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COMMENTARY

EDITORIALS

INTERVIEWS

ORIGINAL PAPERS

Finn et al report an improvement in outcomes for children with Cystic Fibrosis. The clinical parameters FEV1 and BMI are better. There has been a decline in the incidence of chronic Pseudomonas.

McCrossan et al report the findings of a questionnaire that was circulated to both consultants and SHOs on the latter's preparedness for paediatric work. There was discrepancy in the replies between the 2 groups. SHOs rated their readiness for procedures, teamwork, and outpatients as significantly lower than that of the consultants.

Hennessy et al demonstrate that CT scanning plays a vital role in the work-up of suspected lung cancer. They describe 2372 first attendances, 91% had a chest CT scan. 866 patients diagnosed with cancer, all had an abnormal CT scan.

ORIGINAL PAPERS (continued)

THE ROLE OF ENDOBRONCHIAL ULTRASOUND IN EARLY-STAGE NON-SMALL CELL LUNG CANCER

Cullivan et al describe their experience with endobronchial ultrasound (EBUS) in early non-small cell lung cancer (NSCLC). Their study found high rates of nodal discordance in patients who underwent EBUS which contrasts with existing data.

NATIONAL GUIDELINES ON THE PROVISION OF OUTPATIENT PARENTERAL ANTIMICROBIAL THERAPY (OPAT)

Sweeney et al describe the administration of an outpatient parenteral antimicrobial therapy service. It requires a designated team approach. It should include a clinical lead, a nurse, and a pharmacist.

EXPLORATION OF FACTORS ASSOCIATED WITH INTENTION, INITIATION AND DURATION OF BREASTFEEDING

Callaghan et al studied 131 women who intended to breastfeed. 120 women initiated breastfeeding. 86 and 73 women respectively were still breastfeeding at 1 month and 3 months respectively. A longer duration of breastfeeding was associated with a higher education and a lower BMI.

OCCASIONAL PIECES

THE 100 CITATION CLASSICS IN THE IRISH MEDICAL LITERATURE; A BIBLIOMETRIC ANALYSIS

AIRBORNE TRANSMISSION OF COVID-19: IMPLICATIONS FOR IRISH HOSPITALS

VIRTUAL CLINICS IN THE COVID-19 PANDEMIC

RESEARCH CORRESPONDENCE

TREATMENT MODALITIES FOR PRIMARY AND SECONDARY SPINAL MALIGNANCIES

CASE REPORTS

LEUKOCYTE ADHESION DEFICIENCY TYPE 1 DUE TO NOVEL ITGB2 MUTATION

Harvey et al describe an infant with neutrophilia and omphalitis. The infant was subsequently diagnosed with leukocyte adhesion deficiency type 1 (LAD1). A blood stem cell transplant was performed at 4 months with a good outcome.

QUINOLONE-INDUCED BICEPS TENDON RUPTURE

Crawford et al report a case of biceps tendon rupture due to quinolone antibiotic medication. The mechanism is a toxic effect on the collagen fibres.

CASE SERIES

AUTO-DECOMPRESSION - PRESERVED NEUROLOGICAL FUNCTION IN BILATERAL CERVICAL FACET DISLOCATIONS

O'Doinn et al 4 unique cases of bilateral cervical facet dislocation (BCFD). BCFD has a high incidence of severe neurological impairment. The cases that the authors describe had a good outcome because a concurrent lamina fracture resulted in auto-decompression of the spinal canal.

SHORT REPORTS

ENHANCED CARBAPENEMASE PRODUCING ENTEROBACTERALES (CPE) SCREENING IN A PAEDIATRIC POPULATION

Broderick et al report on 917 children who were screened for CPE. Two children were positive, who would have been identified from their history. The authors recommend that children whose only risk factor was admission in the previous year do not require screening.

POEMS

CORONAVIRUS (COVID-19) - IN PRAISE OF THE MEDICAL ARMY

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Covid-19: The Next Steps

J.F.A. Murphy - Editor of the Irish Medical Journal

After seven months we've come to accept that Covid-19 is not going to abate. It is still here, and it remains both infectious and virulent. The overall death rate has been estimated at 0.66%, rising to 7.8% in those over 80 years and declining to 0.0016% in children aged nine years and younger. The hospitalization rates also increase with age, ranging from 1% for those in their 20s, 8% for those in their 50s, and 18% for those in their 80s[1].

Herd immunity is not an option. At least 60% of the population needs to be immune to the virus in order to prevent its spread. In Ireland 5% have been exposed to the virus, which indicates that there is no significant level of immunity in the community.

All countries are now working towards medium and longer-term strategies. The stage that they are at differs from State to State but the direction is the same. There are three interlocking approaches.

The first challenge is living with the virus. This is the new reality of an economic and social life that co-exists with the pandemic. It is a difficult balancing act for all healthcare services and societies. The essence is the re-opening of day-to-day activities as much as possible while containing the Reproduction rate of the virus. The main strategy is the restriction of the movement of people, and a continued ban on large gatherings. The Government's advice is not to travel to other countries unless absolutely necessary. A further measure is the wearing of facemasks on public transport, in shops and shopping centres.

The second challenge is the planning for a possible winter surge of Covid-19. This will be about being better prepared. It is based on learning from one's own knowledge and the experiences of other countries. Boccia et al[2] have recently reflected on why Italy was so badly affected by the virus.

Italy has the most elderly population in Europe and is the second most elderly population in the world after Japan. The proportion of people over 65 years in Italy is 23% compared with 14% in Ireland. Their healthcare system became overwhelmed in Bergamo following a massive viral transmission during a Champions League football match on Feb 19, 2020.

Although Italy has a competent state-run healthcare system, it has only a modest number of ICU beds, 8.4 per 100,000 population. Also being a decentralized country complicated initial containment measures. A uniform approach was not adopted.

Many patients with mild symptoms were admitted to hospital and this resulted in overcrowding and transmission to healthcare workers. There were shortages of facilities, equipment and staff.

Germany has coped better than most other countries in Europe. The crisis was under control within 6 weeks of its first reported death. It has had 9,100 Covid-related deaths in a population of 83 million compared with 45,400 deaths in the UK with a population of 67 million. As of July 27, in Ireland there have been 1764 Covid-19 deaths and 25,881 cases. In children there have been 188 cases (0-4 years), 265 cases (5-12 years), 267 cases (13-17 years), and no deaths.

Ireland benefited from its centralized health system, it's clear and consistent directives, and good public communication.

The comparative mortality rates from Covid-19 are Germany 109 per million, UK 677 per million and Ireland 360 per million.

The third challenge is the ability and capacity to test and trace. This will be very important in the coming months. These tools make it possible to identify local outbreaks at an early stage. This facilitates effective contact tracing and containment. Proactive restriction can be placed on selected institutions or areas. Contact tracing requires 70-90% of the contacts to be traced in order to prevent onward spread[3]. Currently, Ireland has the capacity to test 15,000 individuals per day.

Serological testing in the identification of those who have had prior infection can be helpful for certain groups. It means that a seropositive healthcare worker does not require repeated periods of isolation.

It is reassuring to see the considerable resources and efforts being put in place in order to get children back to school fully at the end of August. The lockdown has placed the greatest restrictions on the lives of children encountered in modern times. It has been the longest school closure in the history of the State. Even during the Second World War schools remained open in the UK. Children's academic progress will undoubtedly have been affected. The educational concerns are greatest for primary schoolchildren. They are unable to participate in self-directing learning. The younger ones can't yet read or are only beginning to read. The consequences are particularly concerning for the 10% of children who have an intellectual disability or other learning impairment such as dyslexia, ADHD, or autism. Regression is a real concern for this latter group of children.

Recently acquired knowledge is vulnerable to loss. All child specialists agree that even short absences from school are damaging, let alone long periods over many months. School is also important in the development of a child's conversational skills, interpersonal skills, and their emotional self-regulation. As they enter post-primary education, friendships become a very influential part of their lives. By August, Irish children will have faced at least 6 months without any formal education. In addition to returning to school, 'catch up' programmes will be needed for some children[4].

