, a person …. whose last name I am not sure I ever knew, made me feel that it was OK to be a fragile human and gave me a sip of humanity when I was most parched. She reminded me that patient care starts with caring for the patient.*

Concluding Remarks

So, cognizant that the main function of the Oration is as an address to the new students, I wish to say that you are very welcome to this amazing hospital. I came here for the first time 44 years ago and have really enjoyed spending the greater part of my working life here. It has been an absolute privilege to care for patients, work with inspirational colleagues, educate students, and undertake research in the Royal Victoria Hospital.

You have chosen to join the professions of Medicine and Dentistry where teamwork and excellent patient care is core. However, please remember that, following in the footsteps of William Harvey, it is very important for you to have an inquisitive mind, be curious and innovative, and challenge the *status quo*. You are all future healthcare leaders. So do get involved in teaching and research alongside your clinical studies.

At this stage, I would like to thank Professor Manoharan and Dr McKinley for inviting me to deliver this Oration and to Hanna Greer for her excellent administrative support. I wish to acknowledge the wonderful and enduring support, friendship and mentoring provided by my current and former colleagues in the hospital and University. I extend my sincere thanks to my wife, Julie, for her very constructive comments during my preparations for today's Oration. I am also very grateful to you all for attending.

So, in ending this Oration, I return to the writings of St Thomas Aquinas:[5]

And let this be enough said on the motion of the heart.

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History

Sir Benjamin William Rycroft: Reflections on Character and Career

Debra R. Milamed, M.S.[1], John Hedley-Whyte, M.D., FACP, FRCA[2]

SUMMARY

Ophthalmologist Sir Benjamin W. Rycroft was a key figure in John Hedley-Whyte's early education and experiences at the RAMC's 31st General Hospital, later Harvard's 5th General Hospital at Musgrave Park outside Belfast, 1940-1942. Rycroft later served with distinction in the Mediterranean Theatre and was honored with the O.B.E. After his return to the UK post-war, he advanced reconstructive treatment of burns, corneal grafting, and the establishment of tissue banks. He was a Fellow of the Zoological Society of London, gifted organist, enthusiastic gardener, and close associate of the Royal Family. In 1964, Rycroft returned to Belfast to give the Craig Memorial Lecture at Queen's University, Belfast, titled "Plastic Surgery and Ophthalmology".

Key Words: Keratoplasty, World War II, Eye banks

INTRODUCTION

We have previously recounted John Hedley-Whyte's boyhood acquaintance with Benjamin W. Rycroft while his father, Brigadier Angus Hedley-Whyte, FRCS was commanding officer of the RAMC's 31st General Hospital at Musgrave Park just outside Belfast during the years 1940-42[1]. Rycroft was not only the hospital's chief ophthalmologist, but introduced John Hedley-Whyte to the natural and physical sciences, and was godfather to his younger brother, Michael[2,3,4,5,6]. Rycroft emphasized to his wartime pupil the importance of overall physical fitness, in addition to a rigorous educational regimen.

EARLY LIFE AND EDUCATION

Benjamin William Rycroft was born on 16 August 1902 at Armley, a Yorkshire village west of Leeds famous for its woolen mill. His father, John Thomas Rycroft (1869-1955) and mother, Annie Elizabeth Hudson (1876-1960) were originally from the town of Bradford in Yorkshire. John Rycroft's occupation was listed as "cashier" and likely associated with banking[7]. The young Benjamin Rycroft attended St. Bartholomew's Church at Armley and became fascinated with its German-built organ which he learned to play with considerable skill, developing what became a lifelong avocation[3,7,8].

In 1919 Rycroft began his study of Medicine at St. Andrew's University. After graduation in 1924, he returned to Bradford, Yorkshire to begin General Practice. His interest then turned

