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Editorial

Deeds not Words

David J Armstrong

'Men of Athens, judge me by my deeds, not my words'[1]. – sadly for Socrates he was judged, unfairly it would seem, by his words, and condemned to death. No such fate awaits anyone trying to fix the Northern Ireland healthcare system at present, but having heard calls for several years for the return of local government, and the appointment of a Health Minister, we now have both[2], and the time for action is upon us. What then, must be done?

I suggest three areas to address, and none will be new.

First, the need for organisational reform, in what we do and how and where we do it. To be succinct, implement the Bengoa report. Some have asked if a report published in October 2016[3] (and before COVID) might not be out of date, and whether another review is required. Surely Northern Ireland cannot need another report telling us we need to reform our structures? The data might be 8 or 10 years old, but the conclusions are the same. A scientist asking for monies to repeat the same experiment with almost identical data, having failed to implement any changes based on the conclusions of two or three identical experiments using data from the same source, is unlikely to attract funding. We need to 'get on' and do it. The title – and conclusion – of the Bengoa Report, 'Systems not Structures' speaks for itself.

Some have interpreted Bengoa as a mandate to close hospitals. This is not only incorrect but a gross misrepresentation of what reform of health services means. We need patients to be seen by the correctly qualified person, in the right place, as soon as possible, with the procedures, medicines and follow-up needed easily available. Not everything can be done in every building. Patients demand world class care from experts, which is absolutely right; experts work in centres of expertise, and we must make it easy for the patient to get to see them. In the days when best care for a myocardial infarction was aspirin and bed rest, every small town could have a cardiac unit. In the days when best care is percutaneous coronary intervention, every small town cannot.

There are two factors which will make this work. The first lies at the door not of doctors, but of politicians – we need better public transport, better roads, better trains, better parking, better access. My patient last week took three buses to get from rural Fermanagh to Londonderry, and three buses home again. Public transport is very poor in some areas, trains services skeletal (and literally non-existent in two out of six counties), and almost none of our major hospitals have direct motorway links. It is not distance *per se* but time which is the problem. Will building better roads and improving train services improve healthcare? I suggest it would make a big difference. It might also go some way to make working outside Belfast a more attractive option for staff who, for personal or family reasons want or need to live a distance from their workplace.

Also important, is making it easier to get patients from the GP surgery or district hospital (DGH) to the specialist centre through the medical infrastructure. Every doctor will remember spending time as a junior working in a DGH trying to 'sell' your sick patient to the on-call registrar in the city, with the suspicion that if they were lying in a bed in the destination hospital they would have been seen already. This has improved hugely over the years, but could be made better still. Arguments over who 'owns' a patient sent straight to ICU, or who went from the Emergency department to another hospital are important, but cannot get in the way of patient care. There must be fast and foolproof ways for GPs to access specialist services for their patients. We are intelligent caring people, and these are resolvable issues.

Second, we need to look after our workforce. Paying doctors more? Absolutely. But read the contributions in the last few issues of this journal and you will see that it is quality of life, and quality of work that is as big a concern as the pay packet in itself. I have discussed this in previous Editorals, but treating medical staff, including locum medical staff, with respect and value is a first step. Human Resource departments must do better. Doctors must be paid correctly, on time. Medical accommodation must be habitable, rotas must take account of life outside medicine, people must be facilitated to have different work patterns and career paths from those of 50 years ago. Otherwise staff will simply leave to work in other countries, where pay is better and work more pleasant. Many have already gone.

The 'work-life balance' concept is perhaps outdated, as foundation year one doctor Grace Kettyle outlines in her contribution to the NI Healthcare section later in this issue. Most doctors feel they are defined to a large degree by their work as a doctor, and that it is part of their life, not something to be pushed aside, viewed negatively, or 'balanced' by other things which must somehow be inherently better. We should not regard work like the English poet Philip Larkin's toad 'squatting on my life…its hunkers heavy as hard luck, and cold as snow'[4]. Doctoring should enrich our lives and those of our families and friends, not reduce quality of life and damage our relationships. If doctors in Northern Ireland have good lives as doctors – in hospital as well as at home, in the surgery as well as on holiday or at the gym – then they

will flourish and be more likely to stay here. 'Work-life fit' is perhaps, as Grace says, a better concept.

Third, and briefly, we need leadership. Political leadership in the first instance. Party leaders call for reform, and councillors from the same party oppose reform at every turn if it changes the way things are done in their constituency. Leaders must lead and educate, not just follow the lowest common denominator. Voters are not stupid, and not as fickle as some imagine when it comes to getting good healthcare. My patient from Fermanagh was happy to get to see me in a specialist clinic in Altnagelvin, but she was very cross that it took six bus journeys and 8 hours of her day to do so.

And of course medical leadership. The role of the medical leader has developed massively over the last twenty or thirty years, but so much change and improvement is still stifled by management and fear of different ways of doing things. New ideas must get quickly and easily from the bedside to the Boardroom and back to every other bedside. The role of the Clinical Leader must be developed further, and the younger generation of doctors in Ulster – those born here, and those who have chosen to make their homes with us here – must be allowed to flourish, to innovate and to make this place an example of how we can turn a broken healthcare service around and make it something to be proud of.

People will look back to the opportunity we have in 2024 to rebuild the health service in Northern Ireland. We – doctors, politicians, patients - will be judged by deeds and not words.

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Northern Ireland Healthcare Crisis

Over the last three issues of the Journal we have heard a range of voices from across healthcare in Northern Ireland commenting on their experience of the pandemic and the widely acknowledged crisis in healthcare provision across the province. With the re-establishment of devolved government in Stormont, including a locally appointed Health Minister, it seems the right time to draw the brief series to a close, with a note of realistic optimism from a doctor in her first year after qualification, working in a hospital outside Belfast, but already pushing boundaries in world class research, teaching and training.

David J Armstrong, Editor

'Today's thinking- transforming tomorrow'

Being a Fermanagh native, I have begun my career as a Foundation doctor in the South-West Acute Hospital, Enniskillen. I was privileged to spend three out of my six years at medical school in this hospital and therefore owe a great deal of my clinical knowledge and skills to those doctors and nurses who took the time to train me. As a medical student, I was mentored by many of the esteemed local clinicians, who are now my colleagues. I also had the unique experience of being a Covid Medical Student, the legacy of which has hugely shaped my thinking and transformed my clinical practice due to the challenging and early frontline exposure to critically ill patients, allowing me to build much skill capacity and resilience. This was one of the most physically and mentally challenging periods that I faced, but opened the doors to high level clinical training, and the acquisition of invaluable guidance from expert mentors.

As we all know, healthcare is one of the major success stories of our time. However, a perfect storm of factors has combined to make healthcare unaffordable and unsustainable in its current state. Undoubtedly, change has already begun to address this crisis, but a period of huge transformation in healthcare is dawning with today's thinking transforming tomorrow.

As one of the young doctors standing on the cusp of such exponential change in the ever-evolving field of medicine, it is crucial to embrace innovation and constantly challenge the status quo. By thinking collectively, by thinking critically, by thinking outside the box and pushing boundaries, we can pave the way for ground-breaking discoveries and advancements that have the potential to revolutionise healthcare and address the current crisis.

My desire to be one of tomorrow's surgeons has challenged me to pursue research that involves new and innovative technologies that can be implemented in an ever-progressing surgical field as well as furthering medical education. I recently co-ordinated a pilot study using Smart Glasses technology by a company called Rods and Cones. The Smart Glasses technology was worn by a trainee surgeon whilst she operated allowing her to connect and communicate with a remote proctor, a Consultant General Surgeon who was located on site in one of our state-of-the-art imaging suites. The proctor as well as twenty medical students from Queen's University Belfast and Royal College of Surgeons Ireland were able to see the live feed of the surgical field through the surgeon's lenses. Support to the operating surgeon was given through real-time communication and the use of annotation using augmented reality technology. The technology allowed us to simultaneously show the visor feed, a panoramic view of the operating room as well as the imaging transmitted through the laparoscopic camera. This pilot study has enhanced and revolutionised the teaching experience of our students within these three short days. The feedback we received from our students will be instrumental in shaping how we embed this teaching initiative going forward with some of the cohort recognising, even in its infancy, that this is the future of surgical teaching. By thinking about this today we are transforming the education of tomorrow's doctors.

Today's thinking and transformation of tomorrow is not exclusive to our medical practice. We must understand the importance of finding healthy equilibrium between professional responsibilities and personal well-being. A balanced life today will lead to a happier and more fulfilled healthcare provider of tomorrow.

A well-known female American surgeon, Ms Jamie Coleman, once quoted, '*my best advice is to stop thinking of work and life as a balance as that implies, they are opposing forces and will only set you up to fail.' She went on to say, 'surgery doesn't stop my life and my life doesn't stop surgery. I am a better surgeon because I am a wife and a mother. And I am a better wife and mother because I am a surgeon.'*

Modern thinking supports Ms Coleman's view, and the traditional concept of work life balance will gradually have to give way to a more adaptable and realistic approach known as work-life fit if we are to retain a sustainable workforce. The work life fit differs from the traditional work life balance in that it does not segregate work form personal life but blends the two in a way more seamlessly allowing employees to customise their work schedules to better align with their personal lives. Healthcare must recognise that a one size fits all approach will not work in tomorrow's world and that flexibility and employee well-being must be prioritised.

As John F Kennedy once said, 'Change is the law of life and those who look only to the past or present are certain to miss the future.' Transformation is not a distant vision; it is happening now!

Grace Kettyle
Foundation Year One Doctor
Western Health and Social Care Trust

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Clinical Paper

Mortality and complications after total hip arthroplasty via the posterior approach for displaced intracapsular hip fracture: Results from a regional trauma centre

Grace EM Kennedy[1,2], Julie Craig[1], Samuel E McMahon[1], Laurence A Cusick[1]

Abstract

Introduction

Total hip arthroplasty (THA) for displaced intracapsular hip fracture is increasingly common. The aim of this project was to determine all-cause mortality rates, rates of significant complications and functional outcomes following THA for fractures.

Methods

An inpatient database search identified all patients undergoing THA for displaced intracapsular fracture in Northern Ireland's regional trauma centre from 2010-2017. Regional electronic healthcare systems were reviewed for evidence of complications.

Results

After exclusions, 345 cases were identified. The median age was 70 years (31 – 91 years).

Median follow-up was 4.3 years (1.6 – 9.3 years). The all-cause mortality rate was 0.3% at 30 days, 3.2% at one year, and 5.5% at two years.

Seven patients (2.0%) experienced dislocations. Most occurred within 60 days; five patients underwent revision.

Radiographic evidence of heterotopic ossification (HO) was seen in 48 patients (13.8%).

Re-operation was required for 16 patients (4.6%). This included 5 dislocations, eight cases of periprosthetic fractures (in seven patients), two cases of infection, and one case of symptomatic HO.

Pre-injury, 96.2% (332/345) were independently mobile, and after one year 78.9% (262/332) of those patients remained so. Pre-injury, 96.2% obtained the maximum functional score (Barthel Index, maximum score of 20), and after one year 78.9% (262/332) of these continued to report a maximum Barthel Index score.

Conclusion

THA for hip fracture holds a 2.0% risk of dislocation and a 4.6% risk of re-operation. HO is common but seldom requires re-operation. All-cause mortality rates and functional levels compared favourably with current literature.

Key words

Hip fracture, total hip arthroplasty

Introduction

Hip fractures are a common and increasing global challenge[1] associated with an increased risk of mortality, particularly in the first six months post-injury.[2] In the United Kingdom (UK), the National Hip Fracture Database (NHFD) reported that 30-day mortality rates remain substantial at 6.1%.[3]

Intracapsular hip fractures affect the region of the femur which is enveloped by the ligamentous hip joint capsule.[4] Following such an injury, the femoral head is at risk of avascular necrosis due to disruption of the branches of the medial and lateral circumflex arteries supplying the femoral head.[5] Thus, intracapsular hip fractures, particularly if displaced, are typically managed with arthroplasty. This may be in the form of a hemiarthroplasty (femoral side only) or a total hip arthroplasty (THA), where both the femoral head and acetabulum are replaced.[4,6] Both approaches endeavour to relieve pain and facilitate early weight-bearing and mobilisation.

THA has been associated with superior post-operative function and lower re-operation rates, compared with hemiarthroplasty.[7] This may be due to erosion of the patient's native acetabular cartilage by the femoral prosthesis[8], and disruption of hip abductor function due to the anterolateral approach typically employed for hemiarthroplasty.[9] However, THA has also been associated with greater risk of dislocation as well as operative time and intra-operative blood loss.[10] Thus, consideration of the patient's pre-

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morbid function and overall health status is paramount when planning management.

In 2011, the UK National Institute of Health and Care Excellence (NICE) introduced guidelines regarding the use of THA for intracapsular hip fractures.[11] These recommended offering THA to patients with a displaced intracapsular femoral neck fracture who can walk independently outdoors with no more than the use of a stick, are not cognitively impaired, and are medically fit for anaesthesia and the procedure.

Northern Ireland's regional trauma centre, the Royal Victoria Hospital (RVH), is one of the highest-volume centres in the UK NHFD, with low 30-day hip fracture mortality rates and relatively high usage of THA for hip fractures.[12] Northern Ireland also has a relatively 'captive' population due to its geographical location, whereby patients rarely travel to healthcare providers outside the region, and regional healthcare systems record all emergency department and inpatient episodes, and all radiological investigations performed in Northern Ireland.

The primary aim of this study was to determine the rate of all-cause mortality in patients undergoing THA for displaced intracapsular hip fracture in this unit. Secondary aims included assessing the rate of significant post-operative complications, and the impact on patient mobility and functional status.

Methods

This retrospective cohort study considered all patients undergoing THA for displaced intracapsular hip fractures in a single regional trauma centre (the Royal Victoria Hospital) between 8 February 2010 and 8 August 2017 as identified from the Fracture Outcomes Research Department (FORD) inpatient database. Telephone follow-up to one year was performed by specialist nurses. Regional electronic systems for healthcare notes and imaging provided information regarding further hospital presentations, complications, and re-operation.

Pre-operatively, patients were medically optimised by a consultant-led ortho-geriatric medical team. All patients underwent a THA with a cemented Exeter (Stryker) femoral stem and an acetabular component with highly cross-linked polyethylene liner, either cemented or uncemented as per surgeon preference. Stainless steel and ceramic femoral heads were utilised at surgeon discretion. Femoral head sized ranged from 22mm to 36 mm. All THAs were inserted via a posterior approach with repair of the joint capsule and short external rotator muscles, either by, or under the close supervision of an experienced arthroplasty surgeon. Antibiotic-impregnated cement and antibiotic prophylaxis were used in all patients. Patients underwent an inpatient post-operative radiograph and were routinely mobilised fully weight-bearing under the supervision of physiotherapists. Patients received mechanical and chemical thrombo-embolic prophylaxis (typically enoxaparin for 28 days post-operatively unless contraindicated, or until resumption of pre-injury anticoagulants if applicable).

Details of the admission, demographics and telephone follow-up were retrieved from the FORD database. Of the 390 patients identified from the database, 45 cases were excluded due to incorrect coding (n=8), duplicate entries (n=5), indications other than acute intracapsular fractures (n=22), THA for pathological lesions (n=4), or patients normally resident outside Northern Ireland who did not receive local follow-up.

Regional electronic systems of medical records and radiology images and reports were reviewed to obtain details regarding all-cause mortality, dislocation, periprosthetic fracture, infection, and heterotopic ossification (HO). Telephone follow-up ascertained details of mobility, use of walking aids and functional status (using the Barthel Index).

Descriptive statistics were calculated using Microsoft Excel (Microsoft Office Excel 2016, Washington, USA). Categorical variables were analysed using Fisher's exact tests) depending upon sample sizes, using GraphPad QuickCalcs (available at https://www.graphpad.com/quickcalcs/contingency1.cfm).

Results

Demographic information

From the database, 345 patients who underwent THA for acute displaced intracapsular hip fracture were identified. This represents 8.6% of the 4005 patients with displaced intracapsular hip fractures admitted to the unit during this period. Usage of THA for this indication rose from 2.3% (9/399) in the period from 8 Feb 2010 to 31 December 2010, to 14.3% (74/516) in 2016, and 15.8% (54/341) of those treated from 1 January 2017 to 8 August 2018. Most patients were female (77.7%), were aged over 65 years (median age 70 years, range 31 – 91 years, interquartile range 64 – 75 years) and were of American Society of Anaesthesiologists (ASA) grade 2 (55.7%, 192/345). A further 37.4% (129/345) were ASA grade 3. Pre-injury, 96.2% (332/345) of patients mobilised without assistance. In addition, 90.7% (313/345) of patients mobilised without walking aids, 7.8% (27/345) mobilised with the use of a stick, and 1.4% (5/345) required the use of a walking frame/ rollator. Pre-injury, 96.2% (332/345) achieved the maximum functional score of 20 on the Barthel Index.

All-cause mortality

At the time of data collection, 306 (88.7%) of the patients were alive (median 4.3 years post-operatively, range 1.6 to 9.3 years), of whom 277 had at least two years of follow-up. Of the 39 patients who were deceased at the time of data collection, 20 patients had two years of follow. Two-year follow-up information was therefore available for 297 (86.1%) of the original 345 patients.

Mortality rates were 0.3% at 30 days (one patient of ASA grade 3), 3.2% at one year (11 patients including three of ASA grade 2 and eight of ASA grade 3) and 5.5% at two years (19 patients including five patients of ASA grade 2 and 14 of ASA grade 3).

Among the 192 patients of ASA grade 2, none had died by 30 days post-operatively, three (1.6%) died by one year, and five (2.6%) died by two years. Among the 129 patients of ASA grade 3, one died by 30 days post-operatively (0.8%), eight (6.2%) died by one year, and 14 (10.9%) died by two years post-operatively.

Of the 39 (11.3%) deceased patients, causes of death were available on regional electronic medical for 19 patients, as outlined in **Table 1**. Only one death occurred within 30 days of surgery, due to a fatal dysrhythmia, having experienced a perioperative non-ST-elevation myocardial infarction.

Major complications

Less than 20% of patients undergoing THA for trauma experienced a major complication, as outlined in **Table 2**.

Dislocation

Seven patients (2.0%) had a hip dislocation during the study period. Of these, four patients experienced two dislocations and three patients experienced three or more dislocations. The median time from arthroplasty to first dislocation was 33 days, with six of these dislocations occurring within 60 days post-operatively (6, 8, 20, 33, 43 and 43 days post-

Table 1: The causes of death as indicated on regional electronic medical records.

Cause of death	Number (Percentage overall cohort) deceased at 30-days post-operatively	Number (Percentage overall cohort) deceased at two-years post-operatively	Number (Percentage overall cohort) deceased during available follow-up period
Cardiac event	1 (0.3%)	1 (0.3%)	2 (0.6%)
Chest infection or chronic obstructive pulmonary disease	0 (0%)	2 (0.6%)	11 (3.1%)
Metastatic or recurrent malignancy	0 (0%)	4 (1.2%)	8 (2.3%)
Single or multi-organ failure	0 (0%)	2 (0.6%)	4 (1.2%)
Intracranial event	0 (0%)	1 (0.3%)	2 (0.6%)
Cause of death unavailable	**0 (0%)**	**9 (2.9%)**	**12 (3.5%)**
Total	**1 (0.3%)**	**19 (5.5%)**	**39 (11.3%)**

Table 2: The incidence of major post-operative complications.

Complication		Number of patients (%)
Dislocation	**Total**	**7 (2.0%)**
	Two dislocations	4 (1.2%)
	Three or more dislocations	3 (0.9%)
Periprosthetic fracture	**Total**	**8 (2.3%)**
	Femur	7 (2.0%)
	Acetabulum	1 (0.3%)
Infection requiring washout	**Total**	**2 (0.6%)**
	Infected wound	1(0.3%)
	Infected haematoma	1 (0.3%)
Heterotopic ossification		48 (13.9%)
Nil known		282 (81.7%)
Total		**345**

operatively) and one dislocation occurring 30 months post-operatively.

Two patients required only closed reduction. Five patients underwent open procedures, including one open reduction, one exchange of the acetabular liner and femoral head, and three cases of acetabular component revision.

Almost all femoral heads were diameters of either 28mm (72.2%, 249/345) or 36mm (27.0%, 93/345). None of the three patients with smaller femoral heads (0.9%) (one 22mm head and two 26 mm heads) had dislocations. The rate of dislocation ostensibly was around twice as likely after use of a 28mm head (2.4%, 6/249) than 36mm (1.1%, 1/93), although this did not reach statistical significance (p=0.68).

Periprosthetic fracture

Eight periprosthetic fractures (2.3%) occurred, including seven (2.0%) femoral fractures in six patients, and one (0.3%) acetabular fracture. All resulted from falls (i.e., none sustained intra-operatively).

All femoral periprosthetic fractures were treated operatively. Two such injuries underwent revision of their femoral component plus cable plating, and four underwent cable plating, with one of the latter sustaining a second periprosthetic fracture one month later, which was subsequently treated with internal fixation. The acetabular fracture was managed non-operatively.

Infection

Two patients (0.6%) required re-operation for surgical site infection, one as a wound washout six days post-operatively and one as a washout of an infected haematoma one-month post-operatively. No patients required revision or prosthesis removal due to infection.

Heterotopic ossification

Radiographic evidence of heterotopic ossification (HO) was seen in 48 patients (13.9%), including two patients who had dislocations. Only one patient with HO (0.3%) required surgical excision due to pain.

Mobility and functional outcomes

Almost all patients (96.2%, 332/345) were independently mobile pre-injury. Of these 332 patients, one-year follow-up found that 262 (78.9%) remained independently mobile, 26 (7.8%) required assistance to walk, one was immobile, 11 were deceased, and the mobility of 32 patients was unknown. Amongst the 13 patients who had required assistance to walk pre-injury, one-year follow-up found that eight patients (61.5%) were able to walk without assistance, four (30.8%) continued to mobilise with assistance, and the mobility status of one patient was unknown.