The development of an effective vaccine is showing promising signs. More progress has been made in 5 months than would normally be made in 5 years. The Phase 1 studies, which test the safety of the vaccine, have been reassuring. The take-away points are no serious side-effects, minor local reactions, and reasonably well tolerated. As the doses of the vaccine were increased, patients developed higher antibody levels. Cell mediated immunity, which is the T cell response, was also identified. We don't know what the response to infection will be like. Modeling based on what the natural immunity levels looks like may be the best approach[5].

Richard Horton[6] concurred that the results of two randomised vaccine trials were encouraging. Both studies found that there was a rapid onset of an immune response within 14 days, with evidence of humoral and cellular response by 28 days. There are, however, signs of a poorer immune response in older subjects and this group may need a second dose.

He does warn that the anti-vaccine campaigners are already mobilizing their opposition to a Covid-19 vaccine. The background promotion of the new vaccine needs to begin now. Public health programmes will be needed to counteract misinformation. All strands of society will need to support and get behind the vaccine when it becomes available.

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Suicide

B.D. Kelly

Department of Psychiatry, Trinity Centre for Health Sciences, Tallaght University Hospital, Dublin 24, D24 NR0A.

Suicide is in decline. Globally, the age-standardised mortality rate for suicide decreased by 32.7% between 1990 and 2016, albeit with variations between countries[1]. The largest outlier is the United States of America, where the age-adjusted suicide rate increased by 33% between 1999 and 2017[2].

Despite the overall improvement, however, approximately 800,000 people still die by suicide each year around the world. This means that suicide remains a key public health problem, even in countries with decreasing rates. Even one death by suicide is one too many. Fazel and Runeson, in a recent review in the *New England Journal of Medicine*, point out that suicide is the foremost cause of death worldwide among people aged between 15 and 24 years[3]. Clearly, there is still much to be done.

In their review, Fazel and Runeson go on to examine various risk factors for suicide across the life-course, ranging from predisposing factors to risk-factors seen chiefly in older adults. They note that individual factors, especially mental illnesses, have the strongest effect on suicide rates across the life-course. Conditions such as depression, bipolar affective disorder, schizophrenia-spectrum disorders, substance use disorders, epilepsy and traumatic brain injury increase the odds of completed suicide by a factor greater than three. Risk is also increased if there is a previous suicide attempt, sexual abuse in childhood, a family history of suicidal behaviour and the death of a parent by suicide in early childhood[3].

A range of other factors are also relevant to varying degrees: genetics, epigenetics, early life adversity, personality disorders, physical health problems, lack of social support, economic factors, life events, effects of the media and access to lethal means[3].

While it is important to be aware of these risk factors, Fazel and Runeson point out that risk models for suicide used in emergency departments to assess people who have harmed themselves generally have a poor balance between sensitivity and specificity and do not provide probability scores. As a result, such tools may increase clinical workloads by requiring psychiatric assessment or hospitalisation in cases of false positive risks of suicide[3]. Therefore, while structured tools can help with assessment, they should not be interpreted as estimates of the probability of suicide.
In terms of prevention, Fazel and Runeson point to various population-based measures including limiting access to lethal means, such as erecting barriers at potential suicide spots, restricting paracetamol pack sizes and restricting access to guns (all of which have been proven effective). Other measures include removing ligature points in psychiatric hospitals and prisons, early intervention in psychosis and, possibly, raising awareness more generally[3].

The evidence base for pharmacological treatments to reduce suicide is generally limited, chiefly because most randomised clinical trials are insufficiently powered to study suicide as an outcome. As a result, most studies tend to focus on proxy outcomes, such as suicidal ideas and depressive symptoms. The most convincing evidence to date is for lithium in bipolar disorder and depression and, possibly, certain medications for opiate use disorders in people with addictions[3].

Fazel and Runeson also point to evidence for psychological therapies, noting that trials of cognitive-behaviour therapy have shown reductions in suicidal thoughts, and trials of dialectical behavioural therapy have shown small reductions in self-harm. In conclusion, Fazel and Runeson recommend a comprehensive approach to the assessment and treatment of suicidality, including regular follow-up, brief psychological therapy and, for people with symptoms of mental illness, pharmacologic treatment as appropriate. Environmental safety is also important, along with assessment by specialist mental health services when indicated[3].

In the European context, it is worth noting that Ireland's overall rate of suicide is not high compared to other European countries: it is the 11th lowest rate of 34 countries, according to the National Office for Suicide Prevention (NOSP)[4]. Ireland's overall figure, however, masks increased rates among certain population groups such as the Traveller community and young people: NOSP points out that Ireland's rate of suicide in young people (aged 15-19) is among the highest in Europe.

Overall, then, despite the fact that Ireland's overall suicide rate is below the European average, suicide and self-harm still remain substantial problems[5]. And while it is not possible to predict suicide at the individual level, it is likely that good primary care, good secondary mental health care and good social care all reduce risk.

In terms of targeted interventions, public health measures such as paracetamol pack size regulations have the most evidence to support them. In addition, Ireland's "National Clinical Programme for the Assessment and Management of Patients Presenting to the Emergency Department following Self-Harm" was introduced to the first emergency department in 2014 to better address management of self-harm, a key risk factor for suicide[6]. This programme aims to ensure that all patients who present to emergency departments following self-harm or with suicidal ideation receive a prompt biopsychosocial assessment; their next of kin receives support and advice on suicide prevention; the patient is linked with the next appropriate care; and both the patient and their general practitioner receive a written plan of care. This programme continues to expand.

Overall, it remains important that there is continued focus on providing greater support to those at risk of suicide and those bereaved. A coordinated, effective and compassionate approach is needed, linking community and state resources with each other[5]. Strategies rooted outside mental health services are vital: identifying and treating alcohol problems and other forms of addiction, addressing homelessness, improving social care, and resolving relevant issues within the criminal justice system[7].

Improving child and adolescent mental health services is an especially pressing priority in relation to suicide in Ireland. The relatively high rate of suicide among young people demonstrates yet again the need for enhanced services for this particularly vulnerable population.

Corresponding Author:
Brendan D. Kelly
Professor of Psychiatry
Trinity College Dublin,
Trinity Centre for Health Sciences,
Tallaght University Hospital,
Dublin 24,
D24 NR0A,
Ireland.
Email: brendankelly35@gmail.com

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Covid-19: The Irish Public Health Experience

C. Ni Bhuachalla, N. Murphy, M. O'Sullivan, M. O' Mahony, C. Buckley,
C. Foley-Nolan, D. Murray, A. Brennan, A. Sheahan

Department of Public Health, HSE – South, St. Finbarr's Hospital, Cork, Ireland.

On behalf of the regional Department of Public Health HSE South.

The Covid-19 global pandemic, caused by highly transmissible novel human pathogen SARS-CoV-2, is unprecedented. At time of writing (29/07/2020), almost 17 million cases have been confirmed worldwide[1]. In the absence of a vaccine or curative treatment, response has largely depended on non-pharmaceutical interventions (NPIs)[2]. Nationally, exhaustive efforts of Public Health departments and widespread societal engagement with NPIs, helped to mitigate risk during containment and delay phases. On June 30th 2020, Ireland reported the lowest 14-day incidence of Covid-19 cases in Western Europe [3]. However, as national NPIs are relaxed, resurgence risk arises[3].

There are 8 regional Departments of Public Health in Ireland and the Health Protection Surveillance Centre (HPSC) provides national oversight for health protection activities. In Ireland, Covid-19 cases are notified to Public Health under Infectious Diseases Regulations 1981; confirmed cases (defined as 'Detection of SARS-CoV-2 nucleic acid in a clinical specimen') are notified electronically from laboratory to the Computerised Infectious Disease Reporting System (CIDR) [4,5]. Transmission classification is defined by the World Health Organisation (WHO) as 'community, local or imported' [6] and the need for 'low levels of community transmission' has been cited recently as a pre-requisite to reopening schools and wider healthcare nationally[7].

Given current knowledge of SARS-CoV-2 transmission dynamics[8], timely testing pathways are critical to enable immediate specialised Public Health control activities. These activities rapidly break chains of transmission and prevent generation of secondary and tertiary cases from an index case of Covid-19. Such activities include; control in complex settings, outbreak investigation, identification of transmission source, risk assessment, contact tracing, case finding, isolation of cases, quarantine/'restricted movements' of specific cohorts and enhanced surveillance, amongst others[2,3]. The European Centre for Disease Prevention and Control (ECDC) advises that these Public Health activities should be adequately resourced, multifaceted, robust, timely, sustained, readily adaptable and supported by extended testing[3].