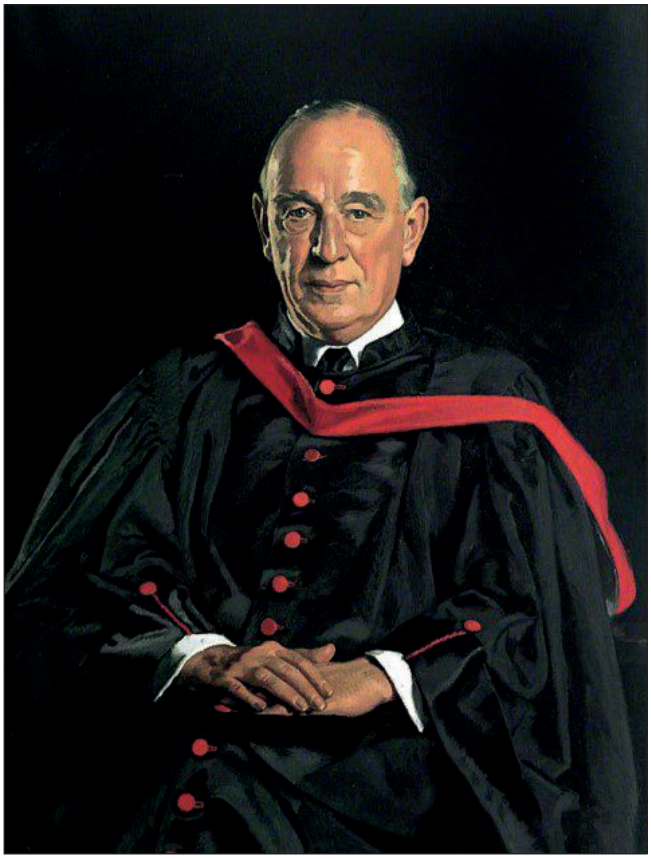

Fig. 1. Sir William Stewart Duke-Elder (1898-1978), GCVO, MD, DSc, FACS, FRCS, FRCP, FRS. Oil on canvas, 1965, 100.4 cm x 90.3 cm. no. LDUCU:E0039, by Edward Irvine Halliday (1902-1984). From the collection of the UCL Art Museum, University College, London and reproduced with their permission.

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to Ophthalmology, which he studied during the week at St. Bartholomew's, London, returning to his Bradford practice for the weekends[7,8,9,10].

In 1924, he married Mary Rhodes, who had been born in Allerton, adjacent to Bradford. Together they raised two sons, Peter and Rodney. After a course of study at Trinity College, Cambridge, Peter also trained in Ophthalmology at St. Bartholomew's Hospital and Moorfields[7,8].

By 1931 Rycroft had been elected to Fellowship in the Royal College of Surgeons. He moved to London after appointment at St. George's Hospital as a clinical assistant to Stewart Duke-Elder who had been knighted in 1933[7,11]. Duke-Elder may have been previously acquainted with Rycroft as a St. Andrew's alumnus, and was in all ways an outstanding mentor[7,11](Fig. 1). Rycroft's hard work and exemplary character led to his Hunterian Professorship and Leverhulme Scholarship of the Royal College of Surgeons, as well as his being named a Lang Research Scholar at Moorfields and Middlemore Prizeman of the British Medical Association[9]. Toward the close of the decade his hospital appointments included the Maidenhead Hospital, King George's Hospital, Ilford, The East Ham Memorial Hospital and London's Royal Eye Hospital[9,10].

CORNEAL GRAFTS

By the 1880s anaesthetics and improved infection control had enabled improved technical accuracy in ophthalmic surgery[12]. Arthur von Hippel's work at Heidelberg formed the basis of corneal grafting[12, 13,14]. The first human-to-human corneal transplant had been accomplished by Austrian Ophthalmologist Eduard Zirm in 1905[7]. Tudor Thomas had pioneered the procedure in England in 1930[15,16,17,18,19](Fig. 2). Rycroft wrote of the variations in both the shape of the grafts and the grafting technique[14]. In 1935 Rycroft described a successful graft performed on a 48-year-old female patient at the Royal Eye Hospital, London with a diagnosis of tuberculous keratitis. A donor eye had become available from a young man with an injury that irretrievably damaged the posterior half of the eye but left the cornea intact. Rycroft attributed the successful outcome of this case to the use of a complete conjunctival flap and constant irrigation with saline[14,20]. Rycroft's growing interest and expertise in this procedure, as well as his recognition of the shortage of donor eye tissue, were to play an important role over the course of his career[7].

THE ZOOLOGICAL SOCIETY OF LONDON

In 1939, Rycroft was granted Fellowship of the Zoological Society of London[21], after proposal by Tropical Diseases Consultant and Zoologist Sir Philip Manson-Bahr, a member of the Zoological Society's Council[22]. Rycroft's Fellowship was seconded by another 1939 Fellow, plastic surgeon Archibald H. McIndoe, later knighted, who was a colleague of Manson-Bahr at the London School of Hygiene and Tropical Medicine[23,24,25]. Manson-Bahr had also proposed