Therefore 79.7% (275/345) of all patients has similar or better independence at one year compared to pre-injury.

Most patients (90.7%, 313/345) also required no walking aids pre-injury. Of these, 195 (62.3%) still required no walking aids at one year post-operatively.

At one year, 65.2% of all patients (225/345) had either similar use of walking aids or less dependence on walking aids, and 22.0% (76/345) required additional walking aids compared to pre-injury. Eleven patients (3.2%) were deceased at one year and the walking aids of 33 (9.6%) were unknown.

Of the 332 patients who achieved the maximum possible functional score pre-injury (Barthel index score of 20 out of 20), 262 (78.9%) maintained a Barthel Index score of 20 at one year, 22 (6.6%) had a decrease in functional score. Functional scores for 39 patients were unavailable and nine (2.7%) were deceased.

Thirteen patients had pre-injury Barthel Index scores less than 20 (range 14-19). At one year, eleven patients reported similar or better Barthel Index scores to pre-injury, and two were deceased.

Therefore, 79.1% of all patients (273/345) demonstrated similar or improved functional scores as compared to pre-injury.

Discussion

As compared to patients undergoing elective THA, patients undergoing THA for trauma have higher risks of mortality and major complications,[13] may be more frail, and be less likely to have pre-operative optimisation.[14] THA has been associated with greater operative time and physiological burden on the patient than hemiarthroplasty.[15,16]

All-cause mortality

Whilst the considered hospital has been noted for low mortality rates among hip fracture patients,[12] the 30-day mortality rate for THA patients in this study was notably low at 0.3%. In this cohort, most patients had only mild systemic disease (ASA grades 1-2), but 37.4% had severe comorbidities (ASA grade 3).

The one-year mortality rate of 3.2% compares favourably with rates of up to 13% reported in the literature.[17] This remains higher than the one-year mortality rate for elective THA,[18] however this may reflect different baseline characteristics and pre-operative optimisation.

Patients undergoing THA are expected to represent a healthier and more active subgroup of hip fracture patients, as per the NICE guidelines.[4] Nevertheless, the low mortality rates suggest that unsuitable patients are not being subjected to undue risks in THA, and that patients are appropriate optimised pre-operatively.

Major complications

Dislocation

Several meta-analyses have reported higher dislocation rates after THA for trauma than after hemiarthroplasty.[17,18]

The dislocation rate of 2.0% in this study compares favourably with rates of up to 7.5% in recent literature[19,20,21,22,23] and 3.9% in a recent meta-analysis. This may reflect the local system where high-volume elective arthroplasty surgeons also perform trauma and provide training under supervision. Of note, another United Kingdom regional database, the Scottish Arthroplasty Register, reported one-year dislocation rates (2.1%) comparable to the present study.[24]

In elective THA, larger head sizes reduce the risk of dislocation,[25] but in the present study the increased risk of dislocation with smaller femoral heads did not reach statistical significance.

In elective THA, dislocation rates are higher after posterior approach than other approaches.[26,27] There is limited evidence regarding the influence of approach on dislocation rates in the trauma setting. However, repair of the posterior capsule in THA for trauma (as is standard practice in this unit) has been associated with decreased dislocation rates.[27]

Re-operation for fracture or infection

In the present study, sixteen cases (4.6%) required re-operation including five (1.4%) for dislocation, eight cases (2.0%) for periprosthetic fractures, two (0.6%) for infection and one (0.3%) for excision of heterotopic ossification.

Ravi et al reported lower one-year re-operation rates after THA for displaced intracapsular hip fractures as compared to hemiarthroplasty (0.2% vs 1.8%, $p<0.001$), after matching for demographics and co-morbidities.[28]

The present study's re-operation rates are comparable to published re-operation rates of 3.3% for periprosthetic fractures[20], and 3.1% revision in the Swedish Hip Arthroplasty Register,[21] but lower than those reported by a recent RCT (7.9% at two years)[29] and the American College of Surgeons National Surgical Quality Improvement Program database (5.3%).[16] Re-operation rates for infection following THA for fracture have been reported to be as high as 8.7%[30] but were only 0.6% in the present study, although selected patients' demographics may affect this.

Heterotopic ossification

In the present study, HO was seen in 13.2% of patients, of whom only one patient required surgical excision. Similarly, Comeau-Gauthier et al, identified HO in 19.9% of patients at 24 months following either THA or hemiarthroplasty for fracture, none of whom required excision.[31] These rates are higher than those reported in other studies,[20,29]possibly due to inclusion of radiologically-identified HO rather than symptomatic HO.

Functional and mobility outcomes

In the present study, most patients mobilised independently with few/no walking aids and high functional scores pre-injury, and the majority maintained these levels at one-year. Maintenance of functional scores compared favourably with published reports of deterioration in functional scores,[19] and reduced ability to mobilise and perform activities of daily living,[20] although the latter study's population involved fewer patients and a higher average age than the present study.

Bhandari, et al compared clinical outcomes following THA and hemiarthroplasty for fracture[29] and concluded that improved results after THA fell below the threshold for a minimal clinically important difference. However, the scoring systems used were designed for primary hip OA and not validated for hip fractures, and post-operative scores were not considered in light of pre-injury ambulatory ability.

The findings in the present study are favourable compared with reported rates of ambulation following hemiarthroplasty described in the literature. Following hemiarthroplasty, non-ambulation has been reported in 4% of patients.[32] being housebound in 23.3%, [33] a reduction in pre-fracture ambulatory ability at one year in 84.8%,[34] and requirement for a walking frame in 42.4%.[34] Comparing THA and hemiarthroplasty, Mariconda et al described a trend (non-significant) for a greater independent ambulation following THA at 12 months, and also found walking aid requirement was significantly lower at four months.[20] Similarly, a recent cohort study reported greater walking support and shorter walking distances following hemiarthroplasty.[35]

Considering Barthel index, one study has reported superior scores following THA than following hemiarthroplasty,[36] however the authors acknowledge the findings should be interpreted with caution given the inherent selection bias. Similarly, a study found 53% of patients undergoing hemiarthroplasty to have a normal-near normal rating (19-20/20) at 12 months,[37] in contrast to 78.8% in the present study. Furthermore, the minimum clinically important difference at 12 months after hip fracture surgery was found to be 2/20.[38] thus, the differences reported in the literature may not be notable to the patient, and we believe this warrants further investigation.

Limitations

Limitations to the present study include its retrospective, single-centre design. Furthermore, whilst the use of regional electronic systems allowed access to details of all inpatient or emergency department activity, ensuring recording of attendance to any hospital with complications, causes of death were only specified for inpatient deaths, resulting in incomplete data for deaths outside hospital.

The present study also lacks a control (hemiarthroplasty)

group, making it difficult to fully evaluate the risks and benefits of THA at this centre, and this represents an area for future work. Subgroup analysis may also wish to consider the merit of using strategies proposed to improve function following hemiarthroplasty, including bipolar components[39] or via a modified abductor-sparing surgical approach, [40] particularly in active, older (>80 years) adults.

Conclusion

In this retrospective cohort study, the one-year all-cause mortality rate following THA for acute displaced intracapsular hip fracture was 3.2%. THA, performed via the posterior approach, was associated with a 2.0% risk of dislocation and 4.6% re-operation rate (1.4% for dislocation, 3.2% for other causes). HO occurred in 13.8% of patients but seldom required re-operation. Overall, a good maintenance of mobility and activities of daily living was seen at one year post-operatively. Therefore, we propose that THA for trauma via the posterior approach with posterior structure repair can be used in suitable patients without putting them at undue risk of major complications or need for revision.

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Clinical Paper

First use of Bedaquiline, Linezolid, and Pretomanid (BPaL) in a family cluster of multi-drug resistant (MDR) TB infection.

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Introduction

Rates of tuberculosis, also known as "consumption" or "the white death", were falling with the introduction of patient isolation, vaccination, and improved general public health in urban areas. However, it was only with the introduction of effective antituberculous therapy since 1946 that individual patients could expect cure. Unfortunately, drug-resistant TB has become a major public health problem, with an estimated 450 000 new cases per annum (2021).[1] Scientific advances in understanding the pathophysiology of TB and potential drug targets have resulted in novel treatment strategies.[2, 3]

Over the past decade, there have been major advances in the treatment of drug- resistant tuberculosis. Previous treatment regimens include a minimum of 18 months of medication, with drugs that have extensive side effect profiles. Prior to 2018, injectable medication was a cornerstone of treatment. Recent studies have shown that shorter all oral regimens are non-inferior to longer regimens and have fewer major adverse effects.[4] The updated World Health Organisation consolidated TB treatment guidelines now recommend shorter all oral regimens as first line where indicated.[5]

Here we present our experience of accessing and using Pretomanid in combination with Bedaquiline and Linezolid to successfully treat two patients with drug resistant tuberculosis.[6] To our knowledge, this is the first use of Pretomanid as part of a recognised regimen in the United Kingdom. Pretomanid has been licenced through the Orphan drug register since 2007, for the treatment of pulmonary extensively drug resistant, or treatment-intolerant or nonresponsive multidrug-resistant tuberculosis.[7] Pretomanid is a nitroimidazooxazine with activity against replicating and dormant mycobacteria through inhibition of mycolic acid biosynthesis and nitric oxide release, respectively.[8]

Recent randomised controlled trials (TB-PRACTECAL[9], Nix-TB[10], and ZeNix[11]) have shown high rates of treatment success with low rates of adverse events using Pretomanid in combination with Bedaquiline and Linezolid, with or without a fluoroquinolone compared to previous standard of care regimens.

TB PRACTECAL showed a treatment success rate of 89% in those receiving Bedaquiline, Pretomanid, Linezolid and Moxifloxacin, and 77% in those receiving Bedaquiline, Pretomanid and Linezolid, compared to 52% treatment success in the standard of care group.[9]

The NIX-TB Trial showed a treatment success rate of 90% with Bedaquiline, Pretomanid and Linezolid and the ZENIX trial had treatment success rates between 84-93% with different dosages of the same drugs.[10, 11]

The TB PRACTECAL trial has also demonstrated significantly lower incidence of adverse events related treatment with BPaL compared to the standard of care (19% vs 59%).[9] Lower levels of toxicity from treatment means monitoring requirements are less intense. Reduced adverse events, reduced monitoring and a shorter duration of treatment have a significant impact on the cost of delivering treatment. The cost of medications for Bedaquiline, Pretomanid and Linezolid for the 6 month treatment course was £39,505, compared to the standard of care which costs £46,089.

In light of this new evidence, and when constructing a regimen to manage our cases of pulmonary drug-resistant TB we were keen to treat our patients in line with WHO recommendations. We have experience using Bedaquiline, and Linezolid, but to our knowledge, Pretomanid has not been prescribed to any patients in the United Kingdom.

The WHO has not yet defined a minimum inhibitory concentration (MIC) for pretomanid. The sensitivity testing for our isolates was carried out at the Irish Mycobacterial Reference Laboratory using two provisional concentrations released in the 2023 EUCAST guidelines.[12] The WHO are making efforts to establish MIC values using epidemiological cut off values, clinical outcome data and PK-PD data.[13]

Cases

We had two cases who we thought would benefit from BPal regimens, both had close contact with a patient who had been diagnosed with extensive pulmonary tuberculosis with the following resistance profile: Resistant to Rifampicin, Isoniazid, Pyrazinamide, Streptomycin, and Levofloxacin. Susceptible to Bedaquiline, Delamanid, Clofazamine,

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Linezolid, Ethambutol, Prothionamide, and aminoglycosides. Of note, the index patient had received repeated courses of levofloxacin monotherapy for "lower respiratory tract infections" prior to TB diagnosis.

Patient A is a 90 year old female with medical history of ischaemic heart disease and cognitive impairment. She had an Interferon-Gamma Release Assay carried out due to the aforementioned contact, which was reactive. Chest x-ray suggested right basal consolidation, and she went on to have a CT of her chest, which showed: "Right hilar and right lower lobe intra-lobar lymphadenopathy. Impacted and dilated airways within the right lower lobe with some associated peripheral consolidation." She was non-productive and unable to provide a sputum sample. She progressed to have a bronchoscopy, which was smear negative, but PCR and culture positive with resistance detected to rifampicin, isoniazid, pyrazinamide, streptomycin and fluroquinolones. Whole Genome Sequencing had one Single Nucleotide Polymorphism difference from the index case, and on culture had the same susceptibility profile, apart from susceptibility to levofloxacin.

After discussion with the British Thoracic Society, drug resistant TB management service (BTS MDRTB), we elected to commence her on Bedaquiline, Pretomanid and Linezolid. It was ultimately decided we would not add levofloxacin to her regime.

She initially suffered from nausea as an inpatient which was managed with anti-emetics and improved with time. She did not miss any doses. Follow up CT chest at two months showed improvement. She did not have a repeat bronchoscopy due to increasing frailty but sputum samples were smear, PCR and culture negative. She was discharged home, with isolation and respiratory precautions, completing 6 months of treatment with no further adverse events. Blood monitoring, ECGs, peripheral neuropathy and Ishihara screens were normal throughout.

Patient B is a 59 year old female with no past medical history of note. She also had a reactive IGRA and therefore went onto have a CT of her chest which showed non-specific enlarged right hilar lymph nodes measuring up to 14 mm and a right lower lobe 5 mm pulmonary nodule. PET Scan showed a mildly avid right hilar lymph node, and biopsy of this via endobronchial ultrasound was smear negative, but PCR positive for TB with genotypic Rifampicin resistance detected. Given her close contact with the index case and Patient A, antibiotic resistances were inferred.

She was also commenced on Bedaquiline, Pretomanid and Linezolid, again after discussion with the BTS MDRTB. There was no growth after 12 weeks of mycobacterial culture.

She initially suffered from gastritis which settled with addition of omeprazole. She completed 6 months of treatment with no further adverse events. Blood monitoring, ECGs, peripheral neuropathy and Ishihara screens were normal throughout.

Discussion

BPaL has displayed superior outcome rates, fewer adverse events, reduced cost and has a shorter duration. Despite being licenced in the UK, Northern Ireland is the only nation of the UK that has been able to access Pretomanid due to commissioning policy in England, Scotland and Wales. We were able to access Pretomanid through a cost per case application to the Trust, presenting evidence of effectiveness, improved side effect profile and reduced cost compared to the standard of care regime. These cases provide further evidence that Pretomanid based regimens should be sought as a more effective and well-tolerated treatment where possible.

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Clinical Paper

Current Practice and Outcomes of Patients Undergoing Surgical Resection for Renal Cell Metastases to the Pancreas in Northern Ireland

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ABSTRACT

Metastatic tumours to the pancreas are rare but most commonly arise from primary renal cell carcinoma (RCC). Contrary to other metastatic malignancies, metastatic RCC demonstrates indolent behaviour; with a long latency between primary tumour presentation and the development of metastasis, as well as a predilection to isolated pancreas-only disease. As such, pancreatic metastasectomy has evolved as a treatment option for patients with metastatic RCC; reported to associate with improved outcomes in selected patients.

The aim of this study was to describe the clinicopathological characteristics and patient outcomes in a series of patients undergoing pancreatic resection for metastatic RCC in a high volume, regional hepatopancreatobiliary (HPB) centre.

Design Retrospective review of all patients who underwent pancreatic metastasectomy for pathologically-confirmed metastatic RCC over an eighteen-year period. Clinicopathological characteristics and outcomes were collected and analysed.

Results Fifteen patients underwent pancreatic resection for metastatic RCC between October 2004 and October 2022. Two patients underwent synchronous nephrectomy and pancreatectomy. In thirteen patients, the pancreas was the only site of metastatic disease. For those with metachronous metastases, the median disease-free interval (DFI) was 126 months from initial nephrectomy.

Five-year disease-free and overall survival were 32.7 % and 63.3 %, respectively. No clinicopathological factor was found to associate with overall survival (OS); however, patients with synchronous metastatic disease had a significantly shorter disease-free survival ($p = 0.029$). Similarly, patients with a longer DFI (≥ ten years) between RCC primary and the development of pancreatic metastases had a trend towards improved OS ($p = 0.074$).

Post-operative morbidity and mortality rates were comparable to that of pancreatic surgery for primary pancreatic pathology.

Conclusion This case series supports the role of pancreatic resection in patients with metastatic RCC, with acceptable rates of morbidity and mortality and favourable patient outcomes. The long DFI between nephrectomy and pancreatic metastases highlights the importance of long-term follow-up for patients diagnosed with RCC.

Introduction

Metastatic tumours within the pancreas are rare; accounting for 2 – 5 % of pancreatic malignancy.[1] Renal cell carcinoma (RCC) is the most common primary tumour to metastasise to the pancreas, with studies reporting close to two-thirds of all pancreatic metastases arising from RCC.[2] RCC is the most common renal malignancy among adults. Approximately 20 – 30 % of patients have metastatic disease at presentation, while 30 – 50 % will develop metastases following potentially curative nephrectomy; of which 2 – 11 % may occur in the pancreas.[3]

Unlike other metastatic primary malignancies that present with disseminated disease, RCC metastases are frequently isolated to the pancreas alone. As such, they may be amenable to surgical resection and this has been reported to improve survival in selected patients with acceptable morbidity and mortality rates when performed in high volume, specialist centres.[4]

Overall, the five-year survival of patients with metastatic RCC has been reported as low as 10 – 15 %;[1] however, a recent systematic review on the outcomes of pancreatic resection for metastatic RCC has reported a five-year survival rate of 53.9 % (26 – 75 %).[4]

The aim of this study was to evaluate outcomes in patients undergoing pancreatic metastasectomy for metastatic RCC in the regional hepatopancreatobiliary (HPB) unit in Northern Ireland and determine if any clinicopathological variables influence outcome in these patients.

Methods

Study Design

This was a retrospective study of patients who underwent pancreatic resection for histologically-confirmed metastatic

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RCC in the regional HPB unit in Northern Ireland between October 2004 and October 2022.

The inclusion criteria comprised a diagnosis of RCC of any histological subtype, the presence of synchronous or metachronous pancreatic metastases and treatment of pancreatic metastases by surgical resection. Patients who met these criteria and had metastatic disease in other organs were also included. Eligible patients were identified from the centralised, regional pathology records. Patients who underwent exploratory-only surgery were excluded, as were patients who underwent pancreatic resection for local invasion from a synchronous, primary RCC.

Outcome variables

Clinicopathological data were collected including patient age, gender, presence or absence of extra-pancreatic metastases, and the interval between primary tumour resection and diagnosis of pancreatic metastases. Histopathology results of the RCC primary and the pancreatic secondary tumour were reviewed to include the International Society of Urological Pathology (ISUP) tumour grade, the number and size of pancreatic metastases, the resection margin (R) status, presence of lymphovascular (LVI) or perineural invasion (PNI) and the involvement of any resected regional lymph nodes.

With respect to the pancreatic resection; the nature of the pancreatic surgery performed, post-operative morbidity and 90-day mortality were collected, as well as the details of any adjuvant therapy received. Post-operative complications were classified according to the Clavien-Dindo classification system,[5] with grade 3 or higher considered as major morbidity. Post-operative pancreatic fistula (POPF) was classified and scored according to the 2016 International Study Group of Pancreatic Fistula (ISGPS) consensus,[6] with Grade B or C considered clinically relevant.

The primary outcome of overall survival (OS) was determined and defined as the time from pancreatic metastasectomy to the date of death from any cause, or most recent date of follow-up if the patient was still alive. Disease-free interval (DFI) was defined as the time from nephrectomy to the diagnosis of pancreatic metastasis, while disease-free survival (DFS) refers to the time between pancreatic metastasectomy and the diagnosis of recurrent disease on imaging. Local recurrence refers to that within the pancreatic bed, remnant or regional lymph nodes, whilst systemic recurrence refers to distant organ sites.

Statistical Analysis

Categorical variables are presented as frequency and percentage, and were compared using Chi-square test or Fisher's exact test, as appropriate. Continuous variables are described as median and interquartile range (IQR) and were compared using the Mann–Whitney U test. Median OS and DFS were calculated using Kaplan-Meier survival estimates and survival curves compared using log-rank analysis. This was presented as median and IQR. Univariate analysis was used to determine if any clinicopathological variable influenced DFS or OS. Variables with a p-value < 0.05 were included in a Cox proportional multivariate hazards regression analysis to identify independent predictors of DFS or OS. Coefficients were reported as hazard ratios (HRs) and corresponding 95 % confidence intervals (CIs). A p-value < 0.05 was considered statistically significant and statistical analyses were performed using the SPSS for Windowsä version 28.0 (SPSS Inc, Chicago, Ill, USA).

Results

Presentation

Between October 2004 and 2022, 15 patients underwent pancreatic resection for metastatic RCC, with a male-to-female ratio of 2:1. The median age at diagnosis of the primary RCC was 54 years (IQR 48 – 62 years), compared to 61 years (IQR 57 – 70 years) for the pancreatic metastasis. The clinicopathological characteristics of the primary tumour are summarised in Table 1 and those of the pancreatic secondary tumour are shown in Table 2.

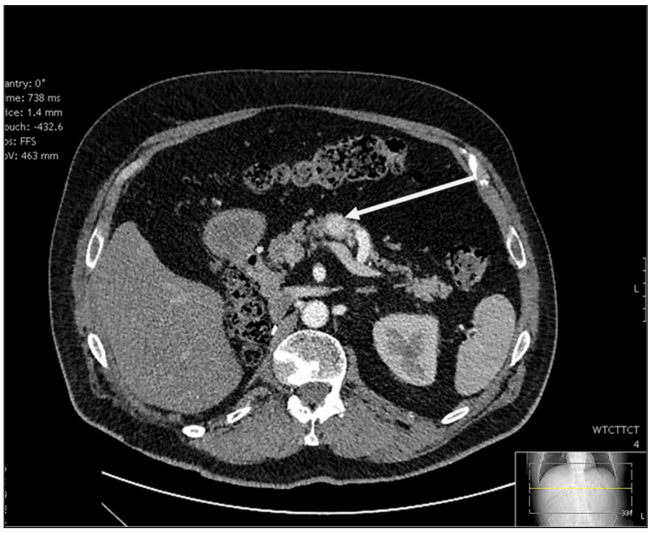


Figure 1
Contrast-enhanced cross-sectional computed tomography (CT) image demonstrating a characteristic arterial enhancing lesion within the body of the pancreas.