The SARS-CoV-2 testing pathway is complex and comprises multiple steps including patient referral, sample procurement, transport of sample to laboratory, testing of sample, reporting of results/notification and appropriate management of those results. Initial national surge capacity issues, affecting various points of the testing pathway, are well documented and posed a significant challenge to all those involved in control activities in various settings[9,10]. However, the considerable cross specialty and cross sectoral efforts invested in developing and implementing the current 'end to end' national testing process are to be commended. It is vital, at a national (and global) population health level, that timely 'test and trace' processes continue to be prioritised. Innovation such as the introduction of an adjunctive national contact tracing app[9,10] is welcome but does not replace the core Public Health activities outlined above.

At time of writing, the current 'Epidemiology of Covid-19 in Ireland' report[6], prepared by HPSC for the National Public Health Emergency Team (NPHET) describes; 25,890 confirmed cases, with 12.94% (3,349) of cases hospitalised, 1.69% (437) of cases admitted to ICU and a case fatality ratio of 5.82%. A total of 2,282 outbreaks are reported, imported cases account for 1.71% (442) of cases, healthcare workers (HCW) account for 32.43% (8,395) of cases and median age of cases is 48 years.

Transmission classification is reported as 65.87% (17,054) due to local transmission (where the source of infection is within the reporting location), 31.6% (8,180) due to community transmission and 2.44% (633) as related to travel abroad. Community transmission is defined as 'inability to relate confirmed cases through chains of transmission for a large number of cases, or by increasing positive tests through routine screening of sentinel samples' [6].

As Ireland 're-opens' the risk of introduction of new chains of transmission increases. Thus, it is critical that selected NPIs are continued[2,3], while living alongside SARS-CoV-2 in a 'new norm'. This is especially important to protect vulnerable cohorts as we remain a susceptible population currently, as demonstrated by recent seroprevalence studies[2]. Mandatory quarantine after travel abroad also plays a vital role[9,10]. Nationally 269 outbreaks in nursing homes have been reported [6]. In our regional experience in HSE-South (Cork and Kerry, population approximately 690,000[11]), and as reported internationally [3,12], Covid-19 has a devastating and disproportionate impact on older age groups. Those with underlying medical condition(s) are also at increased risk of severe illness[6], this highlights the need for targeted services and preventative measures in vulnerable cohort settings.

In our regional experience the Covid-19 epidemic evolved with discrete surges in specific settings. From early March 2020 a spike in travel-related cases was observed. Notifications from hospital and nursing home settings increased rapidly, likely reflecting increased community transmission. On 12/03/2020 Ireland moved into delay phase and schools closed, on 16/03/2020 overseas travel was restricted and on 27/03/2020 a national 'stay-at home' order was implemented[9]. We observed that healthcare and community setting notifications featured prominently in our region up to end of April 2020, with nursing home and residential institution settings of particular concern. Cases in private houses featured throughout. In our region cases declined from mid-March but from May resource-intensive local clusters predominated (e.g., in specific workplace settings). This is consistent with ECDC reports[3].

While occupational exposure risk must be considered, in our experience local transmission within shared accommodation/social settings was also implicated in some outbreak settings (such as workplace and residential institution settings). This is in alignment with international observations[13]. The unique challenges posed by meat factory Covid-19 outbreaks have been described recently[14]. In our experience, migrant workers, particularly those from non-English speaking communities, are especially vulnerable to household spread and development of familial clusters - due to crowded living conditions, and language and cultural barriers. National meat factory outbreak guidance has incorporated multilingual initiatives[15]. This facilitates health protection of wider communities also.

In Ireland, phased relaxation of national NPIs, with increased individual responsibility, commenced on the 18th May[9,10]. The ECDC has outlined a clear framework for avoiding resurgence[3], including a key recommendation that countries are 'prepared to amend strategies rapidly in response to indications of increased transmission'. At time of writing, in response to recent increased Covid-19 activity in Ireland, progression from Phase 3 to Phase 4 has been delayed [7]. Such measures must be underpinned by robustly resourced Public Health services which are fundamental to any effective Covid-19 control strategy [7]. For now, we must optimise our preparedness for the months ahead. As Dr Tedros, Director General WHO tells us 'The second wave is in our hands'.

Corresponding Author:
Cliodhna Ni Bhuachalla,
Department of Public Health,
HSE – South,
St. Finbarr's Hospital,
Cork,
Ireland.
Email: c.nibhuachalla@hse.ie

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Covid-19 and General Practice Part 3:

Interview with Dr. Ray Walley MRCGP FRCGP, Member of the National Covid-19 GP Liaison Committee

The IMO ICGP continue to lead on and support the HSE message emphasising that patients need to promptly seek attention for urgent care.

The IMO secretariat supported by the GP committee have organised continued contractual arrangements for Covid-19 telemedicine consultation for both public and private patients and respiratory assessments till August 10th, 2020.

This is in no way a complete overview of work done but is a summary of some priorities dealt with to date.

How has General Practice continued to respond to Covid-19:

1. The IMO ICGP HSE National GP Liaison Committee continued teleconference meetings with the HSE on a twice weekly basis with periodic additional meetings where required. HSE Meetings are held at 7.30am with IMO ICGP preparatory work done by email and a teleconference at 6pm the preceding evening.
   It is planned to progress meetings to a weekly basis in August.

2. The GP Liaison Committee continued to meet with high level HSE representatives from Chief Clinical Officers Office / Operations / Infectious Disease / Procurement / I.T etc.

3. The Liaison has allowed prompt addressing of organisational and educational issues pertaining to General Practice and community care. It is recognised that General Practice has a cockpit view of Covid-19 prevalence allowing immediate addressing of prompt timely interventions with clinical and organisational answers to the continued optimum management of Covid-19, flattening the curve.

4. The IMO and ICGP separately teleconference to ensure a regular cascade to members changes in algorithms / educational material / contract briefings on issues related to general practice care and provision.

5. Covid-19 prevalence has required that GMS contract changes be prompt, dynamic and fluid. Recent GMS contract changes negotiated by the IMO include;

   a) *Expansion of the qualification age to >70 y.o., down from 75 y.o., for chronic care management. Inclusion criteria include 1-3 of the following disease A Fib / IHD / CCF / COPD / Asthma / Diabetes Mellitus – effective 1/7/20. The new agreement allows for a telemedicine consultation. Both IMO and ICGP advocate face to face consultation as being optimal management of patients however in the context of Covid-19 where prevalence is fluid there was a requirement for a telemedicine option.*

   b) *Acceptance of claim returns for Maternity and infant care claims expanded from 3 to 6 months.*

6. Both IMO and ICGP have recognised the importance of education of all Medical Practitioners and have organised on a weekly basis webinars. It is recognised that knowledge acquisition with Covid-19 is international with it being both fluid and dynamic with education provision having to mirror same.

7. The IMO and ICGP equally contributed to the Department of Health convened leaders forum.

8. It is recognised that Media placement of GP expert opinion is of importance in reinforcing the message of symptoms included in the HPSC algorithm for isolation, referral for testing and contact tracing based on one of the following symptoms; **A high temperature, Cough, Breathlessness, Loss of taste, Loss of smell.**

   The latter is in the context that a patients GP is recognised as the primary first contact for all patients.

   Media GP expert opinion has been of influence on early and accurate engagement on: *''What are Covid-19 symptoms…'',* also on the hashtag *''#wearafacialcovering''* and in advising the public to download the HSE Covid-19 App.

   The IMO and ICGP have ensured that timely opinion is accessible through their respective public relations units. Both have significant presence on social media.

9. The ICGP continue to update its excellent website on a daily basis and is the most up to date information point for GP educational issues.

10. The IMO and ICGP were instrumental on the scaling back of ''presumed Covid-19'' local GP hubs on the basis that they will need to be re-scaleable in the winter months.