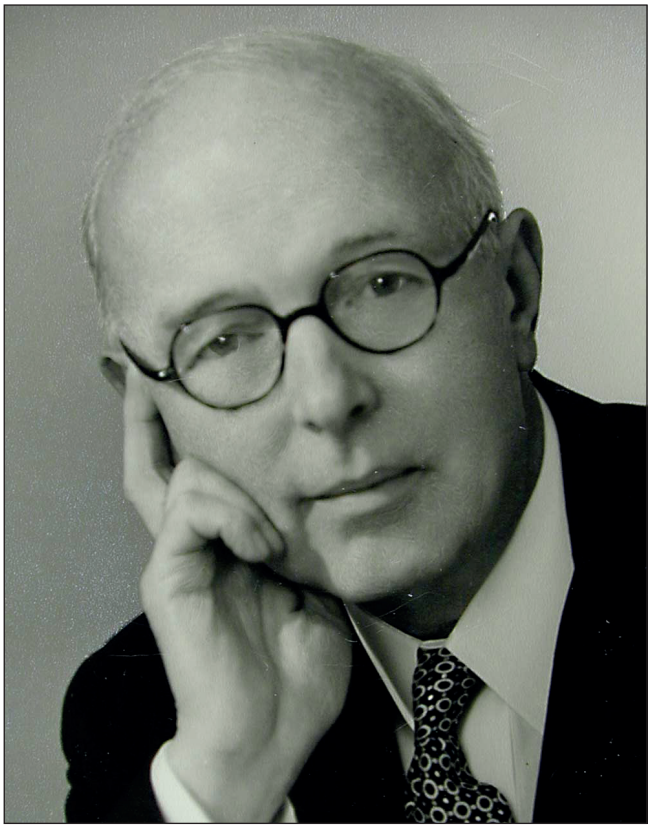

Fig.2. Sir James William Tudor Thomas (1893-1976). Photograph by Max Clifford, ca. 1966. Tudor Thomas was president of the Ophthalmological Society of the United Kingdom 1966-68. From the collection of the Royal College of Ophthalmologists and reproduced with their permission.

McIndoe's Fellowship. Then secretary of the Zoological Society, Julian Huxley, FRS countersigned both Rycroft's and McIndoe's Certificates of Fellowship[25]. After World War II, McIndoe recruited Rycroft to join him at the Queen Victoria Hospital in East Grinstead, Sussex to advance treatment of corneal injuries[7,8,9,10,26]. Rycroft was appointed Honorary Ophthalmologist by the Zoological Society on 20 June 1951[27] and continued to serve as veterinary surgeon and ophthalmologist until his retirement[7,27,28].

WORLD WAR II SERVICE

Rycroft joined the RAMC at the onset of World War II in 1939[7,8,9,10]. As previously noted, he served first in Northern Ireland, at the RAMC's 31st General Hospital[1,2,3,4,5,6]. In July 1940, Colonel Angus Hedley-Whyte arrived to serve as this hospital's commanding officer[29]. Rycroft addressed the importance of testing the night vision of military personnel with a specially-designed apparatus supplied by Brigadier Sir Stewart Duke-Elder, Consulting Ophthalmic Surgeon to the Army[11,30].

After the handover of the 31st General Hospital to the Americans in the Spring of 1942, Rycroft was assigned to the Mediterranean Theatre, serving in North Africa and Sicily. En route to Africa he survived an aerial torpedo attack on his

hospital ship, *HMS Windsor Castle*. He was rescued by the destroyer *Eggesford,* after hours in the water[7,8]. John Hedley-Whyte attributes Rycroft's survival to the very athleticism, swimming ability and stamina he had encouraged in his young pupil at Musgrave Park.

By the Autumn of 1942 the Allied Armies had advanced on North Africa. The general medical plan was to have an ophthalmologist on the staff of each general military hospital with 600 or more beds. Rycroft outlined the administration of the North African Campaign as divided into (1) the First Army Area, (2) the Lines of Communication Area, and (3) the Base Area. The First Army, or forward area (1) held field ambulances, casualty clearing stations, and small and medium general hospitals which were served by approximately three ophthalmologists. These medical units were intended to provide immediate care and prompt evacuation of casualties. The Lines of Communication Area (2) covered territory from the eastern Algerian Frontier to Algiers on the coast, with large hospitals at key ports and railway centers, each with an ophthalmologist. The largest general hospitals, some with over 2,000 beds were located within the Base Area (3). Evacuation of patients to the UK was organized from the Base Area hospitals, directed by Major-General Sir Ernest Cowell, K.B.E. Brigadier John Weddell, C.B.E. arranged for all surgical cases including ophthalmological patients. The stores and supplies for the campaign were centrally located in Algiers[31].

The need for more mobile ophthalmologic units in the First Army forward area was recognized by Major E.C. Zorab, R.A.M.C. who organized a mobile unit to address emergency care and immediate provision and repair of eyeglasses[32]. The contribution of Major Zorab's unit was recognized in dispatches. By the time of the fall of Tunis in May 1943, Field Optical Sections had been established in the forward, communications and base areas and the availability of special ophthalmic supplies such as slit-lamps had much improved[31].

Rycroft reported that in addition to the expected ophthalmologic diseases and injuries of military and civilian practice, he and his colleagues addressed conditions specific to North Africa: ocular myiasis, follicular conjunctivitis, *ophthalmia nodosa* due to implantation of cactus barbs in the conjunctiva, trachoma and dendritic keratitis resulting from high fever[31].

The majority of ocular injuries in North Africa resulted from mortar and shell fragments. Rycroft wrote of the importance of magnets application in the removal of magnetizable particles from the eye[31,33]. A shortage of hand electromagnets in Tunisia provided an impetus for Captain Livingstone R.A.M.C. to develop an electro-magnet from scraps retrieved from a Sherman tank and a Daimler. The Royal Electrical and Mechanical Engineers (R.E.M.E.) and their technicians assisted with construction of giant magnet stands, magnets, Perspex globes, electric eye warmers and other equipment. Rycroft also described the development of anti-mine visors made of Perspex. While sulphanilamide powder was the standard anti-infective, the use of penicillin was investigated[3,31,34].