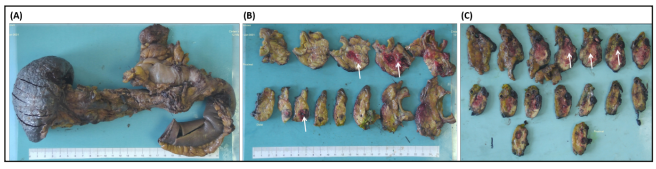


Figure 2
Total pancreatectomy and splenectomy resection specimen performed for multifocal pancreatic RCC metastases.

(A) Posterior view of intact resection specimen.

(B) Sections through pancreatic head. Tumour indicated by white arrows.

(C) Sections through pancreatic tail. Tumour indicated by white arrows

All 15 patients underwent radical nephrectomy; with the majority of primary tumours located in the left kidney (n = 9, 60.0 %). Two patients presented with synchronous pancreas-only metastases (13 %) and underwent synchronous nephrectomy and pancreatic resection. Of the 13 patients with metachronous pancreatic metastases, the median DFI was 126 months (IQR 91 – 157 months).

Most patients with metastases to the pancreas were asymptomatic (n = 11, 73.3 %); diagnosed incidentally on surveillance imaging following nephrectomy (Table 2). Among the four who had symptoms, three presented with abdominal pain and one presented with painless, obstructive jaundice.

Prior to pancreatic resection, all patients had an abdominal computerised tomography scan (CT) demonstrating an arterial enhancing pancreatic lesion (Figure 1). Five (33.3 %) patients had an endoscopic ultrasound (EUS) performed, and two of these had a biopsy obtained confirming a diagnosis of RCC metastasis prior to surgery. Thirteen (86.7 %) had isolated pancreas-only metastases while two (13.3 %) had renal recurrence in the contralateral kidney as well as pancreatic metastases.

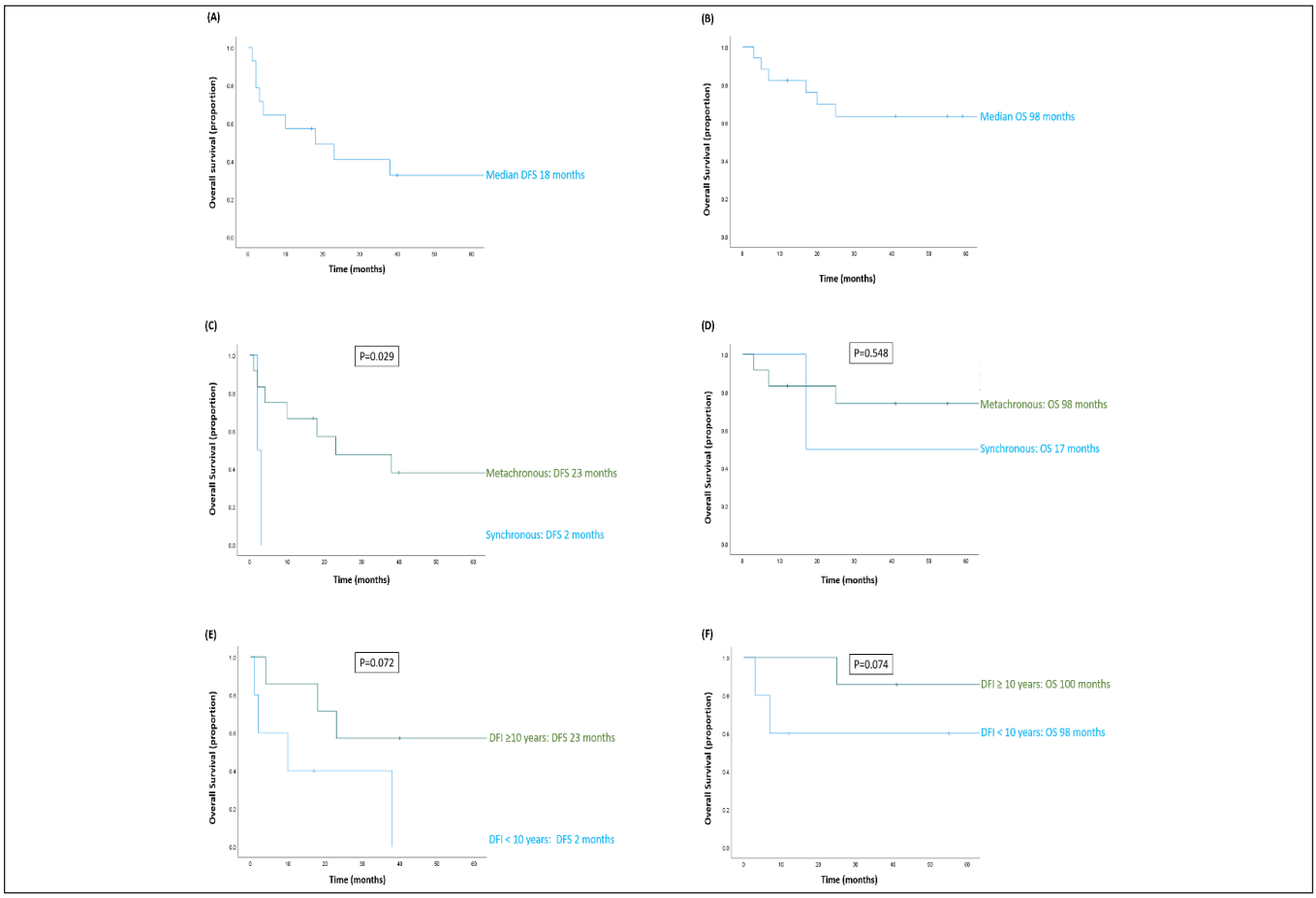
Metastases were located most frequently in the body or tail (n = 9, 60.0 %), followed by the head, neck or uncinate process (n = 3, 20.0 %) of the pancreas. Six patients had more than one pancreatic lesion, and in three patients these were located in more than one region of the pancreas (n = 3, 20.0 %) (Figure 2 A – C).

There was no association between the location of the primary RCC and the site of metastasis within the pancreas (Supplementary Table S1, p = 0.51).

Surgery

Based on tumour location, nine patients (60.0 %) underwent distal pancreatectomy (DP) with splenectomy, three (20.0 %) underwent a Whipple's pancreaticoduodenectomy and three

Figure 3 Kaplan-Meier Survival Curves



(A) Median disease-free survival in patients who underwent pancreatic resection for metastatic RCC.
(B) Median overall survival in patients who underwent pancreatic resection for metastatic RCC.
(C) Median disease-free survival in patients with metachronous pancreatic metastases compared to those with synchronous pancreatic metastases.
(D) Median overall survival in patients with metachronous pancreatic metastases compared to those with synchronous pancreatic metastases.
(E) Median disease-free survival in patients stratified by disease-free interval.
(F) Median overall survival in patients stratified by disease-free interval.

Supplementary Table S1

Primary tumour location and site of pancreatic metastasis.

Location of pancreatic metastases	Location of Primary RCC	
	Left kidney	**Right kidney**
Head/neck/uncinate	**2**	**1**
Body/tail	**4**	**5**
Multifocal	**2**	**1**

Supplementary Table S2

Statistical analysis of clinicopathological variables with respect to disease-free and overall survival.

	Disease-free survival (DFS)		**Overall survival (OS)**	
	Univariate Analysis Median DFS [months (IQR)]	**p**	**Univariate Analysis** Median OS [months (IQR)]	**P**
Gender				
Male (n=9)	23 (4 – 89)	0.426	100 (100-112)	0.156
Female (n=5)	10 (2 – 38)		98 (17 -98)	
Age at pancreas resection				
< 65 years (n=8)	10 (2 -23)	0.148	98 (17 -100)	0.396
≥ 65 years (n=6)	4 (1 – 4)		7 (5 out of 6 alive)	
Primary tumour location				
Left (n=9)	18 (3 – 38)	0.200	98 (25 – 112)	0.839
Right (n=5)	89 (10 – 89)		100 (17 -100)	
Primary tumour Fuhrman grade				
1 (n=0)	-		-	
2 (n=5)	89 (23 -89)	0.187	100 (100 – 112)	0.175
3 (n=5)	10 (3 – 18)		25 (17 -25)	
4 (n=4)	2 (1 -2)		7 (3 -7)	
Primary tumour (T) stage				
T1 (n=2)	23 (2 -23)		3 (-)	
T2 (n=4)	18 (1 -89)	0.933	25 (7 -100)	0.354
T3 (n=8)	10 (3 -10)		98	
T4 (n=0)	-		-	
Primary tumour node (N) stage				
N0 (n=4)	1 (1 – 3)	0.013	7 (-)	0.555
NX (n=10)	23 (10 -89)		100 (25 -112)	
DFI (months)				
< 120 months (n=5)	10 (2 – 38)	0.072	98 (7 – 98)	0.074
≥ 120 months (n=7)	89 (18 – 89)		100 (100-112)	
Interval from primary to pancreatic metastasis				
Metachronous (n=12)	2 (2 -3)	**0.029**	98 (25 – 100)	0.548
Synchronous (n=2)	23 (4 – 89)		17 (-)	
Size of pancreatic metastasis				
< 3cm (n=7)	18 (4 -23)	0.728	112 (25 -112)	0.869
≥ 3cm (n=4)	3 (1 -3)		7 (3 out of 4 alive)	
Type of surgery				
Whipples pancreaticoduodenectomy (n=2)	4 (4 -22)		- (both alive)	
Distal pancreatectomy (n=9)	23 (10 -89)	0.352	98 (25 -100)	0.095
Total pancreatectomy (n=3)	2 (1 -2)		7 (3 -7)	
Pancreatic metastases Node (N) stage				
N0 (n=11)	18 (2 -89)		100 (17 -100)	
N1 (n=1)	10 (-)	0.774	-	0.640
NX (n=2)	23 (23 -38)		98 (98- 112)	
Pancreatic metastases margin (R) status				
R0 (n=7)	38 (3 -38)	0.578	98 (25 -98)	0.157
R1 (n=4)	2 (1 -10)		7 (3 -7)	
Lymphovascular invasion (LVI) status				
LVI present (n=11)	10 (2 -23)	N/A	98 (17 -112)	N/A
LVI absent (n=0)	-		-	
Unknown (n=3)	-		-	
Perineural invasion (PNI) status				
PNI present (n=2)	4 (4 -10)		- (both alive)	
PNI absent (n=3)	3 (1 -18)	0.946	25 (7-25)	N/A
Unknown (n=9)	-		-	
Site of RCC metastases				
Isolated pancreas only (n=12)	23 (2 -89)	0.333	98 (17 -100)	0.668
Extrapancreatic metastasis (n=2)	4 (4 -18)		25 (-)	
Number of pancreatic metastases				
Multifocal (n=6)	18 (3 -89)	0.208	98 (7 -112)	0.701
Single (n=8)	10 (2 -23)		100 (25 -100)	
Clavien Dindo complication ≥3				
Yes (n=3)	18 (18 -89)	0.333	100 (25 -100)	0.893
No (n=11)	10 (2 -10)		98 (17 -112)	

Table 1

Primary TUMOUR Characteristics		
	NUMBER	**%**
Gender (M:F)	10 : 5	66.7 : 33.3
Age at diagnosis (years)	54 (48 – 62)	
Location		
Left kidney	9	60.0
Right kidney	6	40.0
Radical nephrectomy	15	100
Histological subtype		
Clear cell	15	100
WHO/iSUP* grade		
1	0	0
2	4	26.7
3	7	46.7
4	4	26.7
AJCC Tumour (T) stage		
T1	2	13.3
T2	5	33.3
T3	8	53.3
T4	0	0
AJCC Node (N) stage		
N0	4	26.4
N1	0	0
NX	11	73.3
Interval to pancreatic metastases		
Synchronous	2	13.3
Metachronous	13	86.7

Table 2

Characteristics of Pancreatic Metastases		
	NUMBER	**%**
Age at diagnosis (years)	61 (57 – 70)	
Disease-free interval (months)	126 (91 - 157)	
Presentation		
Asymptomatic	11	73.3
Symptomatic	4	26.7
Investigations		
US	7	46.7
CT	15	100.0
MRI/MRCP	6	40.0
PET-CT	1	6.7
EUS	5	33.3
+ biopsy	2	13.3
Tumour Location		
Head/uncinate	3	20.0
Body/tail	9	60.0
Multifocal	3	20.0

Table 2 continued

Type of surgery		
Whipple's pancreaticoduodenectomy	3	20.0
Total pancreatectomy & splenectomy	3	20.0
Spleen-preserving distal pancreatectomy	1	6.7
Distal pancreatectomy & splenectomy	8	53.3
Resection of other organs Subtotal gastrectomy Synchronous nephrectomy	 1 2	
Surgical approach		
Open	13	86.7
Laparoscopic	2	13.3
Tumour size (mm)	25 (19 – 38)	
Number of pancreatic metastases Single Multiple	 9 6	 60.0 40.0
Lymphovascular invasion (LVI)		
Yes	11	73.3
No	0	0
Unknown	4	26.7
Perineural invasion (PNI)		
Yes	2	13.3
No	3	20.0
Unknown	10	66.7
Margin (R) status		
R0	7	46.7
R1	5	33.3
R2	2	13.3
Unknown	1	6.7
Lymph node status		
Positive	1	6.7
Negative	14	93.3

had a total pancreatectomy with splenectomy (20.0 %). Open surgery was the most common approach, with laparoscopic distal pancreatectomy and splenectomy performed in two patients (20.0 %). One patient required a distal gastrectomy as well as distal pancreatectomy due to local invasion of the pancreatic metastasis into the distal stomach.

The overall post-operative morbidity rate was 40.0 %, with 26.7 % (n = 4) developing a Clavien-Dindo grade IIIa or higher complication. Significant morbidity most commonly followed the development of a post-operative pancreatic fistula (POPF) which was observed in six patients (40.0 %). According to the revised ISGPS definition for POPF,[6] 16.7 % (n = 3) developed a grade B fistula requiring insertion of a radiological drain, while the remaining three were grade C POPFs (16.7 %), two of whom required a reoperation for post-pancreatectomy haemorrhage. One patient with a grade C POPF died within 90 days of surgery, resulting in a 6.7 % 90-day mortality rate for the cohort.

Pathology

Histological data for the primary RCCs and pancreatic metastases are summarised in Table 1 and Table 2, respectively. All primary RCCs demonstrated clear cell morphology, with the majority grade 3 according to the The World Health Organisation/International Society of Urological Pathology (WHO/ISUP) grading system for renal cell carcinoma. The median size of the metastatic pancreatic tumour was 25 mm (IQR 19 – 38 mm). Nine patients had a solitary pancreatic metastasis (60.0 %), while six had multifocal metastases within the pancreas (40.0 %). Only one patient was found to have metastatic disease within their resected regional lymph nodes (6.7 %).

Survival

Excluding the 90-day post-operative mortality, median follow-up from pancreatic metastasectomy was 61 months (IQR 16 – 89 months), during which time ten (71.4 %)

patients developed recurrent disease and seven patients died (50.0 %).

The median DFS was 18 months (IQR 3 – 89), with 1-, 3- and 5-year DFS of 57.1 %, 40.8 % and 32.7 %, respectively (Figure 3A). Five of the ten patients (50.0 %) developed recurrence within six months of pancreatic surgery, of which two were alive at last follow-up.

Three patients developed recurrence at a single organ site; either the lung (n = 1) or liver (n = 2) and the remaining seven developed disseminated metastases. In order of frequency, the commonest sites of relapse were the liver (n = 7), contralateral kidney (n = 7), lung (n = 6), bone (n = 3) and pancreatic remnant (n = 2). No patient underwent further surgical resection for disease relapse. Five patients (33.3 %) received systemic treatment for recurrent disease; two with Sunitinib monotherapy and three with combination targeted therapies. Locoregional therapies were utilised in four patients (40.0 %); with radiofrequency ablation (RFA, n = 2) or cryo-ablation (n = 1) used for renal recurrence, and combination transarterial chemoembolisation and RFA utilised in the same patient to manage their liver metastases.

Median OS was 98 months (IQR 25 - 100) from the time of pancreatic metastasectomy; 1-, 3- and 5-year overall survivals were 85.7 %, 70.1 % and 63.3 %, respectively (Figure 3B).

For patients presenting with synchronous, isolated pancreas-only metastases, their OS was 17 months from their synchronous nephrectomy and pancreatic resection, compared to 98 months for those who presented with metachronous pancreatic metastases (Figure 3C, p = 0.548). These patients had a significantly shorter DFS compared to those with metachronous disease (DFS 2 months *vs.* 23 months, p = 0.029).

Survival analysis was limited by the small number of cases. On univariate analysis, no clinicopathological variable was found to associate with OS (Supplementary Table S2). A trend towards improved survival was observed in patients with a longer DFI (Figure 3C - D, p = 0.074). Only one patient had lymph node involvement at the time of pancreatic resection. Their median DFS was 10 months compared to 18 months in node negative patients, and 23 months in those whose nodes were not assessed (p = 0.774). Despite a shorter time to disease relapse, the patient was still alive at last follow-up.

Discussion

Renal cell carcinoma has a tendency to metastasise to the pancreas but displays relatively indolent behaviour in contrast to other metastatic tumours, making surgical resection a viable treatment option. Accordingly, pancreatic resection for metastatic RCC has now been reported in a number of published case series from specialist centres.[1, 3, 7-9] While case numbers are small, results from these series and systematic reviews suggest that pancreatic metastasectomy associates with favourable survival outcomes, and with acceptable rates of morbidity and mortality.[4,9]

This study describes the outcomes of patients undergoing pancreatic resection for metastatic RCC in a specialist HPB centre in Northern Ireland over a consecutive eighteen-year period. Close to one patient per year underwent pancreatic resection for metastatic RCC, representing less than 2 % of all pancreatic resections performed in the region per annum. Results confirm encouraging long-term outcomes in patients undergoing surgery for metastatic disease, with a five-year survival rate of 63 % and a median OS exceeding eight years.

The vast majority of pancreatic RCC metastases are metachronous, with synchronous metastases observed in just two patients in this study. A long latency period between primary nephrectomy and development of pancreatic metastasis is well recognised; with an estimated mean DFI of 105 months based on systematic reviews.[4] In our cohort, we observed a DFI of 126 months following nephrectomy, highlighting the importance of long-term surveillance of patients up to, and even beyond, ten years post-nephrectomy. This is particularly important when we consider that over 70 % of these patients were asymptomatic and had their metastases diagnosed on surveillance investigations.

Radiologically, pancreatic RCC metastases may be difficult to distinguish from primary pancreatic adenocarcinoma. A high index of suspicion is necessary when a solid, hypervascular pancreatic mass is detected on CT or MRI in a patient with a history of RCC (Figure 1). Differential diagnoses include other hypervascular neoplasms such as neuroendocrine tumours. For the majority, an oncological history aids the correct diagnosis. However, most cases are amenable to endoscopic ultrasound (EUS) and biopsy when the diagnosis is uncertain.

Evidence to support the role of surgery in the management of RCC pancreatic metastases is based on small case series, with a lack of randomised or case-control series comparing surgical and non-surgical treatment options. Non-matched controlled cohorts[10] and systematic reviews[2,4] suggest that surgery associates with prolonged DFS and OS compared to conservative management.

Similar to surgery for primary pancreatic malignancy, the aim of pancreatic metastasectomy is to excise the tumour with clear margins whilst preserving as much normal pancreatic parenchyma as possible. The nature of surgery performed depends on the location of the metastatic tumour and whether it is solitary or multifocal, with lesions within the head or uncinate process requiring a Whipple's pancreaticoduodenectomy, while lesions within the body or tail may be resected with a distal pancreatectomy. Enucleation has been described in small isolated lesions[1,3,11] but was not performed in our cohort. This approach is generally avoided due to the high risk of tumour recurrence and significant risk of POPF.[1,11] While metastases may often be multifocal within the pancreas, a total pancreatectomy is not always

necessary provided a clear margin can be achieved. Although a total pancreatectomy does not carry the risk of POPF, this approach is avoided where possible due to the lasting impact of the resulting insulin-dependent brittle diabetes on quality of life.[12] Furthermore, it has been shown that a radical total pancreatectomy or the addition of a splenectomy does not appear to reduce recurrence or associate with improved OS.[4] In our study, the three patients who underwent total pancreatectomy had multifocal metastases throughout the gland. One patient was identified on preoperative CT to require a total pancreatectomy for clearance, while for the remaining two this decision was made intraoperatively.

Unlike primary pancreatic adenocarcinoma, involvement of the regional lymph nodes is an uncommon feature of metastatic RCC and was observed in just one case (6.7 %). Standard oncological resections require excision and assessment of the regional lymph nodes to provide prognostic information and to reduce the risk of disease recurrence. A survival benefit of peripancreatic lymphadenectomy in metastatic RCC has not been established[4] and given the low rates of lymph node involvement associated with pancreatic RCC metastases, routine lymphadenectomy may be of limited value.