Ongoing challenges for General Practice include (in no particular order):

- Access to local Hospital based phlebotomy
- Direct referral Access to all diagnostics incl. Xray, Ultrasound, CT and MRI imaging.
- Access to Acute Medical, Surgical and Paediatric Assessment Units
- Timely provision and resourcing of flu vaccinations in context of expansion of qualifying population
- Prioritising Children's immunisations and maternity care.
- Recognition of the unique challenges posed by Childhood fevers/illness and how both general practice and hospital paediatrics will organise services for the winter.
- Commencing a return to chronic care
- Ensuring GP self and staff care
- Ensuring continued access to PPE
- GP Manpower deficits
- Rostering for out of hours and Hub shifts in addition to surgery shifts.

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Improvements in Clinical Outcomes in Children with Cystic Fibrosis aged Six and 16 years

B.P. Finn[1], S.R. Millar[2], K. Cronin[3], J. Crowley[3], S. Dunne[3], R. Jennings[1], E. Keating[1], C. Murphy[1], D. O' Donovan[1], P. Shanahan[4], C. Short[5], D. Mullane[1], M. Ni Chroinin[1]

1. Department of Paediatrics and Child Health, Cork University Hospital.
2. School of Public Health, University College Cork, Ireland.
3. Department of Dietetics, Cork University Hospital.
4. Department of Physiotherapy, Cork University Hospital.
5. Department of Respiratory Medicine, Cork University Hospital.

Abstract

Aims
Our aim was to assess if outcomes for cystic fibrosis (CF) patients at six & sixteen years of age have improved in the last 17 years looking at FEV_1, BMI and death.

Methods
A retrospective observational study using a prospectively maintained database of CF patients at Cork University Hospital.

Results
84 patients were included in the 16-year-old data and 89 patients were included in the six-year-old data. The mean FEV_1 and BMI (16 years) for the 2002-2007 group was 72.9±21.0% and 18.9±2.53 respectively, 2008-2013 group was 75.4±27.2% and 19.8±2.7 and for the 2014-2018 group was 95.2±16.0% and 22.9±4.1. The percentage of patients (16 years) with chronic pseudomonas status was 37.9% (11/30) in the 2002-2007 group, 51.6 % (16/31) in the 2008-2013 group and 4.2% (1/24) in the 2014-2018 group. The relationship between FEV1 and FVC with BMI remained significant in multivariate analysis (P <0.001). The mean FEV_1 (six years) for the 2002-2007 group was 90.7±16.1%, 2008-2013 group was 99.3±17.9% and for the 2014-2018 group was 100.9±15.8%.

Conclusions
Improvements in FEV_1 and BMI aged six and 16 years are notable as well as a significant decline in the number of patients with chronic pseudomonas.

Introduction

Cystic Fibrosis (CF) is the most common life shortening genetic condition affecting Caucasians[1,2,3]. There is a high prevalence of CF in Europe with a particularly high mean prevalence in Ireland (2.98/10,000) [4,5,6]. Early diagnosis of CF provides opportunities for earlier medical intervention[7]. Lung health is a major indicator of wellbeing in CF which is represented by FEV1 (Forced Expiratory Volume in 1 second)[7]. In 2016, 250 adults (43.9%) and 47 children (8.3%) had chronic pseudomonas aeruginosa infection[7]. Prevalence of CF related diabetes in Ireland is 31.5%[8]. Since 2000, an average of 18 individuals died annually (range: 7-31)[7].

Major recent advances in Ireland include the introduction of new-born screening for CF in Ireland in 2011[8]. Pseudomonas aeruginosa is an early acquired pathogen in CF patients that can lead to chronic infection, more rapid lung function decline and premature death[3,9]. To prevent these poor outcomes, early eradication of pseudomonas protocols have been introduced to aggressively eradicate this organism[10,11,12]. Patient segregation and isolation to reduce cross infection have become the standard of care[13,14]. The use of Ivacaftor and Lumacaftor /ivacaftor (Orkambi) have been a huge milestone in CF care[15-18]. Ireland subsequently gained access to Lumacaftor/Ivacaftor in 2017 for over 12 years with Delta f 508 homozygous. In February 2018, Lumacaftor/Ivacaftor was extended to the 6-11 year old age group and is now available to children over two years of age[8].

The aim of our project was to assess if outcomes for cystic fibrosis patients have improved in our centre since the introduction of these key measures over the past 17 years. We chose two time points to evaluate patients aged six and sixteen years of age. The timepoint of sixteen years of age was chosen as this is the age for children to be transferred to the adult service in our centre. Six years was also chosen so the impact of of new-born screening in 2011 could be assessed.

Methods

We carried out a retrospective observational study using a prospectively maintained database of cystic fibrosis patients in Cork University Hospital (CUH).

The cystic fibrosis nurse specialists have maintained a record of all cystic fibrosis patients since the early 1980s including all patients who passed away during this time in both the paediatric and adult services.

Approval to access the patient's records was granted by the Cork University Hospital Clinical Governance and Audit Office.

Our inclusion criteria included any child who reached 16 years of age between 1st Jan 2002 and 31st December 2018 under the care of the CUH paediatric cystic fibrosis service were included in the 16 years of age cohort.

Similarly, all children under the care of the CUH paediatric cystic fibrosis service between 1st Jan 2002 to 31st December 2018 who reached six years of age during this time period were included in the six years of age cohort.

The outcomes to be measured include; patient demographics including date of birth, date of diagnosis, reason for presentation, genotype and initial sweat chloride result at time of diagnosis. Lung function tests: FEV1 and FVC (Forced Vital Capacity) at sixteen years and six years respectively for each cohort. BMI (Body mass index) at sixteen years and six years for each cohort. Pseudomonas status (Leeds Criteria[19]) classified as never (no previous positive pseudomonas sputum or cough swabs), free from (a previous positive pseudomonas sample but none in over the last 12 months prior to transfer), intermittent (<50% of sputum samples positive in the preceding 12 months) and chronic (>50% of sputum samples positive for pseudomonas in the preceding 12 months). Diabetes diagnosis at sixteen or six years of age depending on cohort where insulin was required as part of their care (CF related diabetes defined on the basis of either a two hour oral glucose tolerance test blood glucose of >/= 11.1mmol/L/ fasting blood glucose of >/= 7mmol/L on two or more occasions or fasting blood glucose of >/=7mmol/L plus random blood glucose level of >/=11.1mmol/L or random BG levels of >/= 11.1mmol/L with symptoms of diabetes mellitus on two or more occasions when otherwise clinically well[20]. Also, the use of CFTR modulators and transplant status: Lung transplant undertaken prior to sixteen years.

Statistical analysis using descriptive statistics followed by linear regression analysis for both univariate and multivariable models was carried out using Stata SE Version 13 (Stata Corporation, College Station, TX, USA) for Windows. Features that displayed a P value of less than 0.05 in univariate analyses were included in subsequent multivariable models.

Results

Sixteen-year-old data

In total 85 patients reached 16 years of age between 2002 and 2018; one case file was unfortunately lost to medical records, leaving 84 cases to analyse. The case file lost was a patient in 2002.

We arbitrarily grouped these patients from a 17-year period into 3 groups- two six-year groups and one five-year group to provide greater statistical strength rather than compare each year. Group 1. 2002-2007 (30 patients), Group 2. 2008-2013 (31 patients) and Group 3. 2014-2018 (24 patients).

Table 1. Clinical and Demographic Characteristics of 16-year-old patients with cystic fibrosis, 2002–2018.

Outcome Measured	2002–2007	2008–2013	2014–2018
Mortality (No of Deaths)	5	1	2
No of Living patients who reached 16 years	n=30	n=31	n=24
Age at diagnosis (mean)	2.0 ± 3.9	1.1 ± 2.9	3.6 ± 4.9
BMI, kg/m^2 (mean)	18.9 ± 2.5	19.8 ± 2.7	22.9 ± 4.1
Pseudomonas status:			
Never (%)	6 (20)	2 (6.5)	5 (20.8)
Free From (%)	2 (6.6%)	8 (25.8)	12 (50)
Intermittent (%)	10 (34.5)	5 (16.1)	6 (25.0)
Chronic (%)	11 (37.9)	16 (51.6)	1 (4.2)
Diabetes (%)	1 (3.3)	4 (12.9)	4 (16.7)
Use of CFTR modulators (%)	0 (0)	0 (0)	6 (25.0)
Forced expiratory volume, L (mean)	72.9 ± 21.0	75.4 ± 27.2	95.2 ± 16.0
Forced vital capacity, L (mean)	82.7 ± 18.8	81.7 ± 22.9	103.1 ± 14.9
No. (%) of patients DeltaF508 homozygous	23/30 (76.7)	24/31 (77.4)	14/24 (58.3)

Mortality: No of children who passed away before 16 years of age. Age at diagnosis, BMI, forced expiratory volume and forced vital capacity are shown as a mean ± one standard deviation. Numbers and % are shown for pseudomonas status and use of CFTR modulators.