The North African Campaign had prepared R.A.M.C. and other Allied ophthalmologists for the campaign in Sicily and Italy which followed. Along with specialized nursing sisters they were integrated into a medical-surgical team under Major General Hartgill, O.B.E., M.C. as Director[31,35]. Rycroft's experiences were the basis for his 1944 monograph, *A Manual of Ophthalmology for Medical Officers*[36].

As lieutenant colonel, Rycroft was awarded the O.B.E. in 1944 by Major General Sir Henry Maitland Wilson, Supreme Allied Commander, Mediterranean Theatre[37,38]. His citation recognizes that:

> "*Rycroft has displayed outstanding zeal and initiative in the planning of the Ophthalmological Services in this theatre. His aim to provide immediate surgical aid for eye injuries as near as possible to the front line, has been achieved with remarkable success whereby speedy treatment has saved the vision of many. He has been very much alive to the needs of the moment and, following the use by the enemy of the Schu mine, which destroys vision by blast, he quickly perfected a protective visor which bide [sic] well to save the vision of those at risk in all theatres*."[38]

John Hedley-Whyte recalls another example of Rycroft's overall bravery and calm, persuasive and charming personality. Just after the *Bismarck* was sunk on 27 May 1941, the Hedley-Whytes were visiting family in Newcastle-upon-Tyne, where they were joined by younger son Michael's godfather, then Major Benjamin Rycroft. The *HMS Dorsetshire* carrying seventy-eight rescued German survivors of the *Bismarck* sinking had been ordered to Newcastle-upon-Tyne[39]. The German prisoners were to be transported by train from Newcastle to Greenwich. The British Admiralty reported their youth and inexperience[40]. Exhausted and restless, the *Bismarck* survivors appeared on the verge of rebellion at the train station, where it was feared they might seize control of the North-East Railroad. The officer in charge had heard that Major Benjamin Rycroft was in Newcastle. A sergeant arrived at Moorfield, the home of John Hedley-Whyte's maternal grandfather, and summoned Rycroft to quiet the prisoners. Brigadier Angus Hedley-Whyte reported Rycroft's success.

RYCROFT AND SIR STEWART DUKE-ELDER

In his account of the ophthalmic services of the British Forces in the Western Mediterranean, Rycroft wrote that Brigadier Sir Stewart Duke-Elder "has always seen to it that every demand for ophthalmic and optical supplies from this theatre has always been met[31]". Four years Rycroft's senior, William Stewart Duke-Elder (Fig.1) was born in 1898 in Dundee, 5 miles south of his family home, the Manse at Tealing. He

was the second of three sons of the Rev. Neil Stewart Elder and his wife Isabella, daughter of the Rev. John Duke, who was also a Minister of the United Free Church of Scotland[11].

In 1915 Duke-Elder began his studies at the University of St. Andrews, where Rycroft was to follow, and in July 1919 graduated M.A. with first class honours in natural science, and a BSc. with special distinction in physiology. On 19 January 1923 he was awarded the M.B., Ch.B. after completion of his medical course at the Royal Infirmary, Dundee and the Royal Infirmary, Edinburgh[11].

Duke-Elder next advanced his career in London, with a progression of appointments at St. George's Hospital during 1923-24. Sir John Parsons, F.R.S., Ophthalmic Surgeon at University College Hospital and at the Royal London Ophthalmologic Hospital known as Moorfields, chose Duke-Elder as his clinical assistant later in 1924. With Parsons' encouragement Duke-Elder obtained a grant for part-time work at the National Institute of Medical Research to investigate the effects of radiation of different wavelengths on components of the eye, particularly in the etiology of cataract and the therapeutic use of ultraviolet light[11]. As a result, in 1927 he was appointed Medical Officer to the Ultraviolet Ray Department. This provided opportunity for clinical application of his research on ultraviolet light. In 1928, he was appointed Surgeon at Moorfield's, where he remained until retirement from hospital staff on medical advice in 1936. He was later to return as Consulting Ophthalmic Surgeon[11].

In 1936 he was also appointed Surgeon Oculist to King Edward VIII. This was followed by subsequent Royal appointments serving King George VI, and Queen Elizabeth II until 1965[11].

Duke-Elder joined the RAMC at the outbreak of World War II as an emergency Lieutenant, and was promoted to Acting Colonel in 1940, then Consultant Ophthalmic Surgeon to the Army at the rank of Brigadier. He was given charge of the Zachary Merton Convalescence Home at Barnstead, Surrey as an auxiliary ophthalmologic hospital to the R.A.M.C. for patients with serious eye injuries and diseases. His wife, Lady Phyllis Duke-Elder, supervised the facility administered jointly by the Red Cross and the St. John Ambulance. Duke-Elder's R.A.M.C. duties included responsibility for personnel, supplies, and visits to overseas RAMC hospitals in all theatres of war[3,11,31]. Duke-Elder received the Bronze Star Medal for assisting the Medical Department of the U.S. Army and was also honored with the stars of Burma, Italy, France and Germany[11,31]. Later in his career he was best known for his seven-volume *Textbook of Ophthalmology*

Fig 3. Sir Benjamin Rycroft presents Mr. Harry Coveney, who was once on the Blind Register, is now able to drive a car, 1963. Left to right: the Queen Mother, Sir Benjamin Rycroft, unidentified, Mr. Coveney. Photograph from the collections of the East Grinstead Museum[47], and reproduced with their permission.