Traditionally, pancreatic surgery associates with significant morbidity and mortality rates. Recent advances in surgical approach and post-operative care have led to a reduction in these rates.[11] The overall morbidity rate of 44.4 % in our study is comparable to that published in a recent systematic review,[9] with rates ranging from 12.5 % to 61.9 %. Morbidity rates as low as 38.5% and mortality rates of less than 5 % have been observed in specialist units performing high numbers of pancreatic resections.[2-4]

Despite improvements in the morbidity associated with major pancreatic resection, not all patients will be suitable for major surgery. Furthermore, recurrence rates following metastasectomy are high; ranging from 39 – 100 % across various single and multicentre studies.[3,4,9] As such, many advocate systemic therapy over surgery. Traditionally, RCC response rates to chemotherapy and radiotherapy have been poor. However, the development of targeted therapies, such as tyrosine kinase inhibitors, mammalian target of rapamycin (mTOR) inhibitors, vascular endothelial growth factor (VEGF) inhibitors, and immune checkpoint inhibitors has led to improved response rates; but non-response remains a problem.[13] As such, combination systemic therapy is recommended.[14]

While no study has compared surgery to immune checkpoint inhibitor therapy, similar survival outcomes with tyrosine kinase inhibitors have been demonstrated compared to metastasectomy.[13] However, surgery has the advantage that it may achieve disease-free control in a proportion of patients compared to systemic therapy, but at the expense of higher morbidity and mortality rates.[13]

Ultimately, due to its low incidence, there is a lack of prospective, randomised or case-control evidence to support surgery over systemic therapies. Formal discussion involving both urological and hepatopancreatobiliary multidisciplinary teams is crucial and findings from our series would suggest that case-selection for metastasectomy is important. While the small numbers have limited identification of prognostic factors in metastatic RCC, we observed a significantly shorter DFS in those with synchronous metastases, and a trend towards improved OS in those with a longer latency period between nephrectomy and development of pancreatic metastases. This is a finding that has been observed by others,[4,9,15] and suggests that synchronous metastases or a short DFI heralds a more aggressive tumour biology. A strategy of selective upfront systemic therapy in these high-risk patients to assess biological response may be more appropriate and avoid pancreatic resection with its associated morbidity in those at risk of early disease relapse. Although not demonstrated in our study, other factors that have been shown to associate with high recurrence rates and worse prognosis include: the presence of extra-pancreatic metastases prior to pancreatic metastases[15,16] and the presence of vascular invasion[11] or lymph node metastases.[11,16]

Despite high recurrence rates, prolonged survival can still be achieved in patients with metastatic RCC. Our recurrence rate was 71.4 % (n = 10) over a median follow-up of 61 months, with a DFS of 18 months. Contrary to other reports of a predilection to single organ recurrence, 70 % of cases in our cohort had disease relapse at more than one site. Despite the high recurrence rate and short DFS observed in this study, the median OS was 98 months and 5-year survival 63.3 %; similar to rates reported by others.[6] These findings highlight that prolonged survival can still be achieved in patients with relapsed metastatic RCC utilising combinational systemic therapies, as well as locoregional treatments to manage oligometastatic disease. Radiofrequency ablation in particular has emerged as a safe and effective modality to manage relapse in the contralateral kidney,[17] as well as the pancreatic remnant,[18] liver[19] or lung.[20]

Conclusion

Our results show that surgery for RCC metastases to the pancreas carries comparable morbidity and mortality rates to that of pancreatic resection for primary pancreatic cancer, yet with a more favourable overall prognosis. The indolent biology of RCC, with long DFI and isolated single site metastases mean that metastatic RCC does not carry the poor prognosis associated with other primary abdominal malignancies. Despite high recurrence rates and a short DFS, prognosis for these patients is favourable. Locoregional therapies may now be added to the armamentarium of surgery, tyrosine kinase and immune checkpoint inhibitors. Similar to the evolution of metastatic colorectal cancer management, a multidisciplinary, multimodal approach may be utilised to control metastatic RCC and achieve excellent patient outcomes.

Key words: Pancreatic metastases, renal cell carcinoma

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Clinical Paper

It takes a village to raise a child- A multidisciplinary approach to promoting paediatric health literacy in cystic fibrosis

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ABSTRACT

Background

In Northern Ireland, approximately 550 people with cystic fibrosis (PwCF) attend the regional paediatric and adult centres within the Belfast Health and Social Care Trust. This autosomal recessive chronic condition necessitates regular clinical monitoring and a high treatment burden, as well as time implications for the maintenance of respiratory devices. Development of health literacy skills at an early age and promoting children with CF (CwCF) to take an active role in their healthcare has many advantages relating to their long-term self-care in preparation for transition from paediatric to adult care, decision-making and partnership engagement with the CF-multidisciplinary team (CF-MDT).

Methods

This study comprised of four individual components, namely (i) an analysis of responses (n=24) to an anonymous questionnaire from the Northern Ireland CF community to determine where PwCF and their carers/families seek healthcare information; (ii) to co-produce paediatric-facing healthcare educational resources, namely colouring/storybooks and animations, relating to the importance of microbiological sampling, nebuliser hygiene and pancreatic replacement therapy (PERT) in conjunction with the CF-MDT, CwCF, parents, students and animators and (iii) assess the readability of these new materials using Flesch Reading Ease (FRE), Flesch-Kincaid Grade Level (FKGL), SMOG Index and Gunning Fog (GF) Index and compare these with paediatric and adult-facing materials available from CF charities, pharmaceutical companies and the scientific literature. The final component (iv) examined parents' and children's knowledge of PERT pre- and post- viewing the bespoke animation.

Results

(i) The findings showed that the CF community relied upon the CF-MDT as their primary source of healthcare information, most frequently consulting the Doctor/CF Consultant (61.5%), the physiotherapist (61.6%), the nurse (57.7%), followed by the CF dietitian (34.6%), as well as the Cystic Fibrosis Trust (38.4%). Pharmaceutical websites were least consulted with 69.2% of respondents never consulting such resources.

(ii) Reflective learning points from this co-production of resources are provided to assist other healthcare teams preparing engaging and effective healthcare information for the paediatric service user.

(iii) The readability of the new paediatric-facing materials prepared by the CF-MDT was appropriate for primary school aged-children and was not statistically different from paediatric-facing information prepared by charities or pharmaceutical companies. A statistical difference was noted in relation to the prepared materials in comparison with adult-facing charity information (p=0.04; 0.02; 0.03; 0.04) and

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scientific abstracts (p<0.0001), which were more complex in terms of readability parameters, FRE, FKGL, SMOG and GF, respectively.

(iv) Following viewing the PERT animation, both parents' and children's knowledge had improved with 50% of children's understanding determined as moderate/little understanding (pre-animation) and 50% very good/ 42 % good (post-animation).

Conclusions

Healthcare professionals are important custodians of healthcare information for their service user population. Paediatric healthcare teams have a responsibility to aid in the development of health literacy skills at an early age and promoting children to take an active role in their healthcare. The use of colouring/storybooks and animations are excellent media to initiate discussions and develop partnerships in paediatric healthcare in an engaging and informative manner. Whilst this study related to CwCF, the findings may be applicable to the health literacy of children of other disease states. For optimum impact, the healthcare team should (i) co-produce these media with the paediatric service user, their families and animation teams and (ii) ensure that the readability, legibility and formats are appropriate, informative and engaging for the target age-group.

Introduction

Cystic fibrosis (CF) is an autosomal recessive condition caused by mutations in the cystic fibrosis transmembrane regulator (CFTR) gene which codes for a protein whose function is to transport chloride and bicarbonate ions across the apical surface of epithelial cells[1]. Mutations in this gene results in an imbalance of ions and surface ion transport causing a build-up of sticky mucus in various organs, particularly the lungs. The resulting impaired mucociliary clearance in the lungs promotes chronic inflammation and infection which ultimately causes damage to the CF lungs[1]. Other organs are also affected which necessitates the condition to be managed by means of a multidisciplinary Team (MDT) approach primarily relating to the treatment and management of (i) ensuring optimal oxygen saturation and respiration, (ii) lung infections, (iii) pancreatic insufficiency; (iv) gut complications, (v) nutritional support, (vi) CF-related diabetes (CFRD), (vii) therapeutic treatment plans involving medications, (viii) airway clearance, (ix) lung transplantation, (x) infection prevention and control, as well as other related clinical needs e.g., gynaecology, obstetrics, genetic counselling[2] (Figure 1). The resulting high treatment burden comprising of oral, intravenous and nebulised medications, respiratory physiotherapy regimes and exercise coupled, with review appointments, in-patient

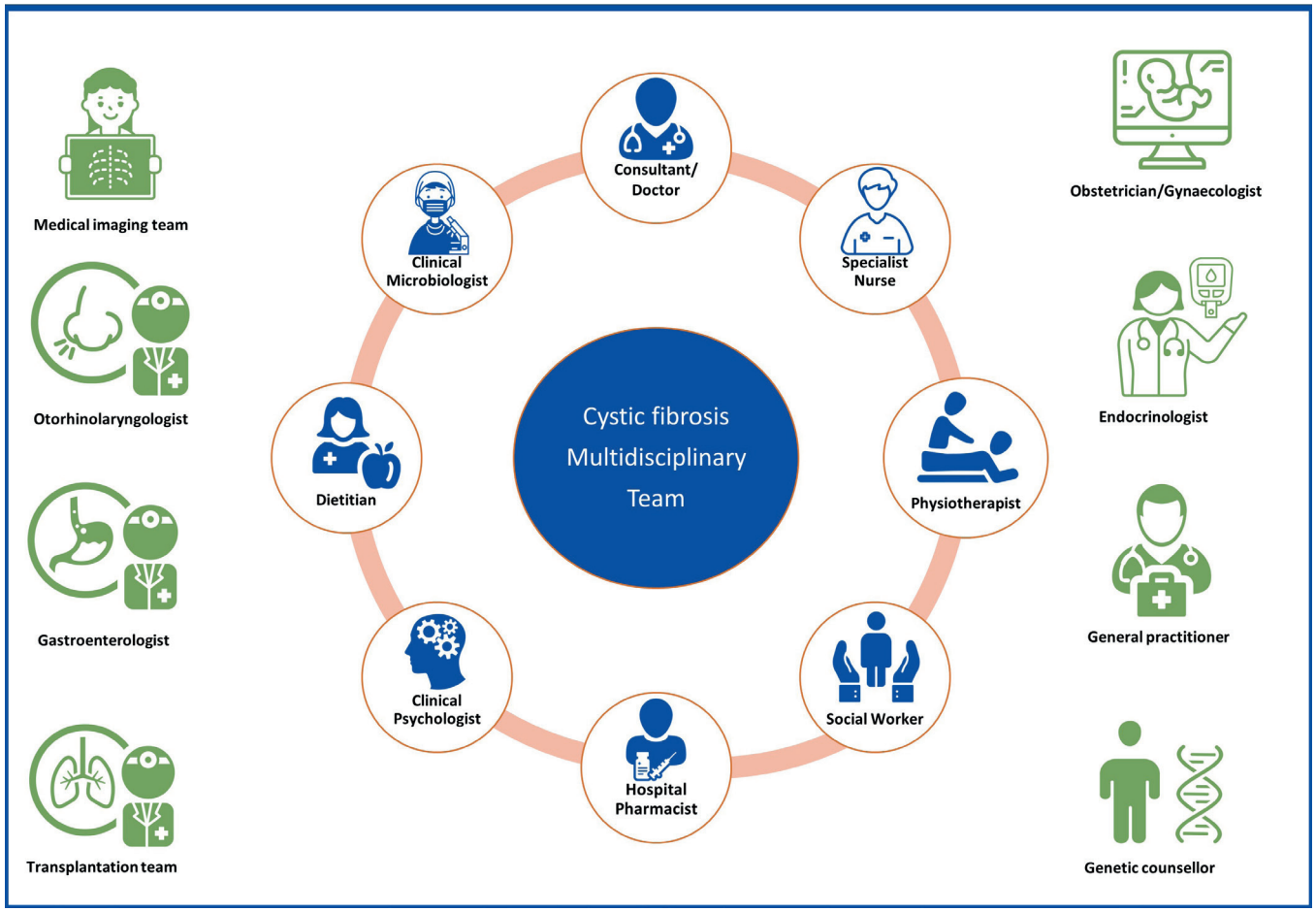


Figure 1:
The structure of the core cystic fibrosis multidisciplinary team and other associated specialisms

stays and the requirement for a plethora of samples to be taken and tests to be performed, all of contribute to patient anxiety, as well as impacting on compliance and adherence.

Health literacy is an important aspect of the management of cystic fibrosis and the role of effective communication and healthcare educational approaches used by the MDT to support individuals with CF and their families plays a fundamental role in alleviating anxieties and empowering individuals to take an active role in their healthcare management[3]. Health literacy has various definitions[4], however a recent systematic review by Liu et al. (2020) defines health literacy as the '*ability of an individual to obtain and translate knowledge and information in order to maintain and improve health in a way that is appropriate to the individual and system contexts*'[5]. These authors also defined three broad themes relating to health literacy in relation to *"(1) knowledge of health, healthcare and health systems; (2) processing and using information in various formats in relation to health and healthcare; and (3) ability to maintain health through self-management and working in partnerships with health providers*"[5].

It has been reported that persons with cystic fibrosis (PwCF) have higher health literacy scores than those of the general public[6], which has been suggested to be due to the frequent interaction between PwCF and the multidisciplinary members of the CF team. Healthcare teams should also be mindful, however, that in the case of PwCF, that the level of health literacy does not directly correlate with educational attainment. It has been reported that, in the case of adolescents and young adult PwCF, higher health literacy capabilities are associated with better health outcomes, lower cost implications and a higher quality of life (QoL)[6]. This has been highlighted by the fact that PwCF with limited health literacy capabilities have been shown to have a trend of lower lung function/ppFEV1, higher chronic colonisation with *Pseudomonas aeruginosa*, more frequent outpatient visits and in-patient stays and greater use of intravenous antibiotics, as well as number and duration of oral antibiotics[6].

Recently, Mindel (2023), reported that children with cystic fibrosis (CwCF), in the age range 8-13 years, who had a "*mature understanding and awareness of their condition*" wanted to participate in their medical care, as they understood the requirement of such care, however they trusted that the medical team would make most of the medical decisions[7]. This study highlighted many facts which were important to children, namely with respect to developing their knowledge, understanding, particularly in relation to the reasoning and practicalities of treatments and procedures. By incurring such inclusivity when providing clinical care for CwCF, this would potentially help to alleviate anxiety associated with a lack of understanding, particularly relating to such treatments and procedures, as well as encouraging shared decision making (SDM)[7,8]. Of note, a Cochrane intervention review relating to the promotion of decision making for the target population of CwCF (aged 4-18) reported that due to the absence of eligible randomised control trials (RCTs), there was a lack of evidence-based findings and hence a need for such trials, as well as the important need to train healthcare professionals and develop models to ensure that CwCF are involved in SDM in a manner that is suitable for their age group[8].

Development of health literacy skills at an early age and promoting children to take an active role in their healthcare has many advantages relating to their long-term self-care in preparation for transition from paediatric to adult care, decision-making and partnership engagement with the healthcare team[8]. The formation and foundations of health literacy is believed to begin in childhood and this is particularly true for children with chronic illnesses[9]. Most healthcare materials in general and for the CF community, target the adult patients or the parent/carers of paediatric individuals and as such, there is a paucity of studies relating to healthcare information for the paediatric audience *per se.*

As such, the goals of the Belfast CF-MDT were to help CwCF to develop their health literacy skills by informing children along with their families of best evidence-based practices relating to their care. These initiatives included the development of bespoke health education story/colouring books and animations, by means of a co-production approach, involving the CF-MDT, CwCF and their families, as well as students from Queen's University Belfast and Ulster University. These materials targeted (i) why it is important to provide a good respiratory specimen, what happens to it when it goes to the laboratory and what does it mean for the CwCF; (ii) why and how to clean the respiratory nebuliser and (iii) the importance of pancreatic enzyme replacement therapy (PERT). From the reflections of preparing these paediatric facing materials practical guidance is provided for other healthcare teams wishing to use a similar communicative co-production approach to the paediatric community in relation to the format and readability of such materials.

Methods

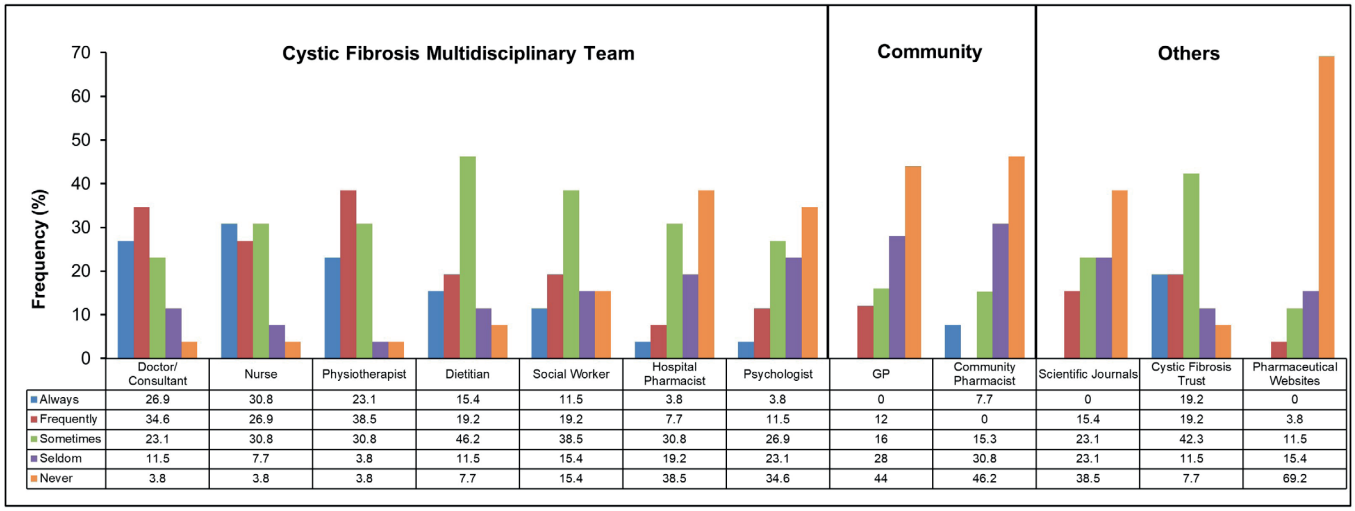
Information sources questionnaire

As part of a service development, quality improvement initiative, voluntary, anonymous questionnaires were completed at outpatient clinics and hospital in-stays, by the Adult and Paediatric CF community in Northern Ireland, to assess the sources of CF-healthcare information consulted. These Likert styled questions asked:-

"How often (Always, Frequently, Sometimes, Seldom, Never) do you

1. Ask the following members of your CF Clinical Team in order to obtain information relating to Cystic Fibrosis?"
   (CF/Doctor/MD/Consultant; GP/Family Physician; CF Nurse, CF Physiotherapist, CF Dietitian, CF Social Worker, Community Pharmacist, Hospital Pharmacist, Clinical Psychologist)?

Figure 2: Results of a questionnaire detailing where members of the cystic fibrosis (CF) community in Northern Ireland (n=27), source healthcare information on CF.



	Doctor/ Consultant	Nurse	Physiotherapist	Dietitian	Social Worker	Hospital Pharmacist	Psychologist	GP	Community Pharmacist	Scientific Journals	Cystic Fibrosis Trust	Pharmaceutical Websites
Always	26.9	30.8	23.1	15.4	11.5	3.8	3.8	0	7.7	0	19.2	0
Frequently	34.6	26.9	38.5	19.2	19.2	7.7	11.5	12	0	15.4	19.2	3.8
Sometimes	23.1	30.8	30.8	46.2	38.5	30.8	26.9	16	15.3	23.1	42.3	11.5
Seldom	11.5	7.7	3.8	11.5	15.4	19.2	23.1	28	30.8	23.1	11.5	15.4
Never	3.8	3.8	3.8	7.7	15.4	38.5	34.6	44	46.2	38.5	7.7	69.2

2. Consult medical/scientific journals to obtain information relating to cystic fibrosis?
3. Retrieve information from the Cystic Fibrosis Trust (UK) website?
4. Consult pharmaceutical websites for information relating to Cystic Fibrosis?