Table 2. Factors associated with forced expiratory volume levels in 16-year-old patients with cystic fibrosis – linear regression.

	Outcome Measured	Coefficient	Std Error	95% CI	P value
Model 1					
	Age at diagnosis	1.21	0.71	-0.20, 2.62	0.09
	BMI	3.21	0.69	1.85, 4.56	<0.001[2]
	Pseudomonas status (yes)[1]	-15.71	5.07	-25.81, -5.60	0.003[2]
	Diabetes	-7.92	8.51	-24.85, 9.01	0.355
	Use of CFTR modulator	22.78	9.96	2.96, 42.60	0.025[2]
Model 2					
	BMI	2.95	0.65	1.65, 4.25	<0.001[2]
	Pseudomonas status (yes)[1]	-10.77	4.83	-20.38, -1.15	0.029[2]
	Use of CFTR modulator	13.59	9.19	-4.70, 31.89	0.143
Model 3					
	BMI	2.77	0.70	1.37, 4.16	<0.001[2]
	Pseudomonas status (yes)[1]	-9.75	5.04	-19.79, 0.28	0.057
	Use of CFTR modulator	11.51	9.66	-7.12, 30.73	0.237

Features that displayed a P value less than 0.05 in univariate analyses were included in multivariable models.
One subject was excluded from analyses due to missing values (Patient no 85-2002 case).
Model 1: Univariate.
Model 2: Adjusted for each other.
Model 3: Adjusted for each other and year of data collection.
[1]Either intermittent or chronic.
[2]P value significant (<0.05).

Table 1 describes the initial results of our patients who reached 16 years of age. Overall, there was a significant increase in FEV_1 from 95.2±16.0% in the 2014-2018 group when compared with 72.9±21.0% from the 2002-2007 group. Similarly, BMI improved over the time frame of our study from 18.9±2.53 back in 2002-2007 to 22.9±4.1 in 2014-2018.

From a pseudomonas viewpoint the number of patients with chronic pseudomonas infection fell significantly from 37.9%in 2002-2007 to 4.2% in 2014-2018. Only one cohort demonstrated the effect of CFTR modulators- the 2014-2018 cohort. 10 patient years of ivacaftor exposure and two patient years of Lumacaftor/Ivacaftor exposure in total.

There has been only one bilateral lung transplant (performed in UK) in a patient attending our centre in this time period- An 11-year old male in 2015 who subsequently passed away at 13 years of age.

Table 2 demonstrates that BMI (FEV 1: P <0.001, FVC: P<000.1), pseudomonas status (FEV1: P 0.003, FVC: P 0.017) and use of CFTR modulators (FEV 1: p 0.025, FVC 0.027) were all significantly related to forced expiratory volume in univariate models. Similar results were found for forced vital capacity data. Subsequent multivariable analysis revealed the relationship between FEV1 and pseudomonas status remained borderline significant (P 0.029 in Model and 0.057 in Model 3). The relationship for CFTR modulators and FEV1 trended to an insignificant relationship (P 0.143 in Model 2 and 0.237 in Model 3). The relationship between FEV1 and FVC with BMI remained significant in multivariable analysis adjusted for each other and year of data collection (P <0.001).

Six-year-old data

Table three demonstrates our results for all patients who reached six years of age between 2002 and 2018. We arbitrarily grouped these patients once again: Group 1. 2002-2007 (29 patients), Group 2. 2008-2013 (30 patients) and Group 3. 2014-2018 (30 patients).

The mean FEV_1 rose from 90.7±16.1 in the 2002-2007 group to 100.9±15.8 in the 2014-2018 group. The mean BMI for the 2014-2018 group was 15.5±1.0, 2008-2013 group was 16.1±1.8 and the 2002-2007 group was 16.1±2.0. Chronic pseudomonas rates fell once from 10.3% in 2002-2007 to 0% in 2014-2018. Only four patients (13.3%) in the 2014-2018 group and two patients (6.7%) in the 2008-2013 group received CFTR modulators.

Table 3. Clinical and Demographic Characteristics of six-year-old patients with cystic fibrosis, 2002–2018.

Outcome Measured	2002–2007	2008–2013	2014–2018
Mortality (N)	2	2	0
No of living patients who reached six years	n=29	n=30	n=30
Time to diagnosis:			
Before or at birth (%)	7 (25.0)	10 (33.3)	13 (48.1)
Before 1 year (%)	10 (35.7)	13 (43.3)	8 (29.6)
Between 1–2 years (%)	6 (21.4)	4 (13.3)	1 (3.7)
>2 years (%)	5 (17.9)	3 (10.0)	5 (18.5)
No (%) of patients DeltaF508 homozygous	19/29 (65.5)	16/30 (53.3)	20/30 (66.7)
BMI, kg/m^2 (mean)	16.1 ± 2.0	16.1 ± 1.8	15.5 ± 1.0
Pseudomonas status:			
Never (%)	17 (58.6)	10 (33.3)	13 (43.3)
Intermittent (%)	6 (20.7)	11 (36.7)	2 (6.7)
Free from (%)	3 (10.3)	8 (26.7)	15 (50)
Chronic (%)	3 (10.3)	1 (3.3)	0 (0)
Diabetes (%)	0 (0)	0 (0)	0 (0)
Use of CFTR modulator (%)	0 (0)	2 (6.7)	4 (13.3)
Forced expiratory volume, L (mean)	90.7 ± 16.1	99.3 ± 17.9	100.9 ± 15.8
Forced vital capacity, L (mean)	94.1 ± 14.6	101.7 ± 15.2	102.8 ± 16.7

Mortality: No of children who passed away before 6yrs of age. BMI, forced expiratory volume and forced vital capacity are shown a mean ± one standard deviation. Numbers and % are shown for time to diagnosis, pseudomonas status and use of CFTR modulators.

Linear regression analysis was subsequently carried out on this dataset also. BMI is a strong determinant with regard to FEV1 (P 0.024) and FVC (P 0.031) levels in 6-year-olds although BMI levels haven't changed to a statistically significant level between the 2002-2007 and 2014-2018 cohorts. None of the other variables displayed a convincing

relationship with FEV1 and FVC. Time to diagnosis was not statistically significant under univariate analysis (FEV1: P 0.507 and FVC: P 0.575). Neither was pseudomonas status (FEV1: P 0.381, FVC: P 0.437), diabetes diagnosis (FEV1 P 0.08, FVC P 0.068) or use of CFTR modulators (FEV 1 P 0.197 , FVC P 0.115) amongst our six year old patients.

Discussion

The group of patients born before the introduction of newborn screening showed no difference in the age of diagnosis between the different cohorts. The most likely reasons for this are that prior to newborn screening the diagnosis of cystic fibrosis was on the basis of characteristic clinical findings and laboratory values, and in the past the diagnosis was often not clear cut on an initial consultation[21]. Equally the age of onset of symptoms is highly variable from antenatal evidence of echogenic bowel to adolescent onset respiratory symptoms. A similar experience was found in the US in 1996 where only two states had introduced newborn screening by that time. The earlier diagnoses provided by newborn screening have not demonstrated an improvement in outcomes for our six-year old patients as of yet as only a very small minority of patients in our 2014-2018 cohort benefitted from screening. Significant Improvements in FEV_1 and BMI are noted over the past 17 years at both six & sixteen years of age. In the past five years, our sixteen year old patients have reached the European Cystic Fibrosis Society (ECFS) recommendation of a BMI >20kg/m2 in adults with CF and matches national figures of an average BMI of 22.3 in 2016[8,22]. BMI, pseudomonas status and use of Ivacaftor/Orkambi medications were all significantly related to forced expiratory volume and forced vital capacity levels in univariate models at sixteen years. The relationship between pseudomonas status remained significant (or borderline significant) in multivariable models at sixteen years, while the relationship for medication use trended to insignificant – but the numbers were low for this variable. A limitation to this study is that we did not collect data on imaging e.g. CT thorax in these patients.