(1932-1954)[41] and later *System of Ophthalmology* in fifteen volumes published 1958-1976[42].

RYCROFT POST-WAR

Rycroft returned to his civilian clinical practice and was appointed consultant ophthalmic surgeon to Park Prewitt Emergency Medical Service Hospital near Basingstoke and the Canadian War Memorial Hospital. He adapted well to Britain's new National Health Service although he did not fully support its role[7,8,9].

Rycroft's Zoological Society colleague, plastic surgeon Sir Archibald McIndoe (1900-1960) had expanded a program for treatment of burns at the Queen Victoria Hospital in East Grinstead, Sussex during the later years of World War II[23,24,26,43,44]. McIndoe had served as a civilian throughout. Corneal injuries were widespread among the burned patients he treated. McIndoe recruited Rycroft to create a Corneo-Plastic Unit in 1947 to provide corneal grafts, lacrimal surgery and procedures on eyelids and eye sockets[7,44,45]. Duke-Elder served on the Editorial Committee of the *British Journal of Ophthalmology* for many years and followed Rycroft's publications in that journal[11,31,32,46].

The Queen was acquainted with Rycroft, likely through Sir Stewart Duke-Elder's association with the Royal Family[11]. The Queen, and later as Queen Mother, staunchly supported his work at the Queen Victoria Hospital, East Grinstead (Fig.3)[47].

Rycroft's second son, Rodney, has recounted the Rycroft family's post-war visits to the Queen Victoria Hospital on Christmas Days, accompanied by his father's former World War II theatre sister, Sister King. There they would assist in feeding the patients and describe the festive Holiday decorations in detail to the visually-impaired[48].

PROMOTION OF TISSUE BANKS FOR CORNEAL GRAFTS

After World War II, awareness of the importance of keratoplasty increased, and technology advanced. Rycroft wrote that "In the United Kingdom, the expansion of this branch of ophthalmic surgery had been sadly hampered by the impact of two wars, the lack of instruments, and the absence of trained personnel"[46]. Welsh Ophthalmologist Tudor Thomas (1893-1976) had initiated an effort in Great Britain before the War for collection of cadaver eyes for corneal grafting, through a registration bureau for donor tissue at the Central London Ophthalmic Hospital (Fig. 2)[15]. Tudor Thomas was associate surgeon in charge of the Hospital's Corneoplastic Department from 1935 to 1940[15,16,17,18,19]. Rycroft noted that there were few deaths providing cadaver eyes in a hospital such as East Grinstead, specializing in plastic and maxillofacial surgery, necessitating the use of donor tissue from outside sources[45].

Rycroft promoted the Corneal Grafting Act of 1952, with a Bill presented to the House of Commons on May 21, 1952. The campaign was supported by the Royal College of Surgeons of England (Sir Cecil Wakely) and by the South East Metropolitan Regional Hospital Board. The cause was promoted by radio, television and public lectures[45,46,47]. Unopposed, it was passed into law on September 24, 1952. To aid its implementation, Regional Centres were established by the Ministry of Health to serve as Eye Banks. Rycroft drew additional attention to the subject with the publication of the 1955 book under his editorship[49].

Rycroft reported the success of the system for corneal transplant developed at East Grinstead, writing that

> "*A sterile set of enucleation instruments complete with a container of liquid paraffin B.P. is always kept ready at the hospital and when a death is reported by the general practitioner or relatives the eye surgeon on duty proceeds to remove the bequeathed eyes…eyes removed up to 10 hours after death are suitable for optical grafts… Cadaver eyes thus obtained may be used up to 10 days after preservation in liquid paraffin at 4°C in the Eye Bank*"[46] .

The Human Tissue Act of 1961 followed[50]. This legislation repealed the *Corneal Grafting Act* and applied the same bequest provisions to all donated tissues from deceased persons[45].

Writing as Clinical Director of the Pocklington Eye Transplantation Research Unit, Rycroft described a successful corneal graft as "one which restores vision and remains permanently and perfectly clear; it must be free from oedema, scar tissue and blood vessels[51]".

RETURN TO VETERINARY SERVICE

Rycroft was appointed Consultant Ophthalmologist to the Zoological Society of London in 1951[27,28]. Oliver Graham-Jones, Senior Veterinary Officer of the Zoological Society of London from 1951, later lauded Rycroft's service as Consultant Ophthalmologist. Graham-Jones had once anaesthetized a tigress for Rycroft's removal of a prolapsed lens. The ophthalmologist's team included an additional anaesthetist, a senior registrar, theatre sister and theatre nurse[52,53]. Rycroft treated ophthalmologic problems that arose in a wide range of animals including small mammals and birds, some of whom would wander freely about his office[28]. In 1961 Rycroft performed a corneal graft on a horse at the London Zoo[28].