Animations & Story/colouring books

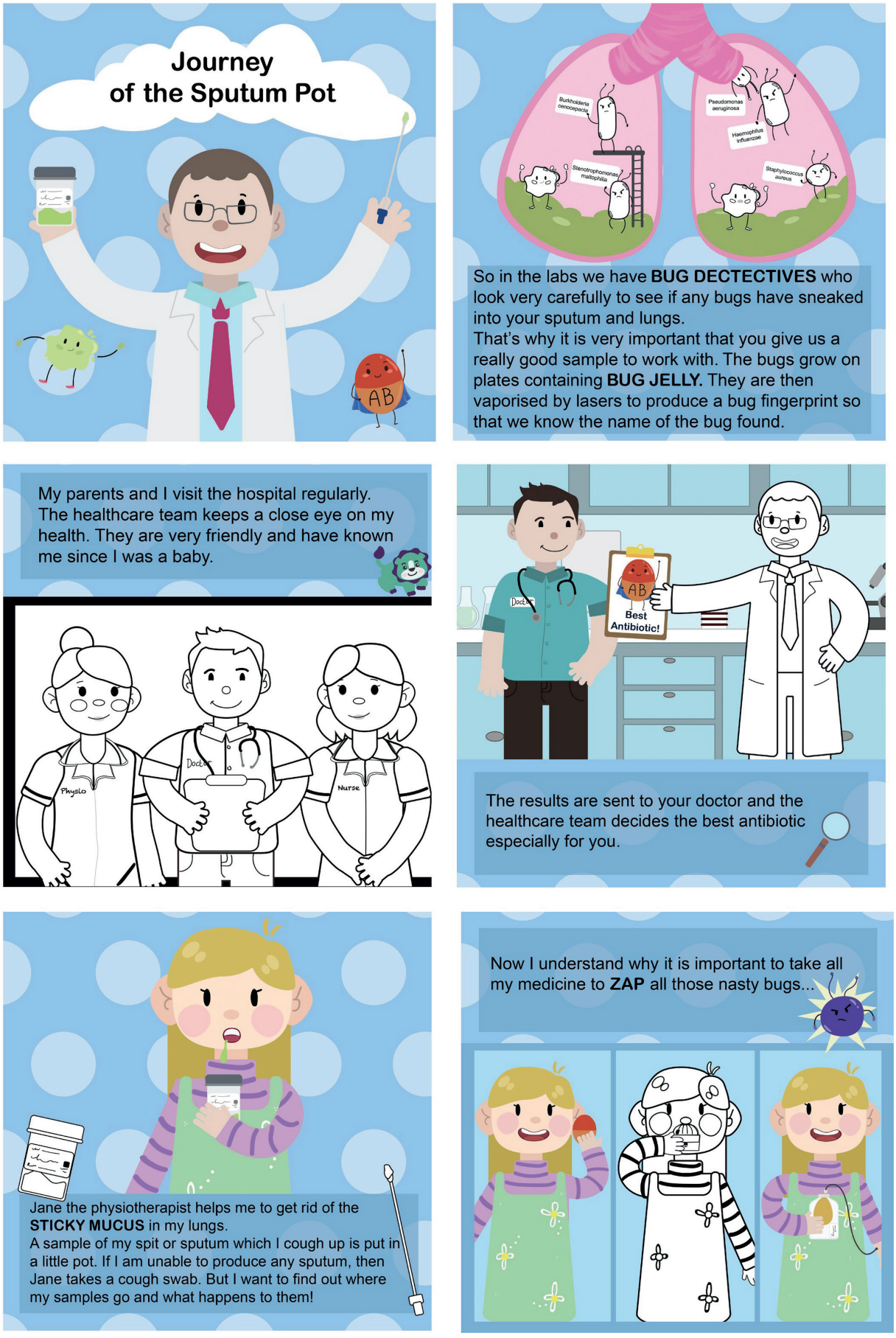
A needs analysis was determined through discussions with the cystic fibrosis multidisciplinary team, which highlighted three priority areas of focus to educate and promote/engage CwCF in their own healthcare responsibilities. Firstly, due to increasing difficulties in obtaining a quality respiratory specimen from children with CF and the future impact on sputum production due to the use of CFTR medicines, there was a need to emphasise to children and their parents the importance of obtaining a respiratory specimen for microbiological analysis. Secondly, our group had recently published peer-reviewed recommendations on how to clean and disinfect nebulisers[10]. Resources were required to promote such best practice relating to nebuliser hygiene and to instil ownership of such practice at an early age. Thirdly, pancreatic enzyme replacement therapy (PERT) is a vital part of treatment in people with cystic fibrosis (PwCF) who are pancreatic insufficient. Symptoms of fat malabsorption, ineffective dosing or poor adherence to PERT, and subsequent poor nutritional outcomes are well documented[11]. The dietetics team wished to educate and re-enforce the importance of adherence to PERT to CwCF as well as their families.

The preparation of animation videos was conducted in stages similar to another study[12]. Stage 1: CF-MDT identified a "needs analysis" of topics which needed promotion and awareness to encourage active participation of CwCF. Stage 2: Script design prepared by the CF-MDT. Stage 3: Storyboards drafted based on the scripts and discussions between the CF-MDT team and animators. Stage 4: Digital media design, where scenes, backgrounds and characters for the educational materials were prepared using Adobe Photoshop[12]. Stage 5: Animation of characters and objects followed by compositing using Adobe After Effects. Stage 6: Rendering of completed animation for mp4 file production, prior to embedding as YouTube videos for circulation. Three animation videos and accompanying story/ colouring books were prepared.

Video 1 was entitled "*Journey of the Sputum Pot*" which lasted 2min 06s (https://youtu.be/c6_UvffZE1c?si=QD9SXpTFFR37YgVm). Figure 3 details excerpts from the accompanying book. This video follows Zara, a CwCF, who initially explains what CF is and its impact in relation to coughing. Zara explains the role of the healthcare team and the fact that Jane, the physiotherapist, helps Zara get clear sputum which is sent to the laboratory. Zara wishes to know what happens the sputum or cough swab when it goes to the laboratory. John, the microbiologist explains why it is important to look at Zara's respiratory samples and what it means for Zara, in terms of selecting the most appropriate antibiotic. The script of this video was written by Clinical Scientist in Clinical Microbiology, BC Millar; healthcare advice was provided by physiotherapists L Alexander and J Bell; animation was prepared by animation students, K Catney and D Toland (supervisors A Parkin & B Coyle) and voices provided by Zara and JE Moore, Clinical Microbiologist.

Video 2: Was entitled "*How to clean and disinfect the nebuliser in cystic fibrosis*", the core content lasted 2m 14 s (https://youtu.be/Pw_w9ZXrHsw?si=lB7bAES4fYUHIbEg). Figure 4 details excerpts from the accompanying book. In this video Zara, a CwCF, explains the role nebulisers play in CF therapy. Zara asks Jane, the physiotherapist, why is it necessary to wash the nebuliser after it is used, particularly when it is going to be used again. Jane, explains why and

Figure 3: Excerpts from the colouring/storybook entitled "*The Journey of the Sputum Pot*"



demonstrates the correct cleaning and disinfection procedure. This video was written by L Alexander and J Bell; facilitation and healthcare advice was provided by BC Millar and JE Moore; animation was prepared by K Catney and D Toland and voices provided by Zara and J Bell.

Video 3: Was entitled "*Food and Enzymes- How it all Works*" (The importance of enzymes in cystic fibrosis) (https://youtu.be/Oyva3Y5PjsQ?si=GYGEZotjt-V19mV1) the core content lasted 2m 46s. Figure 5 details excerpts from the accompanying book. In this video Henry, a CwCF, wants to find out why it is important to take capsules or enzymes when eating. Henry's mum takes him to visit Christine, the dietitian, who explains Pancreatic Enzyme Replacement Therapy (PERT), its role, action, potential side effects if missed and members of the CF team who have knowledge of PERT. This video was written by dietitians C McCabe, W Wright and E Grieve, facilitation healthcare advice was provided by BC Millar and JE Moore; animation was prepared by K Catney and D Toland and voices provided by Henry, Henry's Mum and dietitian C McCabe.

Analysis of Readability of written materials

The readability of the BHSCT materials (n=3) and materials prepared for CwCF from reputable sources namely CF charities (n=8) and pharmaceutical companies (n=7) were analysed and compared with the readability of adult facing PwCF information provided by CF charities (n=10) and scientific abstracts relating to CF (n=10). The subscription software package, Readable (www.readable.com) was used to perform the analyses and was chosen as it is reliable, easy-to-use and widely available[13]. Readability measures included readability grade levels according to the Flesch-Kincaid Grade Level (FKGL), Gunning Fog Index and SMOG Index and readability score according to the Flesch Reading Ease (FRE), as detailed in Table 1. Text statistics and text density were also assessed. These readability measures were chosen as they have been used widely and accepted by scientific and non-scientific communities alike[14-17].

Evaluation of parent and children's knowledge of pancreatic enzymes pre- and post- viewing animation video

As part of a service development, quality improvement initiative, two voluntary, anonymous questionnaires, employing a 5 point Likert scale were hosted on the Northern Ireland Paediatric Cystic Fibrosis Centre closed-group Facebook page. The pre-questionnaire was released two weeks prior to the launch of animation video 3 and the post-questionnaire, following the release of the video, to assess the perceived knowledge of parents and their perception of their child's knowledge of PERT.

Statistics

Statistical analyses were performed on readability and text metrics of paediatric and adult information from all five sources detailed above. For data relating to readability scores (FRE, FKGL, Gunning Fog Index and SMOG Index), a Shapiro-Wilk test for normality was performed followed by a one-way ANOVA with a Tukey's multiple comparisons test between all information sources. For data relating to text metrics, following a Shapiro-Wilk test for normality, normally distributed data relating to words per sentence was analysed by a one-way ANOVA with a Tukey's multiple comparisons test. For analysis of syllables per word which was not normally distributed, a Kruskal-Wallis test and post hoc by Dunn's multiple comparisons test was performed. Statistical significance was set at $p \leq 0.05$. All analyses were conducted using GraphPad Prism 10 for Windows, Version 10.0.0 (GraphPad Software, Boston, USA).

Results

Information sources questionnaire

Twenty-seven questionnaires were completed by the local CF community, in relation to the frequency of asking members of the CF clinical team, the community general practitioner, the community pharmacist or consulting information provided by the charity, the CF Trust, scientific journals or pharmaceutical websites, in relation to cystic fibrosis. The most frequently contacted individuals for such information were members of the CF multidisciplinary team namely the Doctor/CF Consultant, the nurse and the physiotherapist and dietician, as well as the Cystic Fibrosis Trust (Figure 2). Pharmaceutical websites were least consulted with 69.2% of respondents never consulting such resources (Figure 2).

Animations and Story/colouring Books

Animations and story/colouring books (Figures 3-5) were prepared adhering to the criteria detailed in Figure 6.

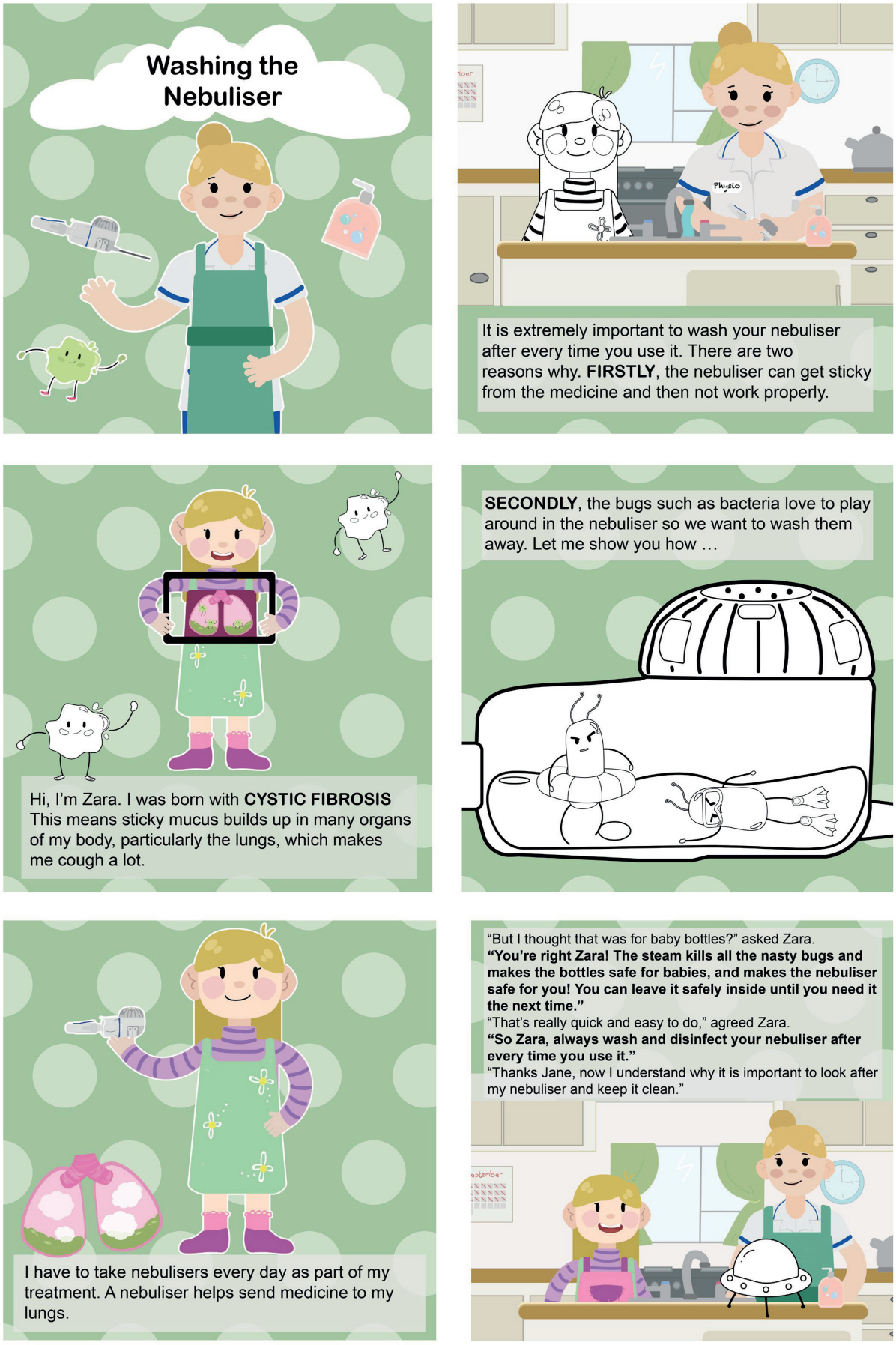
Analysis of Readability of Written Materials

Readability scores and text densities, namely words per sentence and syllables per word for the paediatric-facing and adult-facing materials, relating to cystic fibrosis, are shown in Figures 7 & 8, respectively. In relation to FRE, FKLG, Gunning Fog Index and SMOG Index (Figure 7 A-D) and text metrics (Figure 8 A & B), there was no statistical difference between the three paediatric-facing material sources i.e., those prepared by the charities, pharmaceutical companies and the authors. Statistical significance was noted in comparison of the paediatric sources with the adult-facing charity and scientific abstract resources in relation to readability scores (Figure 7 A-D), with adult-facing materials and scientific abstracts not meeting the target readability levels, for the adult population. In relation to the text metrics, it was noted that there were statistically significant differences, namely that paediatric-facing information contained less words per sentence and less syllables per word, which would contribute to their enhanced readability (Figure 8 A & B).

Evaluation of parent and children's knowledge of pancreatic enzymes pre- and post- viewing animation video

Parent respondents (n=18) to the pre-video questionnaire ranked their level of understanding of how PERT works as

Figure 4: Excerpts from the colouring/storybook entitled "*Washing the nebuliser*"



very good (55.6%), good (33.3%) and moderate (11.1%). When rating their children's understanding, 50% felt they had either a very good/good understanding, whilst the remaining 50% felt they had either moderate, little or no understanding. Parent respondents (n=14) to the post-video questionnaire showed that 12 (85.7%) had watched the video with their child and those who did not were a parent of a baby and the parent of a child who was pancreatic sufficient, so they did not feel it appropriate to watch. Parents ranked their level of understanding of how PERT works as very good (86%) after watching the video, and the remaining 14% had good understanding. All children (n=12) who watched the video, had either very good (58%) or good (42%) understanding of how PERT works. Comments included: "*As we learn about how enzymes will be part of our lives, this is brilliant for us to share with family who are also new to it*"; "*Very informative and a great tool…sometimes we get caught up in just doing it and forget why"; "Easy to understand and designed in a brilliant way to help a child understand easily".*

Discussion

The United Nations Convention of the Rights of the Child (UNCRC), which defines a child as anyone under eighteen years of age[18], came into force in the UK in 1992[19]. The UNCRC has 54 articles which relate to all aspects of a child's life and each of these articles relate to each other[18,19]. Article 12, which relates to respect for the views of the child, has been noted as of particular significance in relation to healthcare practice and medical decisions[18,20]. Healthcare professionals generally recognise the importance and requirement to involve children in various healthcare-related decisions and practices[20], primarily by providing explanations of treatments and procedures. Recently, however, Davies and colleagues (2023) discussed significant barriers to the real-world implementation of this Article 12 and stated that healthcare providers need to actively implement Article 12, rather than provide token gestures to listening to children's views[21]. These authors acknowledged that this may be difficult due to a lack of clear guidelines for medical practice. A recent National Institute for Health and Care Excellence (NICE) guideline[22] entitled "*Babies, children and young people's experience of healthcare*", may in part, provide such a guideline, relating to the importance of ensuring children and young people are listened to and provided with information to enhance their understanding of their condition. Additionally, this would allow children to be involved in decisions regarding their healthcare if they have the competence to do so. Such practices can promote positive experiences for the child which in turn can build trust relationships with healthcare professionals, alleviate anxiousness and distress, particularly before procedures and interventions, promote self-confidence and empower children to manage decisions regarding their own healthcare. It is also important to recognise that children are not defined by their health condition but that they have a life outside of the healthcare setting where they participate in common activities along with other children[22]. This NICE guideline also states that the methods of communication, information and discussions are tailored for the child's age, developmental stage and level of understanding[22].

Important considerations when preparing paediatric-facing materials

When preparing and communicating information for the paediatric community, the team considered several aspects of the content and delivery of the healthcare advice as detailed below and summarised in Figure 6, which other healthcare teams may find useful when preparing such materials.

Encouragement to ask questions

All three videos initially commenced with a CwCF asking a healthcare professional a question who in turn provided the CwCF with the evidence-based information required. This highlighted who was the most appropriate member of the healthcare team from which to seek guidance and also provided an opportunity to convey the friendly and approachable nature of team members. The rationale for such inclusion was to convey the message that the healthcare team welcomes and encourages CwCF to ask questions.

Building partnerships and trust

Videos alluded to the role that family members had in the day-to-day management of their healthcare and the importance of coming for regular reviews with the healthcare team, thereby highlighting that the management of their condition is a shared responsibility between child, healthcare team and parents/carers all working in partnership for the wellbeing of the child. The animated videos and story/colouring books were chosen as they provided healthcare team members an opportunity to establish discussions regarding treatments and practices and provided children the opportunity to discuss and share their experiences with family and careers in their home environment outside of the clinical setting. It is important to allow children, along with their careers and families, to absorb such information at their own pace and in their own environment and then subsequently the healthcare team can re-address the healthcare messages which they are attempting to address[22].

Promoting identity and confidence

The NICE guidelines, as detailed above, promote that the preparation of digital healthcare information is conducted in partnership with children and young people[22]. In this case, CwCF were the primary role players in the animations prepared by our team and the children's families also participated by discussing the scripts and playing themselves in the final animation in the case of the "Enzymes" video. This was important so that other CwCF could identify with the scenarios portrayed.

Delivery to promote engagement and cognition

The ability to communicate with service users who have different levels of understanding and disability issues by

Figure 5: Excerpts from the colouring/storybook entitled "*Food and Enzymes- How it all Works!*"

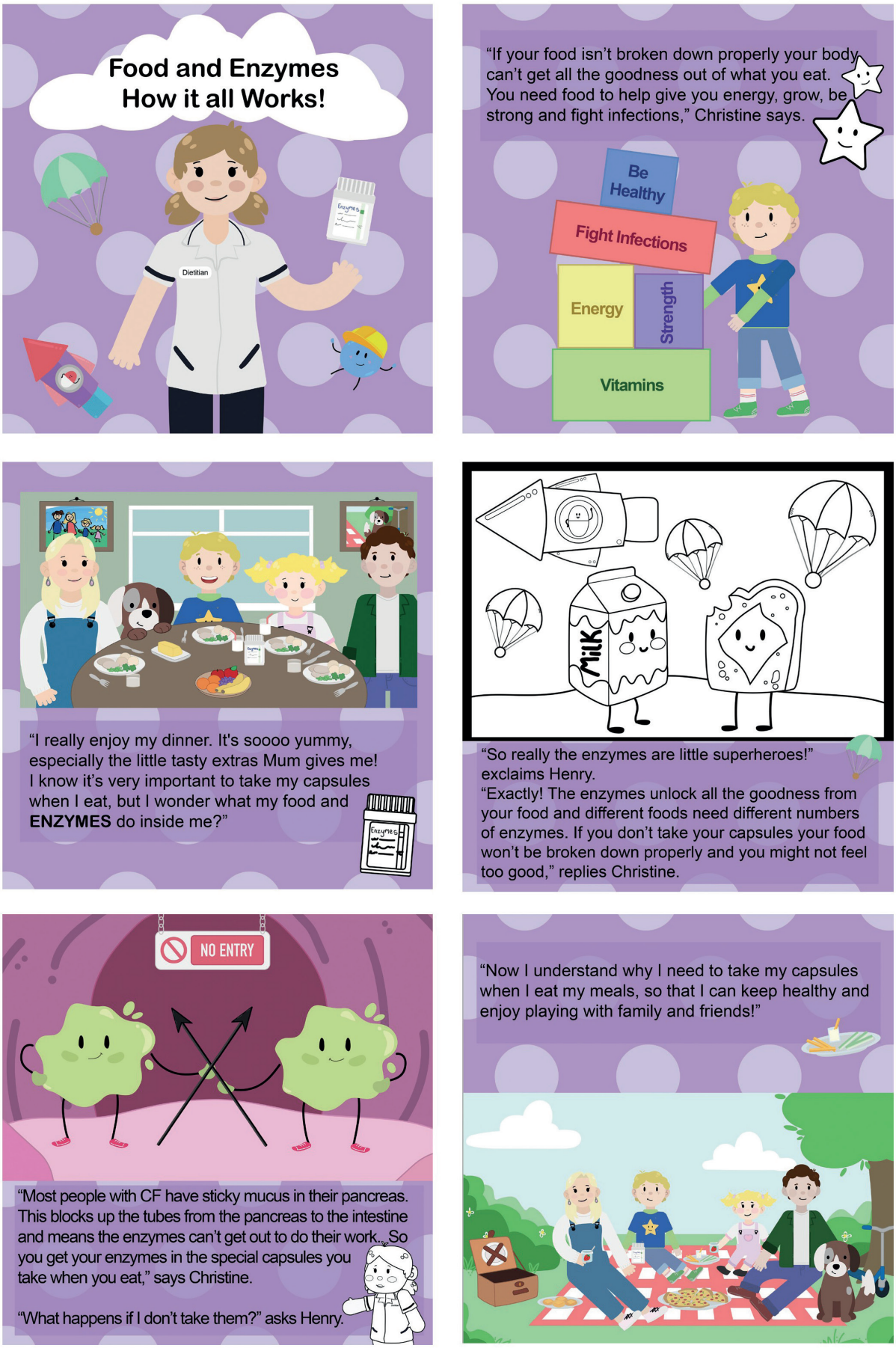


Table 1: Readability formulae used in this study and their associated target score for the general public

Readability Scores	Readability formula	Target score for texts aiming at the general public
Flesch-Kincaid Grade Level (FKGL)	0.39 (total words/total sentences) + 11.8 (total syllables/total words) – 15.59	A text aimed at the general audience should have a grade level of 8 or lower. At Grade Level 8, 85% of the general population will be able to read and comprehend the text.
Flesch Reading Ease (FRE)	206.835 – 1.015 (total words / total sentences) – 84.6 (total syllables / total words)	A target score of 60 or above.
Gunning Fog Index	0.4 [(total words / total sentences) + 100 (complex words / total words)]	Grade level of 8 or below.
Simple Measure of Gobbledygook (SMOG) Index	3 + square root √polysyllabic count in 30 sentences	Grade level of 8 or below.