There is a huge decline in the number of patients with chronic pseudomonas at 16 years of age although the rate of acquiring pseudomonas infection has not changed. This may be related to changes in antibiotic prescribing including use of inhaled therapy leading to pseudomonas eradication. Our low chronic pseudomonas rates are in keeping with national figures of 8.3% from the national CF registry in 2016[8]. Shidhani et al report that they have detected a decline in the overall prevalence of pseudomonas infection in their CF population which we have not detected[23]. The likely reason for this is that both studies were carried out at single centre sites which have different catchment areas in Ireland- we cover Munster while Children's Health Ireland at Crumlin covers Leinster so geography may play a role. However, they describe a similar change in the pattern of severity of pseudomonas infection to our study with a fall in chronic pseudomonas rates[23]. We did not assess in this study whether the prevalence of multidrug resistant bacteria had increased during the same time frame. A further limitation to our study is its retrospective nature. Internationally, our chronic pseudomonas rates as per the Leeds Criteria are lower than the US at 40% in adolescents as of 2015[24].

In conclusion, the real driver behind the more favourable FEV_1 and FVC outcomes we are seeing in recent years are the more optimal BMI levels that we are observing in our patients as demonstrated by our multivariable analysis (Table two). It is hoped that improvements in FEV_1 and BMI will translate into an improvement in the quality of life and longevity in this population as they enter adulthood which we hope would be a finding relevant internationally.
This would suggest that for us to continue to see improving FEV1 and FVC levels at six years of age, a goal would be to increase dietetic support and nutritional supplementation during these initial formative years.

Continued improvement in the outcomes aged 16 years will be accrued when the group diagnosed by newborn screening are assessed (aged 16 in 2027). We look forward to seeing the outcomes in teenagers and young adults in those receiving CF modifiers from early infancy and early childhood and expanding the number of patients who receive modifier therapy.

Continued investment by the Health Service Executive in the maintenance of multidisciplinary teams in designated CF centres as advocated in the National Model of Care for Cystic Fibrosis will be vital to provide state of the art care to children, teenagers and adults with cystic fibrosis.

Corresponding Author:
Bryan Padraig Finn
Paediatric Department, Cork University Hospital, Wilton, Cork.
Email: 112305976@umail.ucc.ie

Declaration of Conflicts of Interest:
The authors of this paper declare that we do not have any conflicts of interest.

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Trainee's Preparedness for Paediatric Work

P. McCrossan[1], A. Nicholson[1], N. McCallion[1]

1. Department of paediatrics, Royal College of Surgeons in Ireland

Abstract

Aim
Compare the opinion of paediatric consultants to paediatric Senior House Officers (SHOs) with regards their perceived level of preparedness for starting work in paediatrics.

Methods
A 5-point Likert scale questionnaire was administered to paediatric consultants and SHOs investigating how well they considered the SHO was performing and how well prepared the SHO perceived themselves for work in clinical paediatrics, respectively. Questions related to procedures, clinical examination, teamwork, history taking and OPD related activity.

Results
50 Consultants and 75 SHOs completed the questionnaire. Using a Mann-Whitney U test, both groups answered similarly to questions relating to clinical examination and history taking ($p=0.51$ and $p=0.15$). However, there were significant differences in their responses to questions relating to procedures, teamwork and OPD related activity ($p<0.05$).

Conclusion
There is a significant disparity between consultant opinion of ability and SHOs perception of preparedness for some of the same skills. More work, focusing on these specific aspects of undergraduate paediatric education needs to be carried out to improve graduate preparedness for this role.

Introduction

Every summer, teaching hospitals employ a new group of trainee doctors. For many new graduates, this will be the first occasion when they have responsibility for their interaction and treatment of patients. Whilst these doctors are still technically, 'in training,' there is an expectation that, in light of their undergraduate medical experience and knowledge, they will be able to perform many duties with limited supervision. A survey delivered to first-year residents in the U.S.A, "suggests the presence of a gap between what students learn during medical school and their clinical responsibilities as first-year residents [1]". There is also a reported discrepancy between graduates' self-assessment and their educational supervisor's assessment of their practice, suggesting possible lack of clarity of expected standards [2].

The process by which the standards of qualifying doctors are determined involves multiple stakeholders. The Irish Medical Council's eight domains of good professional practice [3] outline that doctors require competency in a range of skills in order to adequately perform their duties; scientific knowledge, clinical skills, empathy/compassion, interpersonal skills, ability to teach others, professionalism, management skills and the ability to independently continue their own professional development.

Consultants rely upon a supply of newly qualified doctors on a transitional, temporary basis in order to deliver a full range of services to their patients. Consultants rely upon medical schools or the postgraduate training bodies to guarantee the standard and competencies of the doctor in training that they employ. However, the purpose of the junior doctor is not merely to provide a service. The hospital consultant must provide mentorship, leadership, knowledge and experience to the junior 'under their wing' as part of the postgraduate development of this doctor. Front line hospital consultants often have limited input into undergraduate education and development.

The skills, competencies and training of newly recruited paediatric doctors are key to meeting the standards required in clinical practice. Graduating medical students are comprehensively assessed on their level of knowledge and specific skills, but their own perception of readiness for the role is not examined. In paediatrics, although graduating medical students do not enter the specialty immediately, most do not receive further training in paediatrics prior to starting as SHOs in the specialty.

The objectives of this study were to determine if consultant paediatricians deem that new SHOs starting with their service have been adequately prepared for their clinical role, to determine if doctors working in the role of paediatric SHO perceive they were adequately prepared for work in the field of paediatrics and and to compare consultant's opinion of SHO ability with SHOs' own perceived preparedness for their role.

Methods

This study was a prospective questionnaire-based study of practicing consultant paediatricians in Ireland, doctors entering the basic specialist-training scheme (BST) in paediatrics and new paediatric training SHOs starting in a tertiary paediatric centre (Children's University Hospital, Temple St). The paediatric SHO's included in the study have limited prior experience of paediatrics as they were either entering their first ever paediatric job or entering the training scheme (and so will have had less than 1 years previous experience).

Two similar questionnaires were designed. The first was delivered to current paediatric SHOs to assess how well prepared they felt they were for their job. The SHOs were asked, "My undergraduate training adequately prepared me for…" followed by 8 statements relating to IMC domains of good professional practice. The second was delivered to paediatric consultant physicians to assess how well they felt their current SHO was performing. The consultants were asked, "I feel that my current SHO is displaying the ability to perform at the expected level of an SHO with regards to…" followed by 10 statements, again reflecting IMC domains of good professional practice.

Participants were asked to judge to what extent they agreed with statements using a five-point Likert scale (1= strongly disagree, 2=disagree, 3= neutral, 4 = agree, 5= strongly agree). The questionnaires were administered as paper copies and were also available in Survey Monkey™ online software. (See appendix for copies of the questionnaires).

The SHO survey took place in the Royal College of Physicians Ireland (RCPI), Kildare Street, Dublin in October 2016 during the first of the paediatric 'BST' training days of that academic year. The Survey Monkey™ version was distributed to all paediatric SHOs working in Children's University Hospital, Temple Street (CUH) in February 2017, and eight weeks after they commenced their placement. The consultant questionnaire was distributed to all paediatric consultants employed by CUH and to all members of the RCPCI throughout Ireland via e-mail. The e-mails were sent out in February and March 2017 respectively, 8-10 weeks after the new SHOs had begun their latest job. Two new questions were added to the consultant questionnaire distributed to the whole RCPI to improve comparisons between the SHOs and their supervising consultants. Specifically, we added questions about 'history taking' and 'out-patient consultations' as these were also included in the SHO questionnaire.