Rycroft was a lifelong competitive horseman and owned a number of prize-winning 'jumpers'.

OTHER AVOCATIONS

In 1952, after the death of King George VI, HM Queen Elizabeth, The Queen Mother purchased Barrogill Castle, later known as the Castle of Mey, in Scotland. She began to renovate and restore the castle and estate, and consulted with her ophthalmologist, Rycroft, on the restoration of its gardens[54]. As a young teen, Michael Hedley-Whyte accompanied his godfather on a visit to the Castle of Mey to meet the Queen Mother.

During the 1960s, Rycroft and his wife Mary lived at their small farm, Bishop's Lodge, Berkshire, where he raised Jersey cattle, cultivated roses, and refined his performance as an equestrian[7,8]. He pursued fly-fishing as an additional hobby. The Rycrofts' residence was sufficiently close to Windsor Castle for him to frequently play the organ at St. George's Chapel, of which he was appointed a lay officer[7].

LIFETIME HONORS, FINAL CHAPTERS

Benjamin Rycroft was knighted 11th June 1960 in tribute to his lifetime of accomplishments[55].

In 1960-1961, Rycroft served as President of the Section of Ophthalmology of the Royal Society of Medicine. He traveled more widely and was received by members of the Ophthalmological Societies of Australia, New Zealand, South Africa, France, Italy and Belgium[7]

In February 1964, as Clinical Director of the RCSE's Pocklington Eye Transplantation Unit, he delivered the Hunterian Lecture to the Royal College of Surgeons, titled "Contemporary Views on the Surgery and Biology of the Corneal Graft" [56]. Rycroft reported that in the years since the passage of the 1961 Human Tissues Act[45,50] organization of donated corneas was shifted from the Ministry of Health to the Royal National Institute for the Blind. Corneal bequests were typically about one hundred per week, and at the time of the Hunterian lecture over 35,000 donor bequests had been registered[56].

Later in 1964, Rycroft returned to Belfast, where he had once served at the 31st General Hospital, to give the Craig Memorial Lecture at Queens University Belfast, titled "Plastic Surgery and Ophthalmology" and published in this journal[57]. The lectureship had been endowed by James Andrew Craig (1872-1958), a past president of the Ulster Medical Society and the Irish Ophthalmological Society[58,59].

In 1965, Rycroft gave the Doyne Memorial Lecture, titled "The Corneal Graft—Past, Present and Future" to the Ophthalmological Society[60,61]. He wrote of the problems posed by post-graft membranes and neovascularization. This lecture also provided an excellent opportunity for Sir Benjamin to cite the research of his son Peter Rycroft who by this time was recognized on his own with a post at the Pocklington Eye Transplant Unit of the Institute of Ophthalmology[62,63,64].

Sir Benjamin Rycroft visited the United States in early 1966, where John Hedley-Whyte recalls meeting with his former teacher and lifelong family friend in Boston. Rycroft consulted with ophthalmological specialists at the Massachusetts General Hospital.

Rycroft died of a sudden myocardial infarction on March 29, 1967[7,8]. His Memorial Service on May 2, 1967, was held at St. George's Chapel, Windsor Castle where he had often played the organ[47]. Sir Benjamin Rycroft's son, Peter Vere Rycroft, FRCS, widely regarded as his successor, died in a tragic accident the following year[65].

EPILOGUE

In recent years regulations concerning posthumous organ donation in the United Kingdom have shifted to an "opt-out" policy, i.e. consent is assumed unless otherwise indicated or the deceased falls within a category of persons who are excluded from donation[66,67]. Corneal donation may be accepted from some persons excluded from donating other tissue or organs[66]. Northern Ireland's "opt-out" law became effective June 1, 2023[66, 67]. Public awareness and education will be vital to its success[68,69].

ACKNOWLEDGEMENTS

The authors thank the curators of the Art Collection, University College London, for assistance with the portrait of Sir William Stewart Duke-Elder. The authors thank Mr. Jonathan Parrett and Ms. Judith Burns, Museum Managers, East Grinstead Museum, for assistance with the photograph of Rycroft with the Queen Mother and his former patient. The authors thank the Royal College of Ophthalmologists for permission to reproduce the photograph of Sir Tudor Thomas. The authors thank Ms. Ann Sylph, Librarian, and Ms. Natasha Wakely, Archivist, of the Zoological Society of London, for providing details of Sir Benjamin Rycroft's service to the London Zoo. Finally, the authors thank Dr. Benjamin Wilcox for his meticulously researched biographical paper about Rycroft[7] which encouraged John Hedley-Whyte to further explore and distill his recollections of this extraordinary ophthalmologist and personal mentor.