Readability formulae are taken from Readable.com

Note: 4–6th grade = British school age equivalent of 9–12 years; 7–9th grade = British school age equivalent of 12–15 years; 10–12th grade = British school age equivalent of 15–17 years; >12th grade = British school age equivalent of 17 years and over[14].

using a variety of communication modalities both verbal, digital and non-digital is a competency which has been recently recognised in the revised standards of proficiency for allied healthcare professionals[23]. Additionally, in the General Medical Council Professional Standards for Doctors, Good Medical Practice emphasises the importance of communication and sharing evidenced-based information with patients in a manner appropriate to their communication needs so that as to support them to "*engage in meaningful dialogue and make informed decisions about their care*"[24]. In this case, the videos provided an aural and visual presentation of key information and accompanying bespoke subtitles and were used to ensure that members of our CF community who had hearing difficulties were provided with this information in an accessible and accurate format as autogenerated subtitles may provide inaccurate wording.

When preparing materials for children it is important to be mindful that children have different cognitive abilities and not all have reached the same level of reading. The team therefore decided to prepare two forms of media, namely animations and colouring/ storybooks. Scripts were written in a simple syntactic style to aid understanding.

Children are primarily influenced by their experiences, particularly in relation to what they feel and see[25]. As such, it is important to use imagery both which is attractive and objects and people with which the children are familiar with. In the preparation of these materials, complementary colours for background elements were used as to not cause distraction and contrasting colours were used for characters to allow them to stand out. Attention to detail was made in relation to the healthcare setting so that the CwCF could identify the out-patient clinic which they attended, with imagery of a monkey, lion and tree in the animation similar to that the art detail on the walls of the clinic. Children could also recognise specific pieces of respiratory equipment, sample collection swabs, containers and medications which all are encountered routinely within the healthcare activities.

Animations have been used to deliver healthcare related educational materials on a range of topics[26-28]. One such example was a study which examined an animated educational video prepared for children aged between 5-11 years, undergoing a MRI without sedation, which successfully improved children's knowledge of the procedure, reduced children's anxiety, retained attention and was described as enjoyable[26]. Animations provide the opportunity to deliver information in a fun and engaging manner which is believed to stimulate children's imagination and enhance learning outcomes[25]. The animated characters namely, the healthcare professionals were modelled on the real-life people i.e., the dietitians, the physiotherapist and the microbiologist, as well as the CwCF and their family members. The voice-overs for the animations were provided by the healthcare team, CwCF and a mother of one of the CwCF, which again provided a familiar environment for the CwCF. To further promote engagement with the materials, anthropomorphism was used in relation to antibiotics, mucus, enzymes and bacteria. The animation of characters and animation movement and anthropomorphism significantly impacts the viewer's visual attention and cognition[29,30].

In relation to the story books, attention was given to the font style used, namely Arial at a large size of 24, to aid with letter and word identification[31]. It is important to consider typography in relation to children of different ages, reading abilities and reading difficulties such as dyslexia, in relation to font style, size, spacing between words, letter and lines, weight of typeface and the use of uppercase letters, as these parameters can influence motivation and legibility of text[31-33]. Story/colouring books have been previously used to deliver healthcare guidance in relation to asthma to children and have been shown to provide opportunities for discussions

Table 2: Health literacy resources for children with cystic fibrosis

CF Trust	
Seb's Best Game (my Daddy has CF)	Storybook https://www.cysticfibrosis.org.uk/the-work-we-do/information-resources/resources-for-children-and-young-people/rosie-and-seb Cartoon animation https://youtu.be/UJxHbcHciPg?si=mu42TeSPp3pD9AW3
The Lost Collar Investigation (my Mummy has CF)	Storybook https://www.cysticfibrosis.org.uk/the-work-we-do/information-resources/resources-for-children-and-young-people/rosie-and-seb Cartoon animation https://youtu.be/fA7r_RDeYcI?si=R-eMHkMHdz49v7eO
The A to Z of cystic fibrosis- What is cystic fibrosis?	Video & animation https://youtu.be/AVg24S_pSmo?si=35wE1TrIer_kTSOv
CF- What's it all about? A film for children	Cartoon animation https://youtu.be/ZIhyAkUx69U?si=xyamkGsI_Zp2mCYI
Getting Nosey about CF with Oli and Nush	Cartoon animation https://youtu.be/WuI72eMrIQI?si=wbiyibEenQ5DmnGH
Cystic Fibrosis Western Australia	
CF Smart Good Clean Hands	Animation/song https://www.youtube.com/watch?v=d-WVOBTW6iA
Foundation Care	
Huxi meets her super team Huxi goes on vacation! The amazing story of Huxi a panda with cystic fibrosis	Three story/colouring books Contact: Foundation Care https://www.foundcare.com/Patients/Educational_Resources.html
San Diego Chapter, CFF CureFinders	
SD Chapter CFF What is cystic fibrosis?	Animation https://youtu.be/FMAOEOmLoUE?si=oyusQSWBJbpfIstZ
Boomer Esiason Foundation	
Big Air Jerry	Comic book contact https://www.esiason.org/
Big Air Jerry: Exercises with Cystic Fibrosis	Cartoon animations https://youtu.be/wMXICsQIQU4?si=34sQnCS5qVO4MIFY
Big Air Jerry: Does his Daily Cystic Fibrosis Treatments	https://youtu.be/BqQr1jYt_38?si=U18fJE-ofnPaqI4z
Big Air Jerry: and Teamwork	https://youtu.be/liUinNavxWw?si=rQ3w-3FNYCu6E0s9
Big Air Jerry: Learns to Stay Positive	https://youtu.be/N8cLDLa35FQ?si=aE8jmw4HdbdM75tK
Big Air Jerry: Episode 6: Compliance– Organize Your Pills	https://www.youtube.com/watch?app=desktop&v=yw14_A6qW5E
Big Air Jerry: Episode 7: Nutrition and Snacks	https://youtu.be/qFGOgU-ROT4?si=uXxP1BTVovgcoG5O
Big Air Jerry: Episode 8: Compliance – Nebulizer Medications	https://youtu.be/DmSYhnKx2WU?si=ImRHu1Z5FxOL4N24
Big Air Jerry: Episode 9: Traveling with Cystic Fibrosis	https://youtu.be/wl0R8WSmlig?si=wjcnsVVRmw3KMGq8
Big Air Jerry: Stays Hydrated	https://www.youtube.com/watch?v=JkNfpuJA8Tk
Big Air Jerry: Compliant with Cystic Fibrosis	https://youtu.be/UvN0lXL597w?si=IGeVI5-rvyc4skZO
Jumo Health	
Understanding Cystic Fibrosis	Comic book style video https://youtu.be/pNAr3jb7qYQ?si=7WieII4gqCljLhEr
Genentech	
Who am I?	Storybook https://cfsmart.files.wordpress.com/2015/11/pulmozymestorybook.pdf
Chiesi	
The 7 steps to staying well with CF	Information book https://chiesicysticfibrosis.co.uk/wp-content/uploads/2021/06/7_Ways_to_Stay_Well_with_CF%E2%80%93for_Kids_2020_IE-CF-2000037_for_resources_section.pdf For animation contact Chiesi UK
Vertex Pharmaceuticals Inc.	
Eugene's Big Book of CF Words Causes and Impact of CF Progression in the Lungs Impact on the Digestive System Impact on Bones, Kidneys, and Hearing	Comic books/videos available from https://www.cfsource.com/videos-resources
Visiting the CF Care Center	Animation https://www.cfsource.com/videos-resources
Meeting the CF Care Team	Animation https://www.cfsource.com/videos-resources
PARI	
Meet Mo, the Pesky P.A. Bug!	Animation https://youtu.be/hNFeFyaAVu0?si=WILnZ2dvwDKhj6NS
BBC Teach	
Living with cystic fibrosis- I can't go to school Jasper's Story Living with Cystic Fibrosis	Animation https://youtu.be/F3nH4GV2Zy0?si=x_xLLR8z2C1pNpge Storybook Glynne, A & Jain, N, 2017; (Publisher Franklin Watts)
Royal Brompton and Harefield Hospitals, UK	
Transition Animation film 1	Animation https://youtu.be/MPJW63Ygieg?si=KPagC0DFVN7M5k5c
Transition Animation film 2	Animation/video https://youtu.be/vSoutcJWJP4?si=waXT_H012tBpFVRV
Belfast Health and Social Care Trust (Authors)	
Journey of the Sputum Pot	Colouring/Storybook https://www.cfnebulisercare.com/colouring-books.html Animation https://youtu.be/c6_UvffZE1c?si=QD9SXpTFFR37YgVm
Cleaning the Nebuliser	Colouring/Storybook https://www.cfnebulisercare.com/colouring-books.html Animation https://youtu.be/Pw_w9ZXrHsw?si=1QDoo-RdSoMVBta1
Food and Enzymes: How it all works!	Colouring/Storybook https://www.cfireland.ie/support-resources/resources/publications Animation https://youtu.be/Oyva3Y5PjsQ?si=cMIhxmTYVj2QcPIX

Figure 6: Key points to consider when preparing engaging and effective healthcare information for the paediatric service user.

	**Co-production** (healthcare team, children, family/careers, animators)
	**Evidence-based** (scientific literature critically examined by healthcare team)
	**Promote asking questions** (clearly convey who to ask for healthcare advice)
	**Build trust & partnerships** (material should facilitate discussion between service user and healthcare team)
	**Promote identity & confidence** (through involvement and clear instructions)
	**Plain language script** (checked with readability calculators)
	**Clear Take home messages** (why, how and implications for the service user)
	**Familiarity** (hospital environment, people, equipment)
	**Anthropomorphism & Animation** (engagement & cognition)
	**Duration of animations** (less than 3 minutes)
	**Subtitles** (prepare bespoke subtitles for the animations as autogenerated text is not always accurate)
	**Typography** (appropriate for reading ability of children)

between children and the healthcare team, as well as opportunities for the children to share such information with family members[34].

Reliability of healthcare information

It was of interest and encouraging to note that the local CF community most frequently consulted the healthcare team, primarily, the CF consultant/doctor, nurse and physiotherapist for healthcare information, followed by the UK CF charity, Cystic Fibrosis Trust. It is important that healthcare information is provided by a reliable professional or charity evidence-based source[22]. It is also of interest to note, that although pharmaceutical websites contain a reliable source of information, that in the case of the local CF community who completed the questionnaire, the majority never consulted such websites (69.2%), potentially reflecting that many such websites are for healthcare professionals only and restricted to certain global areas[35]. Furthermore, online materials which are children-facing in relation to cystic fibrosis, is limited or difficult to find (for some key resources see Table 2). As such, these points further enforce the responsibility of the healthcare team to provide such children-facing resources.

Access to evidence-based information

The video entitled "*How to clean and disinfect the nebuliser in cystic fibrosis*" evolved from an evidence-based recommendations prepared by the Northern Ireland Working Group on Nebuliser Care and Hygiene in Cystic Fibrosis[10]. This working group comprises of healthcare professionals from both the adult and paediatric CF multidisciplinary teams within the Belfast Health and Social Care Trust. It was also evident from previous research in relation to nebuliser care within the adult CF community that there were a variety of approaches being practiced, some of which were not optimal and that some adult PwCF were unsure of how to clean their nebulisers due to the fact they were never personally informed as a child and that the responsibility remained with their family members to clean the nebuliser[36]. It is important to instil best practices at an early age to promote ownership and responsibility of their own healthcare and good habits. The resources prepared on why and how to clean nebulisers shared such best practice, not only with the CwCF, but also their parent/career. Indeed, an adult PwCF informed the team that when reading the storybook to their non-CF grandchild it encouraged them to regularly clean and disinfect their nebuliser.

Readability of written healthcare information

It is important that the any information that the healthcare team prepare is targeted to the general age-related readability level and delivered in various digital and non-digital communication media formats. In relation to health literacy in general, it has been documented that the quality of health-related materials prepared to guide and inform patients and families, is varied[37]. Furthermore, the readability of online

Figure 7: Box-and-whisker plots comparing readability scores calculated from analysis of paediatric-facing healthcare information relating to cystic fibrosis prepared by cystic fibrosis charities (n=8); pharmaceutical companies (n=7); the authors' materials (n=3) and adult-facing materials (n=10) prepared by charities and scientists in the form of scientific abstracts (n=10). (A) FRE; (B) FKGL; (C) Gunning Fog Index; and (D) SMOG Index. Boxes represent IQRs (25th to 75th percentiles) and bars represent the medians. Whiskers represent the 10th and 90th percentiles and coloured dots represent outliers outside these percentile ranges. Statistical significance is shown where a p value of <0.05 (5%) was considered as statistically significant. The dashed red lines represent the target readability score for the general population. For the FRE, this is ≥60 and for the FKGL, Gunning Fog Index and SMOG Index this is ≤8 for the general population (i.e., approximately secondary school students).

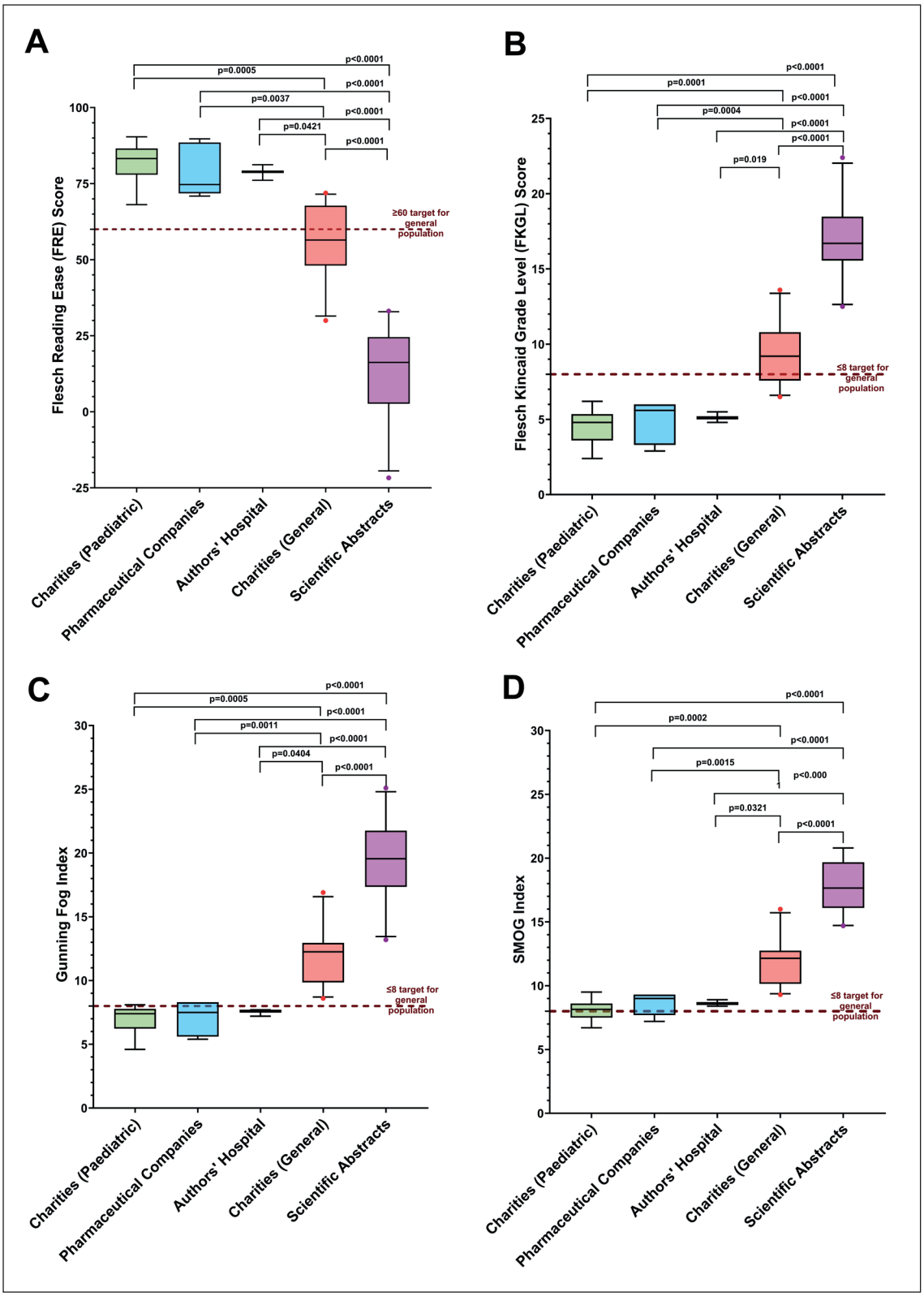
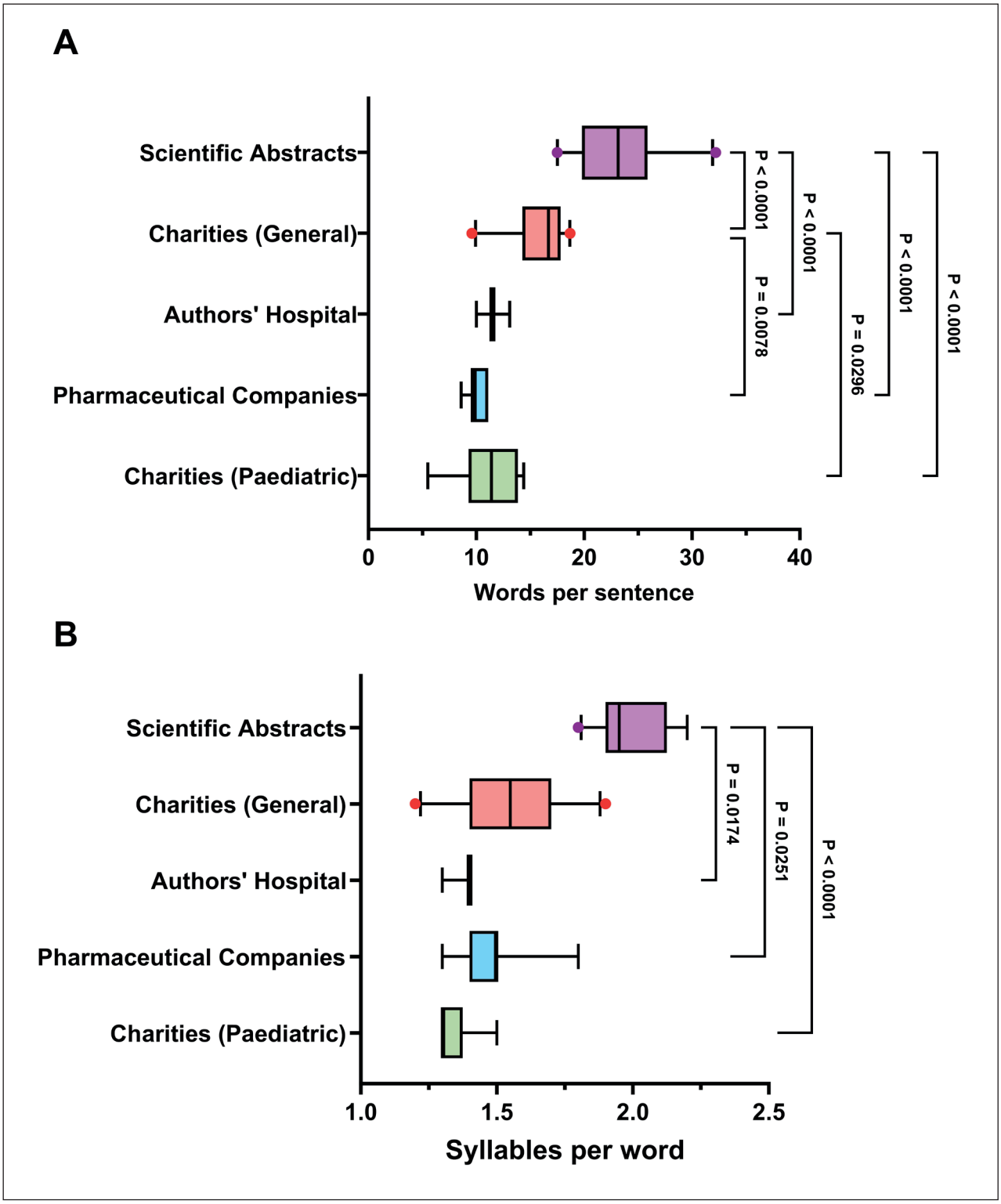


Figure 8: Box-and-whisker plots comparing text metric scores calculated from analysis of paediatric-facing healthcare information relating to cystic fibrosis prepared by cystic fibrosis charities (n=8); pharmaceutical companies (n=7); the authors' materials (n=3) and adult-facing materials (n=10) prepared by charities and scientists in the form of scientific abstracts (n=10). (A) words per sentence and (B) syllables per word. Boxes represent IQRs (25th to 75th percentiles) and bars represent the median. Whiskers represent the 10th and 90th percentiles and coloured dots represent outliers outside these percentile ranges. Statistical significance is shown where a p value of <0.05 (5%) was considered as statistically significant.



materials healthcare information, as well as those prepared by healthcare providers, in relation to the adult population have been deemed "fairly difficult" due to the fact that they exceed the target readability parameter for the FKGL level for the general population, which is eighth grade[38]. Although readability does not necessarily correlate with understandability, it is important that the composition of written materials is prepared at a reading level appropriate for the target audience, which from the analyses of these three materials was appropriate for the reading abilities of children of upper primary school age.