Questionnaires were anonymous so neither consultant nor SHO could be identified. Ethical approval was obtained through the CUH and the RCPI Research and Ethics Committees'.

Results of the Likert scale questions were analysed using descriptive statistical analysis. Mann Whitney U used to test association between the SHO and consultant responses.

Results

Response

There were 51 consultant responses (from a total of 247 consultant paediatricians registered with the RCPI), 14 from CUH and 37 via RCPI e-mails (21% response rate). There were 75 SHO responses. Of a total of 79 paediatric SHO members of the RCPI paediatric BST training scheme, 66 completed paper copies (84% response rate). A further 9 SHOs currently working in CUH completed the questionnaire online, via SurveyMonkey™ from a total of 25 SHOs working in the hospital (some of whom had already completed the questionnaire at the BST study day).

Table 1. Number of responses per Likert score for each question on the SHO satisfaction questionnaire (n=75).

Question	Procedures	History Taking	Clinical Examination	Emergencies	Out-Patients	Teamwork	Prioritising	Continued professional development
Likert 1	19	0	0	7	3	7	5	1
Likert 2	27	0	4	30	17	12	20	5
Likert 3	15	8	8	18	12	17	19	13
Likert 4	13	47	47	17	39	33	29	41
Likert 5	1	20	16	3	2	6	2	15
Median Likert Score	2	4	4	3	4	4	3	4

The SHOs were asked, "My undergraduate training adequately prepared me for…" followed by 8 statements relating to IMC domains of good professional practice; procedures, history taking, clinical experience, emergencies, out-patients, teamwork, prioritising and continued professional development. Table 1 presents how the SHOs responded to these eight statements by use of a 5-point Likert scale.

Table 2. Number of responses per Likert score for each question on the consultant satisfaction questionnaire.

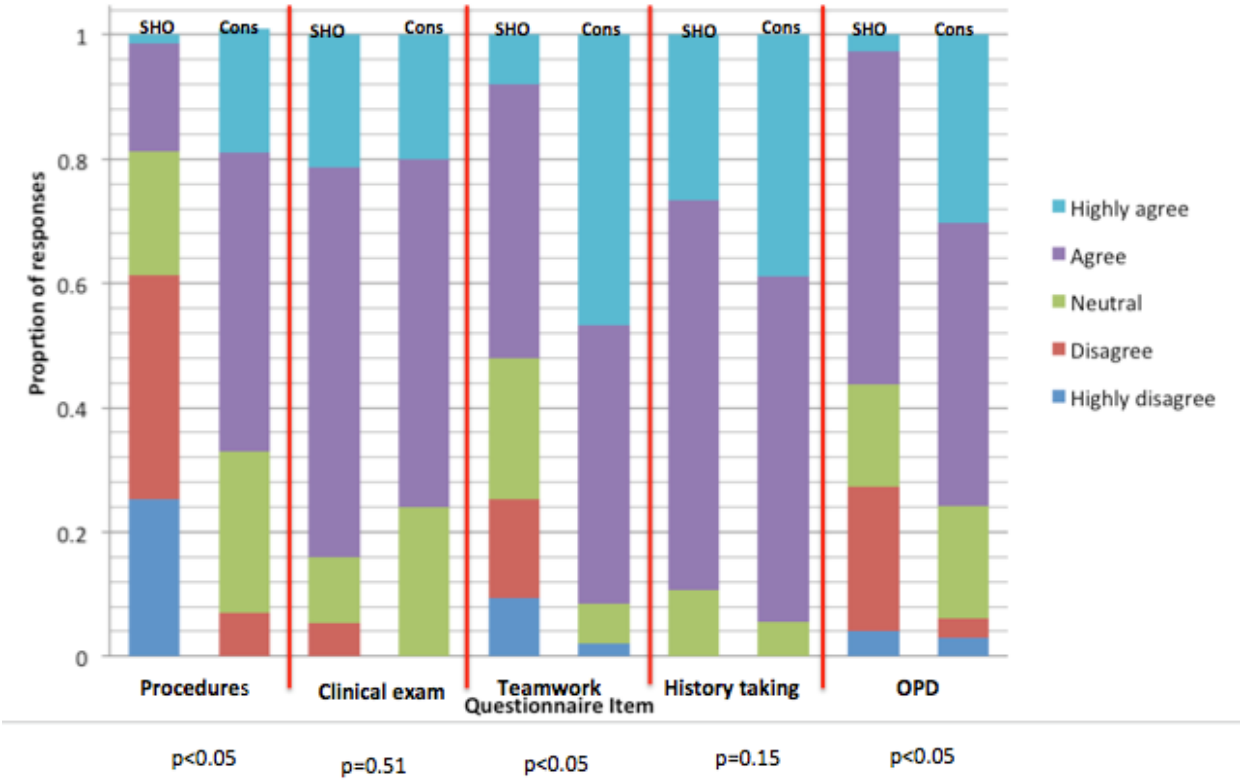
Question	Safety (n=51)	Communication (n=51)	Team work (n=51)	Work load (n=51)	Knowledge (n=51)	Professionalism (n=51)	Clinical Exam (n=51)	Procedures (n=51)	History Taking (n=37)	Out-Patients (n=37)	Relating to patients (n=14)
Likert 1	0	0	1	1	0	0	0	0	0	1	0
Likert 2	0	1	0	1	2	0	0	3	0	1	0
Likert 3	4	6	3	9	8	8	12	12	2	6	2
Likert 4	24	25	21	23	30	17	28	22	20	15	7
Likert 5	23	19	22	14	9	25	10	9	14	10	4
Median Likert Score	4	4	4	4	4	4	4	4	4	4	4

The consultants were asked, "I feel that my current SHO is displaying the ability to perform at the expected level of an SHO with regards to…" followed by 10 statements, again reflecting IMC domains of good professional practice; safety, communication, teamwork, workload, knowledge, clinical examination, history taking, out-patients and relating to patients. Table 2 presents how the consultants responded to these ten statements by use of a 5-point Likert scale.

Comparison of consultant satisfaction with SHO satisfaction comparison

There were five questions, which appeared on both the SHO and consultant satisfaction questionnaires. These related to: 1. Procedures 2. Clinical examination 3. Teamwork 4. History taking 5. Out-patient consultations.

Figure 1. Proportion of responses to the questions, which appear on both the SHO and consultant satisfaction Likert scale questionnaires, with comparison between SHO and consultant responses to the same question (Mann-Whitney U).



Discussion

The purpose of this study was to compare the opinions of paediatric SHO doctors and consultants with regard SHOs preparedness for work in paediatrics. It was therefore important to capture these opinions near the beginning of their first job when the SHO's experience of paediatrics was limited and would reflect what they were taught in their undergraduate degree. Overall, we found a disparity in the opinion of SHOs and consultants with regards how well prepared they were for work in paediatrics.

Consultants expressed satisfaction with current SHO performance in all areas reflecting aspects of the IMC's domains of good professional practice. This is reassuring as, ultimately; patient safety is the highest priority when supervising a colleague. In contrast to our findings, the literature shows that program directors have had concerns in the past with regards to medical students' preparedness for clinical work [4]. A common theme found is that they are more prepared for the affective aspects and not so much the cognitive aspects [5]. The difference between these studies and our own is that they investigated undergraduate students prior to commencing work whereas we investigated the opinion of consultants on a qualified doctor, eight weeks into their latest job.

There is limited literature exploring specifically a paediatric trainee doctor's view on their undergraduate experience and preparedness for the job. However, it is well known that undergraduate experience is very important when deciding on a career in paediatrics [6]. In two studies of postgraduates views on their preparedness for work, less than 60% of graduates agreed that their medical school had prepared them for the medical jobs undertaken when qualified [7, 8]. A study at the University of Edinburgh set a questionnaire based on 13 major 'foundation programme' [9] learning outcomes, administering it to both graduates and their own educational supervisors. Graduates felt well prepared for consultation and communication skills but less prepared for acute care and prescribing [10].

This is consistent with our study, which demonstrated that paediatric SHOs were most satisfied with 'history taking' and 'physical examination' but least prepared for 'emergencies' and 'procedures'.