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Curiositas - Medicine in the Kitchen

QUIZ 1

1. **At which hospital did Alexander Fleming discover penicillin?**
2. **Why is frequent dosing of penicillin more important than achieving a high peak concentration, like some other medication?**

Sarah Lafferty[1], Rebecca Lafferty[2]

QUIZ 2

1. **Which type of honey is used medically?**
2. **What antimicrobial properties does this honey have?**

Sarah Lafferty[1], Rebecca Lafferty[2]

QUIZ 3

1. **Which enzyme does grapefruit inhibit?**
2. **Name a commonly prescribed drug class affected by grapefruit?**
3. **Why are patients with metallic heart valves advised to avoid grapefruit?**

Sarah Lafferty[1], Rebecca Lafferty[2], Lauren Venning[3]

QUIZ 4

1. **Which neurotransmitter does caffeine antagonise?**
2. **How does caffeine affect alertness?**

Sarah Lafferty[1], Rebecca Lafferty[2], Lauren Venning[3]

1. *Locum Specialty Doctor Diabetes and Endocrinology, Ulster Hospital Dundonald*
2. *Specialty Doctor Diabetes and Endocrinology, Ulster Hospital Dundonald*
3. *Locum Senior House Officer, Ulster Hospital Dundonald, Upper Newtownards Road, Belfast, Bt16 1RH*

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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

1) St Mary's Hospital, London
2) Penicillins exhibit time dependent killing whereby bactericidal activity correlates with the duration that free drug concentrations remain above the minimum inhibitory concentration (MIC) of the target organism (T>MIC), rather than the peak concentration achieved. Once the MIC is achieved, increasing the dose further does not significantly boost bacterial killing. Penicillins act via inhibiting bacterial cell wall synthesis through binding to penicillin-binding proteins which become saturated at relatively low concentrations. Anything beyond this adds little additional benefit but may increase the adverse effects. Given the short half-life of penicillins (30 – 60 minutes), long dosing intervals in patients with normal renal function risk sub-MIC concentrations and reduced efficacy. These factors are especially important in severe infections or in sites with limited drug penetration and thus maintaining consistent exposure above the MIC is essential and more beneficial than intermittent high dose regimes aimed at achieving high peak concentrations. Other antibiotics, such as aminoglycosides, use concentration dependent killing and do rely on achieving high peak concentrations as bacterial growth remains suppressed even after drug levels fall below the MIC. In those circumstances, achieving a high peak concentration with once daily dosing maximises efficacy while allowing drug levels to fall low enough between doses to reduce toxicity.

1. *Tilanus A, Drusano G. Optimizing the use of beta-lactam antibiotics in clinical practice: a test of time. Open Forum Infect Dis. 2023;10(7):ofad305. doi:10.1093/ofid/ofad305*
2. *UCLA Health Antimicrobial Stewardship Program. Antimicrobial Fundamental Concepts. Los Angeles: UCLA Health; 2017 Nov 9 [cited 2026 Feb 10]. Available from: https://asp.mednet.ucla.edu/file/3108/Antimicrobial_Fundamental_Concepts.pdf*

QUIZ 2

1) Mauka honey, from the *Leptospermum scoparium* tree in New Zealand and South East Australia
2) Manuka honey has various desirable antimicrobial properties. Its activity is multifactorial and assists in reducing the risk of bacterial resistance, a common challenge we face today. Firstly, manuka honey produces an osmotic effect, due to its high sugar content and low water activity, which dehydrates bacterial cells and suppresses their growth. Furthermore, its acidic pH creates a hostile environment to many pathogenic microorganisms. An added distinguishing feature of manuka honey is its high content of methylglyoxal (MGO). This unique compound provides non-peroxide antimicrobial activity that remains effective even when diluted by wound exudate, unlike many conventional honeys. Additionally, manuka honey also produces low level hydrogen peroxide via glucose oxidase and thus yields localised antimicrobial properties. It has demonstrated activity against a range of organisms and can also help reduce inflammation and promote wound healing by maintaining a moist environment and aiding autolytic debridement.

1. *Kapoor N, Yadav R. Manuka honey: a promising wound dressing material for chronic nonhealing discharging wounds: a retrospective study. Natl J Maxillofac Surg. 2021;12(2):233–7.*
2. *Haynes JS, Callaghan R. Properties of honey: its mode of action and clinical outcomes. Wounds UK. 2011;7:50–7.*

QUIZ 3

1 & 2) Grapefruit inhibits the cytochrome P450 3A4 (CYP3A4) enzyme. CYP3A4 is responsible for first pass metabolism of many oral medications. Inhibition of intestinal CYP3A4 reduces pre-systemic drug metabolism, leading to increased oral bioavailability and higher plasma concentrations. This effect can significantly increase the risk of dose related adverse effects and toxicity. Grapefruit inhibition is irreversible and thus enzyme activity only recovers as new enzymes are synthesised, meaning its interaction may persist for 24–72 hours after ingestion. Drugs commonly affected include statins, calcium channel blockers, immunosuppressants, antiarrhythmics, and some benzodiazepines.
3) R-warfarin is metabolised by CYP3A4. Inhibition of this pathway may increase the anticoagulation effect, increasing INR. Patients are advised to avoid completely.