Involving children as co-designers

In these initiatives, the CF-MDT involved participation of CwCF when recording the voice-over for the animations. Such participatory involvement could be further expanded when designing future healthcare media to involve children further in the process as co-designers. When developing digital technologies for children including animations and interactive applications, CwCF participation throughout all the various design stages of healthcare materials will help to develop age-appropriate products in terms of design and content. The inclusion of different age groups of children as co-designers has many advantages, both to the child and the healthcare team[39], particularly if further interactive technologies are used. The child can further develop their health literacy and the team can gain an appreciation of a situation from an individual child's perspective, in terms of their knowledge, concerns and needs, and factors which influence or promote their participation in healthcare situations, something which an adult alone cannot fully interpret[39]. In such participatory design, the child can be involved in the storyboard design, in the case of animation videos, and in other interactive communication technologies which will further enhance and promote healthcare professional-child interactions, with the objectives to improve children's understanding and participation in clinical procedures and tests[39].

In conclusion, paediatric healthcare teams have a responsibility to aid in the development of health literacy skills at an early age and promoting children to take an active role in their healthcare. The use of colouring/storybooks and animations are excellent media to initiate discussions and develop partnerships in paediatric healthcare in an engaging and informative manner. For optimum impact, the healthcare team should co-produce these media with the pediatric service user, their families and animation teams.

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Disclosure of Conflict of Interest

None to declare. The authors declare that the project was conducted in the absence of any commercial, financial or other relationships that could be construed as a potential conflict of interest.

Key words: animation, communication, cystic fibrosis, health literacy, paediatric, readability

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Medical Ethics

Ethics – A matter of principle?

Michael Trimble

Part 1: Principles and principlism

Abstract

Discussion of bioethical issues using the four principles approach proposed by Beauchamp and Childress is now standard practice in the UK. This paper first documents the history of principlism before considering its impact and reviewing some criticisms of the approach. A future paper will examine some of the philosophical difficulties arising from principlism in greater depth.

The ubiquity of principlism

When considering medical ethics in the UK, it is hard to avoid the 4-principle approach advocated by Beauchamp and Childress. Beauchamp and Childress' *Principles of Biomedical Ethics*, first published in 1979 and now in its eighth edition, remains one of the most influential textbooks of ethics in the English-speaking world.[1] The four ethical principles proposed are beneficence, nonmaleficence, autonomy, and justice. These principles are argued to mediate between high-level moral theory and low-level common morality, providing a working framework with which to analyse ethical questions. Their influence has been pervasive. The approach, also known as principlism can be found in popular general medical textbooks, such as *Kumar and Clark's Clinical Medicine.*[2] It is the framework suggested by the UK Clinical Ethics Network for hospital and Trust clinical ethics committees to use in their practical evaluation of ethical issues.[3] It is even advocated to students hoping to study medicine in their preparation for medical school interviews.[4]

It seems as if these principles are now accepted as self-evident, requiring no further justification, and sufficient – no other principles need be considered. But where did the 4-principle approach come from? How were these principles selected and others, such as sanctity of life, excluded? Who are Beauchamp and Childress?

The origins of principlism

This paper will review the origins of principlism as described by John H Evans[5] and will consider some of the strengths and weaknesses of the approach. Given the profound impact and influence of principlism on contemporary bioethical debate the philosophical and ethical implications of principlism will merit consideration in some detail and will be dealt with in a separate paper. Evans begins his history in the 1950s as concern among the scientific community grew regarding the potential for scientific advances to be applied to the practice of eugenics. The idea of eugenics is, of course, much older. The word was coined by Francis Galton in 1883 and G.K Chesterton was classifying it as an evil in 1922.[6] What was new was the rapid advance of science. Watson and Crick had determined the structure of DNA in 1953. Hopes of further breakthroughs prompted debates regarding the genetic fitness of the population, eventually leading to the prospect of human genetic engineering (HGE). Evans sees this as a time when the scientific community were 'trying to expand their jurisdiction beyond the discovery of facts about nature to a more active role in public affairs.... These geneticists were part of a broader community of scientists attempting to find the meaning and purpose of human existence in evolution and biology, to create a secular "scientific" foundation upon which to re-establish our system of ethics… If human beings could no longer look outside nature for purpose and direction- as most theologies had done- the foundation for ethics was to be found in the "objective" facts of evolution… Society could no longer use a discredited traditional religion for its base: a new human-based scientific religion was needed to save society.'[7]5 This ethical overreach by the scientific community did not go without challenge from both philosophers and theologians. One of the main differences in outlook between the theologians and the scientists was the importance given to means as opposed to ends; in particular the ends to which HGE would be deployed. In brief, many of the philosophers and theologians held that if means are inconsistent with society's ends, then they should not be used. This difference lead to further disagreements between the two groups including disagreements as to how the debate should be constructed. In brief, the scientific community favoured *formally rational* debate where the focus is on how best to achieve agreed or assumed ends (goals), whereas the theologians and philosophers sought *substantially rational* debate where the appropriateness of the ends was included in the discussions. Formally rational debate may be described as 'thin', and substantial rational debate as 'thick'. We will consider the subject of formal and substantively rational debate in greater depth in the second paper.

A key moment in this history was the establishment in the United States of America of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The commission met in the Belmont Conference Center in Elkridge, Maryland, from 1974-1978 and published its report, *Ethical Principles and Guidelines*

for the Protection of Human Subjects of Research, in 1979. (7)

This report may be viewed as the immediate precursor to the 4-principle approach. The commission had been established to consider the question of ethics in medical research when human subjects were involved. The commission proposed that certain basic principles were key. These were:

> Respect for Persons – defined as the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.
>
> Beneficence – defined as an obligation to both not harm and to maximize possible benefits and minimize possible harms.
>
> Justice – 'in the sense of "fairness in distribution" or "what is deserved."'

One of the commission's staff members was philosopher and ethicist Tom Beauchamp. At this time, he and James Childress, a graduate of Yale Divinity School and theological ethicist, were both on faculty at the newly established Kennedy Institute of Ethics at Georgetown University. While Beachamp was working on the *Belmont Report* he was also writing the first edition of *Principles of Biomedical Ethics* with Childress. With reference to the *Belmont Report,* Beauchamp recalls 'This drafting was done at exactly the same time Jim and I were drafting Principles, and the drafting of one would deeply influence the drafting of the other in areas of research ethics and general principles.' [8] It should be noted that Beauchamp's co-author, James Childress, warns against conflating the *Belmont Report* 's three principles with the four principles presented in *Principles of Biomedical Ethics* [9] but it does seem to be part of the story.

The use of guiding principles in ethics is not new. In his book the *The Right and the Good* philosopher W.D. Ross proposed a series of what he termed 'self-evident ethical principles'. These were respect for persons (including oneself), fidelity and honesty, justice, reparation, beneficence, and non-maleficence. [10] Whilst there may be some overlap between Ross's self-evident principles and those proposed by the Belmont Report, there is a difference in terms of how they are derived and how they are applied. Beauchamp describes the thinking behind the development of their approach. He and Childress cite what they term a 'common morality theory' consisting of general moral norms which apply everywhere in life.[11]

Alternative principles

Other bioethicists have proposed their own principles. H Tristram Englehardt Jr proposed that the principles of permission and beneficence were sufficient (In this instance, permission for the physician to act replaces autonomy).[12] Engelhardt recognises the challenges of bioethics in a morally diverse society and admits his own religious perspective which gives shape to his principles. In their *Clinical Ethics: A Practical Approach to Ethical Decisions in Clinical Medicine*, Jonsen, Seigler and Winslade suggest there are four key topics for consideration in ethical questions: Medical Indications, Preferences of Patients, Quality of Life, and Contextual Features.[13] Whilst there is relatively little in the literature regarding this method, it is felt to offer some advantages over Beachamp and Childress' method in terms of clinical applicability.[14] (Sokol, 2008) Influenced by both Ross and Beauchamp and Childress, Robert Veatch also proposed his own set of principles: beneficence, nonmaleficence, fidelity, autonomy, honesty (veracity), and avoiding killing.[15] The four principles of Beauchamp and Childress may also be contrasted with those identified by the European BIOMED II project regarding "Basic Ethical Principles in European Bioethics and Biolaw" – these being autonomy, dignity, integrity and vulnerability. Of note, dignity here includes the 'inviolability of life' and restrictions on 'interventions in human beings in taboo situations'.[16]

Principles and morality

Beauchamp and Childress deny that the set of four principles constitutes the full set of universal norms of common morality. Rather they have been selected from the larger set of principles in the common morality for the purpose of constructing a normative framework for biomedical ethics. Common morality is comprised of principles together with rules, virtues, ideals, and rights and all of these are necessary for a fully formed moral outlook. An important point to note is that 'none of the principles is morally weighted or placed in a hierarchical order of importance,' so that 'questions of weight and priority must be assessed in specific contexts.'[17] Beauchamp resists the criticism that principlism is merely a method rather than a conceptually shaped theory. However, it clearly does function as a method and Beauchamp himself describes it as such elsewhere. (17) Despite the appeal to common morality, elsewhere he states 'I make no presumption that bioethics is integrally linked to philosophical ethical theory. Indeed, I assume that the connection is contingent and fragile. Many individuals in law, theological ethics, political theory, the social and behavioural sciences, and the health professions carefully address mainstream issues of bioethics without finding ethical theory essential or breathtakingly attractive.' [18] He notes the difficulties posed by 'the lack of distinctive authority behind any one framework or methodology, the unappealing and formidable character of many theories, the indeterminate nature of general norms of all sorts' opining that 'moral philosophers have not convinced the interdisciplinary audience in bioethics, or even themselves, that ethic- theory is foundational to the field and determinative in practice.' He concludes with his doubts as to 'whether ethical theory has a significant role in bioethics.'

The impact of principlism

How do others view the impact of principlism on bioethical debate? The influential British medical ethicist Raanan Gillon, emeritus professor of medical ethics at Imperial College London, and past editor of the Journal of Medical Ethics, is a strong advocate for principlism. He contends that 'Ethics needs principles—four can encompass the rest'. Moreover, he feels that respect for autonomy should be "first among equals" [19] Gillon see the principles as a means to avoid what he regards as 'two polar dangers'. These are moral relativism and moral imperialism. (Gillon, 2003,309) Those who hold that there are indeed some moral absolutes will find this concerning. However, it is difficult to see how a practitioner following the four principles without some firmer basis for belief can avoid moral relativism. In a later paper, Gillon acknowledges that 'the approach does not provide universalisable methods either for resolving such moral dilemmas arising from conflict between the principles or their derivatives, or universalisable methods for resolving disagreements about the scope of these principles'.[20]

Another defender of principlism is Ruth Macklin, distinguished university professor emerita at Albert Einstein College of Medicine in New York City.[21] In a paper published in the Journal of Medical Ethics, she contrasts the use of principlism with the more intuitive approach described by Leon Kass as 'the Wisdom of Repugnance' [22], dismissing the latter as simply 'the yuk factor'. [23] Macklin also supports Beauchamp and Childress' contention that the principles are based on a perceived 'universal morality' which is distinct from and superior to any 'community-specific morality'.

Objections to principlism

Whilst principlism has been widely adopted as the norm and has many influential proponents, not everyone supports the approach. Richard Huxtable, Professor of Medical Ethics at the University of Bristol, UK, highlights four criticisms of principlism.[24] First, he notes that the four principles can be seen to set forth a position that is not simply Western but in fact Anglo-American. (This will be dealt with in depth in a following paper.) The second criticism noted by Huxtable is that the principles are inapplicable in certain instances, for example, when the patient lacks autonomy. The third objection is that they are inconsistent, the example given being the conflict between autonomy, beneficence, non-maleficence, and justice when considering ap patient's request for medical assistance to die. Finally, they can be seen as an inadequate framework for resolving ethical difficulties as the cannot help resolve issues such as assisted dying as noted above. Moreover, they are 'incapable of detecting errors and inconsistencies in argument.' Huxtable concludes this paper recognising that 'one might see the principles as offering a framework and language through which conflicting viewpoints can be expressed and explored and then through which consensus or at least compromise might be achieved'. However, it must be realised that principlism 'offers only a starting point for, and not the end point of, moral deliberation.' John Harris agrees with Huxtable, noting that 'whilst the principles constitute a useful "checklist" they also 'allow massive scope for interpretation and are not wonderful as a means in detecting errors and inconsistencies in argument.' [25]

Others find more substantial problems with principlism. Green notes an 'almost deliberate avoidance of deep engagement with basic theoretical issues in ethical theory'.[26] This includes a 'sweeping under the rug' of the potential conflicts between those who hold to a utilitarian position and those who favour a deontological approach. Clouser and Gert also find principlism lacking. 'At best, "principles" operate primarily as checklists naming issues worth remembering when considering a biomedical moral issue. At worst, "principles" obscure and confuse moral reasoning by their failure to be guidelines and their eclectic and unsystematic use of moral theory.' [27] Rather than a coherent account of morality the principles, as described in *Principles of Biomedical Ethics*, are merely 'chapter headings for a discussion of some concepts which are superficially related to each other.' And in practice, 'function as hooks on which to hang elaborate discussions of various topics'. In the absence of an adequate overarching moral theory, the '"principles" are de facto the final court of appeal.'

The first part of this paper has reviewed the history of principlism and considered some concerns regarding its acceptance as the standard approach for bioethical debate. A particular concern has been its tendency to lead to thin debate and formal rationality without a deeper consideration of moral theory. This will be dealt with in greater depth in Part Two.

Part Two of this article will follow in the next issue of the Ulster Medical Journal.

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Medical History

Radar to Radiology

John Hedley-Whyte, MD, FACP, FRCA [1], Debra R. Milamed, MS [2]

INTRODUCTION

In November 1940 while waiting to board the Stranraer to Larne ferry, I[1] heard two Glaswegian builders discussing radar. My mother thought they were Glaswegian builders going to build a radio station. When I got to Hut 1 at Musgrave Park I looked up "radar" in my 1939 *Encyclopaedia Britannica*[1]. There was no mention of radar in any of the nineteen 1939 volumes[2].

At Hut 1, Musgrave Park[3,4] I was initially assigned for tuition to Benjamin Rycroft. Rycroft was already internationally known for his therapeutic replacement of human tissue[5,6,7,8,9]. Later to be knighted, Rycroft explained to me the principles of radar: "The critical need was for reliability and range." Rycroft recounted how Robert A. Watson-Watt had pioneered the use of the radio echo method as a strategic military weapon, building on the earlier work of Professor Edward V. Appleton and the Radio Research Board[10]. I was later to learn that Appleton was knighted in 1941[11]. Appleton won the 1947 Nobel Prize in Physics[12]. Watson-Watt was knighted in 1942[13].

AIR DEFENSE RESEARCH, RADAR

In 1934, Dr. Harry Egerton Wimperis, Director of Scientific Research of the U.K. Air Ministry, along with his colleague, A.P. Rowe, considered potential protection systems for Britain against German bombers. Director Wimperis proposed the creation of a Committee of Research on Air Defense under Professor, later Sir Henry Tizard, KCB[10,14] (Fig. 1). The Tizard Committee recommended the intensification of their experimental program and in 1935 a dedicated laboratory was built at Oxfordness on the Suffolk coast[10]. In 1936 the research group was relocated to a larger facility at Bawdsey Manor near Felixstowe, where 240 foot-tall towers were built. By March 13, 1936, they were able to locate aircraft flying at an altitude of 1,500 feet from a 75-mile distance[10]. RAF pilots were trained to use the radar apparatus and in 1937 construction of a chain of twenty coastal stations was begun. By April 7, 1939, the chain of twenty stations "from Ventnor to the Tay started their continuous watch, which was never interrupted during the war except at one station which stopped for a short time owing to an unexploded bomb"[10]. The network of radar stations was known as the Chain Home (CH) stations. They were a component of the network known as the Dowding System controlling transmission of information and orders during German attacks[15,16].

Figure 1.

Sir Henry Tizard, KCB, FRS (1885-1959), oil on canvas by Cuthbert J. Orde (1888-1968) . Presented to Imperial College, London, by the Civil Engineering Department, 1955. Leader of the Tizard Mission to the United States, August 1940. Every effort has been made to trace or contact all copyright holders.

Dr. J.T. Randall, together with H.A.H. Boot, Physicist at Birmingham University, developed the cavity magnetron capable of producing a reliable output of hundreds of kilowatts in short pulses[10]. This small radio transmitter emitted ten-centimeter radiation at an intensity one thousand times greater than that produced by United States devices[10,17].

John D. Cockcroft, of St. John's College (Fig. 2), working at Cambridge's Cavendish Laboratory[18,19,20] joined the coastal radar defense effort. The team adopted Butement's 1.5

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Figure 2.
John D. Cockcroft (1897-1967), FRS 1936, Nobel Prize in Physics, 1951. Oil on canvas, 1944, by Rodrigo Moynihan (1910-1990), 50.8 cm x 40.6 cm. From the collections of the Imperial War Museum, London, IWM Art LD 5852; transferred from the War Artists' Advisory Committee, 1947, and reproduced with their permission.

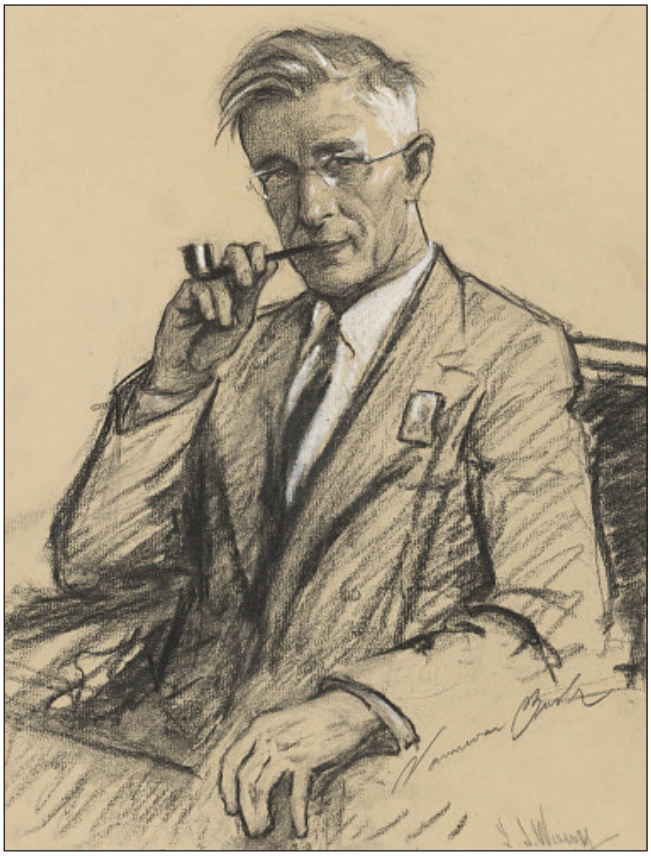

Figure 3.
Vannevar Bush (1890-1974), Charcoal and chalk drawing on paper, 51.5 cm x 38.5 cm, 1945 by Samuel Johnson Woolf (1880-1948). National Portrait Gallery, Smithsonian Institution, no. NPG.80.253 ©Estate of S.J. Woolf. Reproduced under Creative Commons License.
Born in Everett, Massachusetts, Vannevar Bush joined the Department of Electrical Engineering at the Massachusetts Institute of Technology (M.I.T.) in 1919. In 1922 he was a co-founder of the company that became Raytheon. In 1932 he was appointed Vice-President of M.I.T. and Dean of its School of Engineering. Following FDR's suggestion, he was elected to the Presidency of the Carnegie Institution, Washington, D.C., in 1938. He became chairman of the National Advisory Committee for Aeronautics. As inaugural Science Advisor to FDR, Vannevar Bush chaired the National Defense Research Committee (NDRC) and the Office of Scientific Research and Development (OSRD), responsible for the advancement of radar and the Manhattan Project.

metre experimental radar equipment designed for coastal detection[10]. Six sets of this equipment were erected in the Shetland Islands. These devices could detect fully-surfaced submarines up to 25 miles away and aircraft up to 70 miles[17].

On August 29, 1940, the group formally titled the British Technical and Scientific Mission, known as the Tizard Mission, sailed for North America. Tizard himself had departed for Ottawa in mid-August to privately meet with officials to discuss Canadian scientific participation in the war[21]. The team, which included Professor Cockcroft, brought with them a metal box containing secret information and a prototype cavity magnetron. During the following weeks the Tizard Mission traveled between Cambridge, MA, Washington D.C., New York, New Jersey and back again to Washington[10,17,18,22]. They met with the Microwave Committee of the U.S. National Defense Research Committee concurrently exploring deployment of radar in defense[23].

The Anglo-American Assemblage of Professors of Theoretical Physics was assembled in Washington D.C. Vannevar Bush (Fig. 3), investment banker-scientist Alfred L. Loomis[24] and FDR were paying and authorizing for all activities[10,17,22]. Sir Joseph Larmor, Lucasian Professor Emeritus now returned to Ulster (Fig. 4)[25,26] told Rycroft who later told me "Anglo- or U.S. they all appeared to have Princeton or Cambridge, U.S. and U.K. degrees." Einstein[27] or Rutherford-trained[20] they were on the payrolls of Harvard, Princeton, Birmingham, Cambridge and the Massachusetts Institute of Technology (M.I.T.). Tizard's committee was flown to Boston to avail themselves of the all expenses paid largesse of Vannevar Bush, Alfred L. Loomis and FDR. It was agreed to invite from California Professor E.O. Lawrence, who had won the 1939 Nobel Prize in Physics[24,28].

The first week in October 1940, when the Tizard Mission visited Washington, D.C., they met with Vannevar Bush, James B. Conant, President of Harvard University, E.O. Lawrence and K.T. Bainbridge, General Electric Scientist and

Figure 4.
Sir Joseph Larmor FRS, FRSE (1857-1942), oil-on-canvas, 1940, 101 cm x 86 cm, by Frank McKelvey (1895-1974). From the collection of the Naughton Gallery, Queen's University Belfast, no. QUB 52, and reproduced with their permission.
Born in County Antrim, his family moved to Belfast in 1860. He was educated at Queen's Belfast where he received a BA in 1874 and MA 1875 in Mathematics and Experimental Science. As a Johnian, he was appointed Lucasian Professor of Mathematics in 1903. Larmor was elected Conservative MP for Cambridge University in 1922. From the outbreak of World War II until his death on May 19, 1942 he held a position of great responsibility as a liaison between King George VI and FDR.

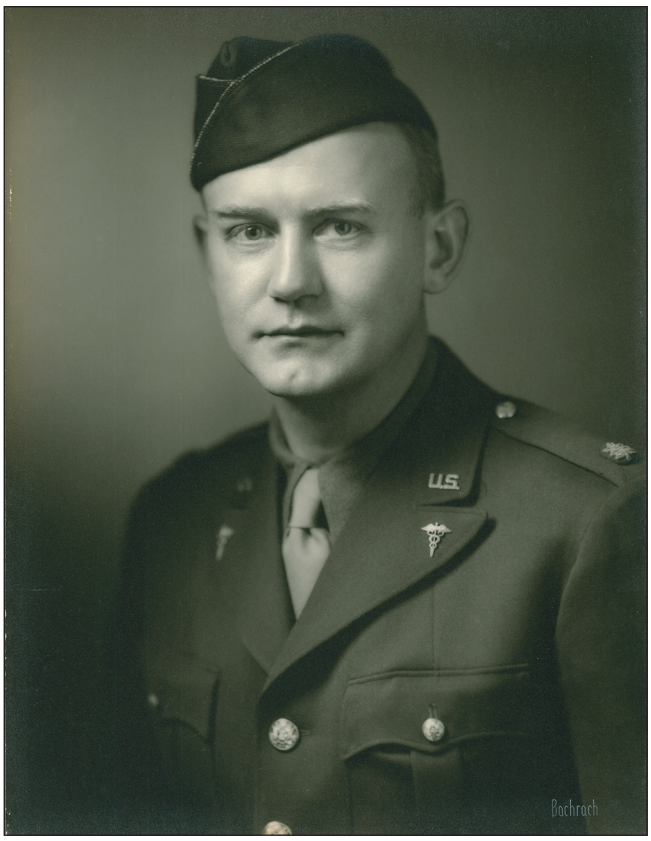

Figure 5.
Magnus Ingvald Smedal, M.D. (1905-1981), ca. 1944, photograph by Bachrach Photographers, Boston, MA, courtesy of the Smedal family and reproduced with their permission. Wisconsin-born, Magnus Smedal transferred from Medical School of the University of Wisconsin in 1927 to graduate M.D. from Harvard in 1929. After serving as Chief of Radiology at Harvard's 5th General Hospital at Musgrave Park, his distinguished war record led to three Battle Stars for heroism in France at D-Day and at the Battle of the Bulge. Post-war he returned to Boston with the rank of Colonel. He served as Treasurer, then President of the New England Roentgen Ray Society.

Engineer[10,17,24,29]. At the U.S. Naval Reserve Laboratory the Tizard Mission was shown 8 meter radar in action. Aircraft were being picked up over 50 miles from Washington D.C. and followed to landing. Vannevar Bush saw reports, costs, and estimates, for bigger, long-range multimeter radar devices that aided the Allies in winning the WWII Battle of the Atlantic[30].

During the 'Belfast Blitz' in April 1941, there were six Chain Home radar stations in Northern Ireland, including one at Downhill[31]. By the end of 1941 additional radar stations were added including one to monitor the shipyards at Belfast[31].

Years later, My father-in-law, then RAF Flight Lieutenant George Stanley Waller of 502 (Ulster) Squadron, related how Whitley bombers had been rebuilt to fly at lower altitudes to evade radar designed to detect enemy aircraft[32]. Advances in radar increased the safety of medical transport by land and sea, and air evacuation of casualties throughout the world[33,34,35,36,37,38,39].

MUSGRAVE PARK, SIR JOSEPH LARMOR

Soon after my arrival in Belfast before Christmas in 1940, Benjamin Rycroft himself introduced me to Sir Joseph Larmor (Fig.4)[25,26]. Larmor was, together with Max Rosenheim (later enobled)[5], discussing roles of U.S. Army and American forces scheduled to arrive through Belfast, very soon to deploy throughout Northern Ireland[40].

Now residing in Northern Ireland, Sir Joseph Larmor was a facilitator for both FDR and the British Cabinet. Sir Joseph wanted to know who, if anyone, of the British would likely be anti-American.

Lucasian Professor Emeritus Sir Joseph Larmor died on 19 May 1942 and was deeply mourned[25,26].

RADIOLOGY AND TEACHING

In spring 1942, in Hut 1 at Musgrave Park, USAMC Lt. Col. Magnus I. Smedal asked me if he could discuss with me Mendeleev's Periodic Table. I replied that I knew about the heavier elements. I asked "Why can't we talk about cyclotrons"[41]?

Dr. Magnus I. Smedal (Fig. 5) always said that he was an electrician who bragged about uses of electricity and the Bragg Effect[41,42,43]. At Musgrave Park he explained to me how Radiology was key to Abdominal Surgery, Ophthalmology, and Orthopaedics, and was even more important in time of war. Smedal's three WWII Battle Stars were well deserved[44]. Smedal set up complex functioning electrical equipment within three hours of the first US troops landing on Omaha Beach. By 13 June 1944, the first mobile X-ray unit was in operation. Smedal used to tell Harvard, M.I.T. and Lahey Clinic staff, students, nurses and residents that image taking and making can change history. During his World War II service, Smedal also worked with tuberculosis expert Col. Theodore Badger, USAMC, in diagnosis and treatment of tuberculosis in Allied troops and civilian refugees[45,46]

In the European Theater of Operations, X-ray machines were routinely used to diagnose combat and non-combat-related trauma and treat disease[46,47,48]. To assure the availability of radiographic images, U.S. medical officers from other specialties were trained in this modality and troops without training were taught to be competent X-ray technicians. Chest surgery was advanced, and the use of the X-ray facilitated removal of foreign bodies from the heart[46].

Because of strict US regulations for the transport and deployment of X-ray machines and supplies, most were required to be obtained in the UK. The U.S. Senior Consultant in Radiology, Col. Kenneth D.A. Allen, MD, and Dr. A.E. Barclay, Consultant to the British Ministry of Health, arranged for three-week training courses for selected U.S. radiologists at pre-eminent British radiologic centers. These courses were designed to facilitate liaison between the British and American radiologists, who were initially resistant to the use of British X-ray equipment. The US Senior Consultant also arranged meetings for all US Radiologists in Britain. The first such meeting was held on 22 May 1943 at the British Institute of Radiology, Welbeck Street, London. Brigadier D.B. McGrigor, RAMC, Consultant in Radiology to the British Army, educated his British and American colleagues on the importance of standardization of X-ray equipment. This talk was intended to make the American radiologists more amenable to the use of British equipment. Another such meeting was held at the same location on 7 December 1943, and attended by 56 radiologists, including then Lt. Col. Smedal[46]. While Chief of Radiology at the 5th General Hospital, Smedal produced a working manual for the effective operation of a hospital X-ray department[46].

At the end of WWII, Col. Magnus I. Smedal returned to M.I.T. and Harvard as senior consultant radiologist, later Department Head. He led the Radiology Department at the Lahey Clinic[44,49] affiliated with the Harvard-M.I.T. Cyclotron[41,44,49], and contributed much to particle acceleration in the treatment of cancer[50,51,52,53,54,55,56,57]. Smedal would order and personally interpret the images that turned out to be crucial in the patients' management.

EPILOGUE

Rapid advances in radar and related technologies, and collaborative efforts between government and academia helped assure Allied victory in World War II.

Dr. Smedal's mentorship continued until his death in 1981. The Harvard University-Massachusetts Institute of Technology Program in Health Sciences and Technology, founded in 1970, was of great interest in our discussions[58]. The wartime challenges of incompatibility of medical and other equipment components, and operator training were remediated by the establishment post-World War II of the International Organization for Standardization in Geneva[59]. Dr. Smedal recognized the importance of standardization of medical equipment and congratulated his former pupil when I became active in this area[60].

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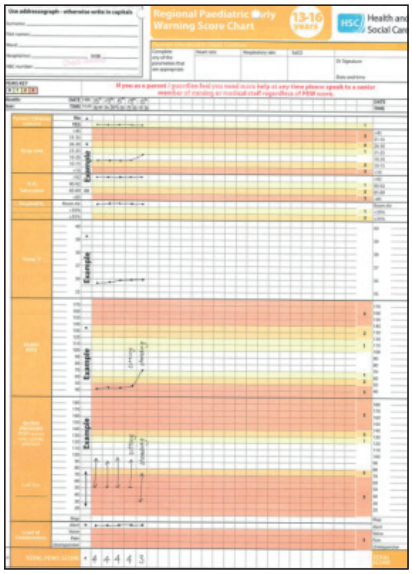
Curiositas - Teenage Kicks

QUIZ 1 - UG quiz

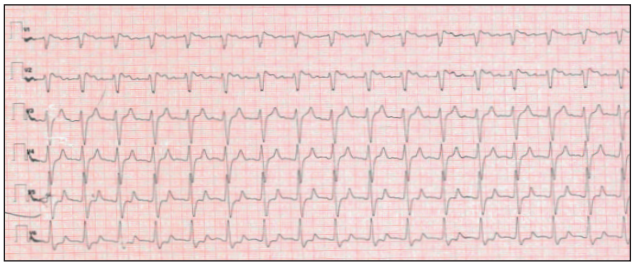


A 13-year-old female presents to the emergency department following a dizzy spell. On examination she is noted to have a significantly low weight. Her observations are as outlined on the chart above.

1. What is the most likely diagnosis?
2. How is this condition managed and what guidelines can be used to guide medical management?
3. Why has there been a rise in incidence since the pandemic?

Lauren Wilson (Year 4 medical student, QUB), Nicola Kocwin (APNP, RBHSC), Dr Christine Sloan (Paediatric Trainee, RBHSC), Dr Katherine Murtagh (Consultant Paediatrician, RBHSC)

QUIZ 2 - PG quiz



A 12 year old girl presents to emergency department after being found collapsed in her bedroom.

1. What abnormality is noted on her ECG and what might this indicate?
2. What is the management of this case within paediatrics?
3. What is the HEEADSSS framework and why might this be useful in assessing adolescents?

Abi Wallace (Year 4 medical student, QUB), Dr Naomi McClelland (Paediatric Trainee, RBHSC), Dr Seana Molloy (Consultant Paediatric Intensivist, RBHSC), Dr Katherine Murtagh (Consultant Paediatrician, RBHSC)

QUIZ 3 - Historical quiz

1. How is this teenager best remembered?
2. What might have added to his risk taking behaviour?

Abi Wallace (Year 4 Medical Student, Glasgow Medical School), Dr Stephen Mullen (Consultant Paediatrician, RBHSC) Dr Andrew Thompson (Consultant Paediatrician, RBHSC).
Acknowledgements: Pictures supplied by Ellen Thompson

QUIZ 4 - And Finally…

1. Who are the adolescents depicted on mural A?
2. *'Teenage dreams so hard to beat'* (mural B) is a lyric from which song?
3. What significant development in medical education took place in 2021 in the city which links the answers to the above questions?

Lauren Wilson (Year 4 medical student, QUB), Manpreet Kaur (Year 4 medical student, QUB), Dr Peter Mallett (Clinical Academic Consultant Paediatrician, QUB/RBHSC) Dr Ben McNaughten (Consultant Paediatrician, RBHSC)

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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. This young person is bradycardic, hypotensive and hypothermic with significant postural changes in heart rate suggesting medical instability. Whilst other causes of weight loss and collapse must be considered this presentation is typical of an Eating Disorder (ED). The most likely diagnosis is Anorexia Nervosa. This is the most common ED in young adolescents. Others include Bulimia Nervosa, binge eating and ARFID (avoidant restrictive food intake disorder).[1]

2. Management requires a MDT approach with the initial aim to ensure medical stabilisation.[2] Optimal care is provided in community settings by dedicated ED teams. When medical instability is significant, hospital admission may be required. Physical stabilisation is achieved by refeeding. *"Food is medicine."* [2] If the patient refuses feeds the application of the relevant legal framework with psychiatric input may be needed, to deliver life-saving treatment.[2] The New MEED guidelines were published in 2022 and have replaced the MARSIPAN guidance. They apply to both paediatric and adult patients and provide a framework for assessing medical risk.

3. There was a significant increase in the incidence of ED in young people as a result of the COVID-19 pandemic. Suggested reasons include the disruption of daily and educational routines, social isolation, familial stress and increasing health anxiety.[3] Nonetheless, the incidence of ED over the preceding ten years was already rising. A major contributory factor is thought to be the increased usage of social media, and its link to increased body image dysmorphia.[4]

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QUIZ 2

1. This ECG shows QRS widening and QTc interval prolongation. Causes of these abnormal findings include structural cardiac defects, sodium-channel blocking, and drug toxicity.[1] This patient's parent reported a history of self-harm and mental health difficulties. Tricyclic antidepressant medications (TCAs) were in her home. TCAs can cause blockade of myocardial sodium channels, making TCA poisoning a probable cause for intraventricular conduction delay, prolonged QTc interval and arrhythmia in this case.[1]

2. This case was managed as suspected TCA overdose. TCAs (including Amitriptyline) are the second most common cause of drug-overdose associated death in the UK.[2] Wide ranging clinical effects include anticholinergic, cardiovascular, and CNS effects. Prompt recognition and treatment is essential. Gastric lavage and activated charcoal are indicated if within one hour of ingestion. Standard resuscitation procedures are advised including airway management and ensuring haemodynamic stability. Alkalinisation using sodium bicarbonate remains the standard of care. Other specialist management options include potential use of lidocaine, lipid therapy or ECMO in refractory cases.[3,4] Following intensive medical stabilisation, this patient required crisis mental health assessment and follow up.

3. Home, Education/Employment, Eating, Activities, Drugs, Sexuality, Suicidal ideation and Safety (HEEADSSS) is a recognised psychosocial interview framework that allows a better understanding of a young person's situation and needs. This tool is regarded as a cornerstone of adolescent care.[5] It can help highlight areas of risk including in relation to substance misuse, mood and mental health. Prompt recognition of adolescent difficulties can allow earlier targeted intervention and safety planning.

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QUIZ 3

1. Samuel Scott is believed to be the first casualty in the story of the Titanic. He was part of the riveting gang who arrived early at Harland and Wolff shipyard on the morning of April 20th 1910. Later that day, Samuel slipped off a ladder and tragically fell to his death. Following a public campaign, the unmarked grave in Belfast's City cemetery finally received a fitting headstone, just over a century after his death

2. Samuel Scott was 15 when he died, falling into the adolescent age bracket (10-24 years of age). Adolescent males are more likely to be involved in traumatic accidents than their female counterparts, and the cause of trauma in this age group differs from both paediatric and adult cases.[1] In 2023, the most common

cause of trauma in adolescents is a road traffic accident (RTC). In 1912, vehicle use was a fraction of todays, and it is likely the commonest cause of trauma in adolescents was different.[2] Falls tend to be the second most common traumatic mechanism of injury in adolescents. Risk-taking behaviour in adolescent males is higher than any other age group and is a contributory factor in their higher mortality rate.[1,3,4] Physiologically, the pre-frontal cortex does not mature until the early 20's and this area is essential for decision making. This impacts on adolescents appreciating risk and can lead to increased impulsivity.[3] As a young adolescent male, it is likely Samuel experienced these reduced perceptions of risk and a stronger inclination to focus on reward leading to his untimely, traumatic death. Over 100 years on, mortality rates within adolescent populations have not shown a significant decline compared with other age groups. This points to a need for better health education and interventions to reduce trauma and subsequent mortality within this age group.[4]

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QUIZ 4

1. Arguably Northern Ireland's most famous teenagers – these are the 'Derry Girls'. 'Derry Girls' first aired in 2018 on Channel 4 and has become one of the channel's most popular and widely acclaimed shows. The series follows a group of typically innocent and naive teenagers in their journey through adolescence. The series was based in a fictional school, Our Lady's Immaculate College. Filming occurred across many Belfast locations including Hunterhouse College, a cross community all girls' grammar school in Belfast. Set during the politically unstable background of early 1990's life in Northern Ireland, it has received praise for sensitively and eloquently highlighting the ongoing challenges of the legacy of conflict-related and inter-generational trauma.[1]

2. This is a lyric from 'Teenage Kicks'. 'Teenage Kicks' was released in 1978 and was the debut record from the band The Undertones. The Undertones are a rock band whose original members were born in Derry. Despite their most prominent era being in the late 1970's and 1980's, their brand of post-punk music focused not upon the political climate, but on timeless issues of adolescence, love, and relationships. Influential BBC Radio 1 DJ John Peel famously identified 'Teenage Kicks' as his all-time favourite song shortly before his death in 2004.

3. August 2021 saw a new chapter unfold at the Magee Campus in Derry as the Ulster University opened its doors to the first 70 students at the new School of Medicine. Based in a recently-renovated historic listed building, it is only Northern Ireland's second medical school – and its first graduate-entry medical school. This 4-year postgraduate degree hopes to address the relative shortages of doctors within Northern Ireland. As soon as 2025, the first batch of UU doctors will graduate having taken the GMC's Medical Licensing Assessment and joining the roughly 8,000 other UK medical graduates at the start of their careers as doctors.[2,3]

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Game Changers

WHAT'S IN A NAME? DECIPHERING THE TAXONOMY OF BACTERIA, FUNGI AND PARASITES CAUSING INFECTION

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Microbial taxonomy, encompassing bacteria, fungi and parasites, is becoming more and more complicated, largely due to the application of newly emerging molecular methods, including whole genome sequencing. Presently, the List of Prokaryotic Names with Standing in Nomenclature lists 30,808 species from 4,954 genera.[1] In addition to this, there are a further 9,006 species from 2,196 genera, which are not validly published names.[1] Classification of these organisms has relied on phenotypic diversity, small subunit ribosomal RNA and more recently, genome-based classification.[2] Whilst only a small proportion of these organisms have ever caused human infection, it is daunting for the physician and surgeon to have an appreciation of (i) where these organisms are positioned taxonomically, (ii) how they are relate to each other and (iii) any recent modifications to their name. More recently, employment of improved molecular tools allows for the reclassification and splitting of established genera into new bacterial genera, with new names, which has the potential to cause confusion amongst doctors using the conventional name. An example of this is the Gram-positive anaerobe, *Clostridium difficile*, which was reclassified and renamed as *Clostridioides difficile* in 2016.[3] Other examples of recent bacterial nomenclature revisions include *Mycobacterium abscessus* to *Mycobacteroides abscessus*, *Enterobacter aerogenes* to *Klebsiella aerogenes* and *Ochrobactrum anthropi* to *Brucella anthropi.* For a full list of bacterial taxonomical revisions, please see Prinzi and Moore.[4]

A freely available online tool, LifeMap,[5] (https://lifemap-ncbi.univ-lyon1.fr/) is available for interrogation, which allows the reader the opportunity to input a microbial name of interest, utilising zooming and panning tools to determine where the organism of interest is positioned taxonomically, as well as describing the most up-to-date taxonomical name (Figure 1). Employment of such a tool may aid in a better understanding of microbial taxonomy of infection-causing pathogens and an improved lexicon aiding better communication amongst physicians/surgeons and scientists.

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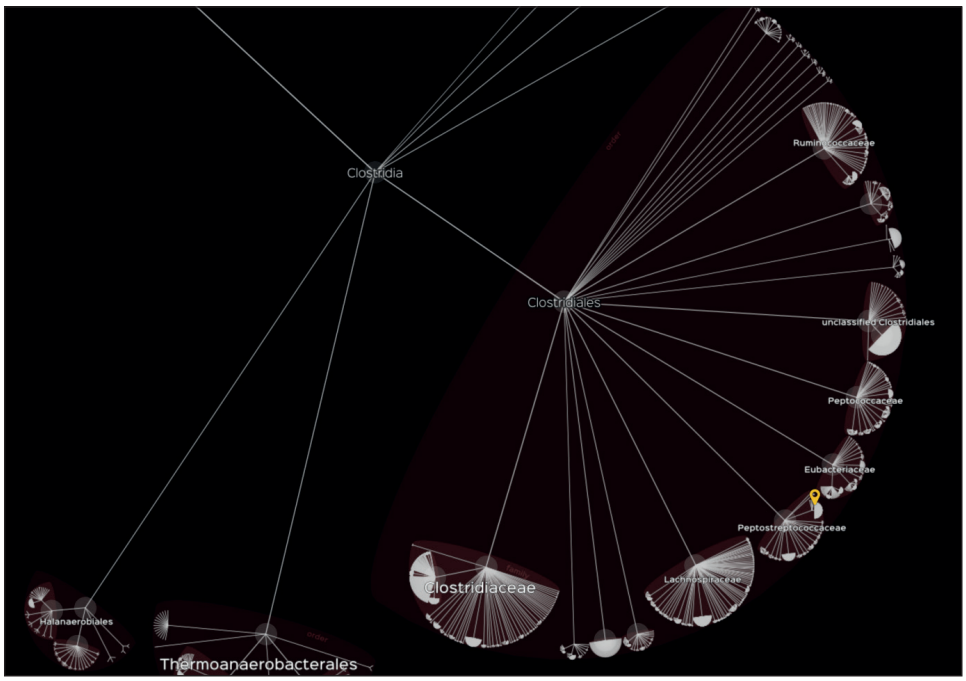

Figure 1:
Description of the taxonomical lineage of *Clostridioides* (*Clostridium*) *difficile* ( ), as displayed by LifeMap (NCBI version).[5]

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Cover Image:

The entrance of Antrim Area Hospital which opened in 1994, as a result of the amalgamation of the Waveney Hospital (Ballymena), Masserene Hospital (Antrim) and the Moyle Hospital (Larne).