1. *Bailey DG, Dresser GK. Interactions between grapefruit juice and cardiovascular drugs. Am J Cardiovasc Drugs. 2004;4(5):281–7*
2. *Hanley MJ, Cancalon P, Widmer WW, Greenblatt DJ. The effect of grapefruit juice on drug disposition. Expert Opin Drug Metab Toxicol. 2011;7(3):267–86*
3. *National Institute for Health and Care Excellence (NICE). [Internet]. Anticoagulation – oral: management – warfarin. Clinical Knowledge Summaries. Manchester, UK: NICE; 2025. {cited 2026 Feb 18). Available from: https://cks.nice.org.uk/topics/anticoagulation-oral/management/warfarin/*

QUIZ 4

1)Adenosine
2)Adenosine typically promotes sleep and suppresses stimulation by reducing neuronal firing. Caffeine, a central nervous system stimulant, acts as a competitive antagonist of adenosine receptors, particularly A_1 and A_{2a} receptors in the brain and thus prevents adenosine mediated inhibition. This leads to increased neuronal activity and perceived alertness. It also results in increased release of excitatory neurotransmitters such as dopamine, noradrenaline, GABA and acetylcholine which all also contribute to alertness. Whilst the above factors in theory improve overall alertness, there are caveats to this. Environmental and genetic factors result in a variation in how caffeine pharmacokinetics behaves. Caffeine is primarily metabolised in the liver by the cytochrome P450 1A2 (CYP1A2) enzyme. There is significant genetic variation in the CYP1A2 gene, resulting in individual differences in caffeine metabolism. In addition, CYP1A2 is affected by pregnancy, smoking and various medications. Moreover, regular consumption of caffeine can lead to increased tolerance and thus reduces the effects caffeine is famous for having.

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Game Changers

THE CAPSULE SPONGE: A NOVEL TEST FOR EARLY DETECTION AND RISK STRATIFICATION IN BARRETT'S OESOPHAGUS

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The capsule sponge is poised to revolutionise the diagnosis and management of Barrett's oesophagus (BO). Consisting of a capsule attached to a string, it can be administered by trained nursing staff in a clinic setting.[1] The capsule is swallowed and after several minutes the coating dissolves in the stomach, allowing an enclosed sponge to expand. The sponge is then withdrawn through the oesophagus by pulling on the string, collecting oesophageal cells, which can be analysed for biomarkers in a laboratory.[1] The biomarker TFF3 is suggestive of intestinal metaplasia and hence the presence of BO, whilst p53 and atypia are high-risk biomarkers suggesting the potential presence of dysplasia or oesophageal adenocarcinoma (OAC).[2]

Gastro-oesophageal reflux is a risk factor for BO, the precursor of OAC. It would not be practical to offer an endoscopy to everyone with reflux; however, it may be possible to offer capsule sponge testing to individuals with reflux to determine those with positive biomarkers who would benefit from endoscopy. The BEST3 trial, conducted in primary care, showed that the offer of a capsule sponge and TFF3 biomarker test to patients with reflux improved the detection of BO ten-fold compared to usual care.[3] Detection of these additional BO cases could help reduce progression to OAC. A Scottish prospective cohort study examining patients with reflux who had been referred to secondary care for non-urgent endoscopy found that capsule sponge biomarker testing for TFF3, p53 and atypia successfully identified those patients who required endoscopy.[4] 27% of patients underwent endoscopy, representing a significant reduction.[4]

The capsule sponge also has a potential role in surveillance of patients with known BO. At present, patients with BO undergo regular endoscopic surveillance, which is invasive and expensive. The DELTA and NHS England trials investigated risk-stratifying patients under BO surveillance into low-, medium-, and high-risk categories based on capsule sponge p53/atypia results and clinical risk factors. The positive predictive value for dysplasia/OAC in the high-risk group was 37.7%, and the negative predictive value for dysplasia/OAC in the low-risk group was 97.8%.[5] In the future, high-risk patients could undergo endoscopic follow-up, medium-risk patients could alternate between endoscopy and capsule sponge, and low-risk patients could undergo capsule sponge-only surveillance.[5]

Over 350 capsule sponge tests have been performed in Northern Ireland as part of implementation pilots within the United Kingdom, however the capsule sponge is not yet used here as part of usual care. The BEST4 trial is currently underway in the United Kingdom, examining whether use of the capsule sponge, both in screening patients with reflux symptoms for BO, and in surveillance of patients with known BO, could reduce mortality from OAC. Going forward, the capsule sponge has the potential to transform the detection and surveillance of BO, provide substantial cost savings to the health service, and save lives from cancer of the oesophagus.

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ISSN 0041-6193

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What will it look like? Birch Hill Centre for Mental Health, a new development to centralise the Northern Health & Social Care Trust's inpatient mental health services.

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