A UK study from 2006, similar in methodology to our own, demonstrated that many of the affective domain aspects of performance were rated highly, however, performance in the cognitive aspects was rated lower [11]. These UK house officers rated their own ability higher than their consultants' rating of their ability, which is in contrast to our findings. This could be due to our consultants not being fully aware of their SHOs cognitive capabilities and being overly generous in their responses. This is borne out in the finding that SHOs rated their preparedness for 'procedures', 'teamwork' and 'outpatients' as significant lower than the consultants.

The results of our study are limited by the relatively poor response rate, particularly for the consultant questionnaire. However, we consider the sample size of 51 consultants to be sufficient from which to draw conclusions and make comparisons to the 75 paediatric SHOs. Another limiting factor is that there is no appropriate standardised questionnaire available. To the best of our knowledge, there have been no previous studies investigating paediatric doctor's views on their undergraduate preparation and so this was a novel questionnaire.

Our study adds to the literature as most other studies tend to suggest that consultants more commonly view the juniors 'ability' less than the junior perceive themselves. These results identify potential issues for new doctors starting in paediatrics that may reflect confidence levels rather than ability and warrants further investigation at both under- and postgraduate level.

In conclusion, consultants were satisfied with all aspects of their SHO performance. SHOs, on the other hand, consider themselves underprepared for many aspects of their job, particularly in 'procedures', 'emergencies' and 'prioritising'. There is a significant disparity between consultant opinion of ability and SHOs perception of preparedness for some of the same skills ('procedures', 'teamwork' and 'out-patients'). More work, particularly at undergraduate level, focusing on these specific aspects of paediatric education needs to be carried out to improve graduate preparedness for this role.

Due to shift-patterns and ever-increasing work demands, consultant may have limited direct interaction with many of their trainee doctors and therefore do not have an accurate knowledge of their ability only 8 weeks into post. We should also consider that trainees might set too high an expectation upon themselves, one that is not set by their consultant supervisors. In practice, it is likely to be a combination of both these factors. In the future, expectations of SHOs should be made explicitly clear when they start their new job. This can be achieved by having a formal educational meeting with their designated consultant supervisor to discuss their new role with regular review of their progress throughout the post. This would ensure that expectations are shared between both parties and made clear clear. These meetings also allow the opportunity for formative feedback to ensure that set standards are met.

Declaration of Conflicts of Interest:

I confirm there are no conflicts of interest related to this paper.

Corresponding Author:

Dr. Patrick McCrossan

Academic Clinical Lecturer at Queens University Belfast.

Email: mccrossp@tcd.ie

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Optimal Timing of CT Scanning in the Rapid Access Lung Cancer Clinic

M. Hennessy[1], D. Ryan[2], S. Clarke[2], C. Higgins[3], M. Logan [4], E. O'Brien[2], R. Morgan[2]

1. Dept of Medical Oncology, Beaumont Hospital, Dublin
2. Dept of Respiratory Medicine, Beaumont Hospital, Dublin
3. Cancer Data Department, Beaumont Hospital, Dublin
4. Dept of Radiology, Beaumont Hospital, Dublin

Abstract

Aims
To investigate whether a 'CT first' approach to Rapid Access Lung Cancer Clinic (RALC) review could be feasible in an Irish context.

Methods
A retrospective review of our institution's Lung Cancer Database was performed. All RALC first attendances from 2012-2018 were identified. Timing of CT was assessed as well as CT imaging findings.

Results
Total first attendances in this period were 2372, of whom 91% had CT thorax as part of their evaluation. 866 patients (37%) were diagnosed with lung cancer, all had an abnormal CT. 1290 patients (54%) underwent CT but did not have lung cancer after clinical work up. 34% of patients diagnosed with Lung Cancer had their CT scan post RALC. Time to diagnosis was longer in those who had post RALC CT (34.5 versus 21 days)

Conclusion
CT scanning plays a vital role in the RALC pathway. Initial delays in obtaining CT can result in delayed time to diagnosis. These findings warrant close consideration when devising future national lung cancer policy.

Introduction

Lung cancer is the leading cause of cancer deaths in Ireland, representing approximately 20% of all cancer mortality[1]. Lung cancer kills more Irish people every year than breast and colon cancer combined and, despite recent advances, the prognosis is poor with a one-year survival of 37% and a 5-year survival of 13%[2,3]. This is largely because the disease presents at a late stage, with two thirds of new lung cancer cases in Ireland diagnosed at stage III or greater[4]. Since the introduction of the National Cancer Control Programme (NCCP) and centralisation of cancer services in eight sites nationwide, there has been a doubling in five-year survival rates in patients treated in those centres as opposed to those treated in non-dedicated sites[5]. However, delays in diagnosis, staging and commencing treatment still play a role in the poor outcomes for patients with lung cancer[6,7].

Rapid Access Lung Clinics (RALC) were established by the NCCP in 2009 to improve the standard of care for lung cancer in Ireland. The aim of the RALC is to provide access to respiratory specialists as well as rapid diagnostics and to expedite the assessment of patients with clinical suspicion for lung cancer. The current indications for referral to the RALC are

abnormal chest x-ray suggestive of lung cancer or red flag respiratory symptoms, such as haemoptysis. Most patients are referred by their general practitioner (GP). A central Key Performance Indicator for the RALC is that all patients referred are seen within 10 working days and the most recent data from the NCCP suggests that 99% of patients are seen with 15 working days[8].

Though referral to RALC expedites time to patient review, time to subsequent diagnosis and treatment are often prolonged as patients await investigations such as CT Thorax which is mandatory in lung cancer diagnosis. We have previously found that approximately 1 in 3 patients attending the RALC are diagnosed with lung cancer and, while many of the remainder have other lung conditions or nodules that require surveillance[9], these patients do not require urgent review within the RALC timeframe. The proportion of patients that undergo CT imaging who are seen in RALC nationally is not known, though it is likely to be high.

The National Optimal Lung Cancer Pathway (NOLCP) in the NHS published by the Lung Clinical Expert group in 2017 suggests that if a patient has an abnormal chest x-ray or high clinical suspicion of lung cancer from their GP, the maximum wait to CT Thorax should be 3 days[10]. Some NHS initiatives such as the RAPID (Rapid Access to Pulmonary Investigation) programme, have prioritised next day access to CT scanning and have reduced time from GP referral to clinic review with a fully reported scan to just 4 days. This has helped to almost eliminate delayed diagnosis and improve 14 day and 21 day multidisciplinary team (MDT) discussion targets by 44% and 72% respectively[11]. Time to assessment in the RALC in Ireland is broadly in line with NCCP guidelines[8] but timely access to a reported CT Thorax and its impact on time to diagnosis and completed staging, essential for MDT decision making, has not been evaluated.

We investigated the impact of timing of CT scan following referral to the RALC on time to diagnosis for patients with lung cancer and whether a 'CT first' approach to RALC review should be the aim for all appropriately referred patients.

Methods

The standard referral pathway for RALC patients to CT is that an order is placed by the respiratory physician after the patient has undergone assessment in the RALC. In cases where the referral is considered particularly high risk (i.e. definite mass on CXR) the CT is ordered following review of the RALC referral and prior to RALC assessment. A number of dedicated CT slots are available to the coordinator who receives the referral. The aim is for patients to be seen in the RALC within 10 days of referral, in keeping with NCCP guidelines, and this is regardless of whether or not CT has already been obtained. The CT protocol that is used is a contrast enhanced scan of the thorax to the level of the adrenal glands, 1mm soft tissue and lung windows with axial MIP(Maximal Intensity Projection)of lung windows, sagittal and coronal bone windows.

Following institutional ethics approval, we conducted a retrospective review of the Beaumont Hospital Lung Cancer Database. We identified the total number of lung cancer cases diagnosed in our institution from 1st January 2012 to 31st May 2018 and identified those patients that were assessed and diagnosed through the RALC. All patients who attended the RALC for the first time from 1st January 2012 to 31st May 2018 were eligible for inclusion into our study. Patients were excluded if they did not attend their appointment for first RALC review, if insufficient data was available, or if no radiological investigations were performed.

We divided patients diagnosed with lung cancer through the RALC into two groups, those who had a CT prior to clinic review and those who had a CT performed after clinic review to identify the effect this had on timeliness to diagnosis following receipt of GP referral. We used median time to diagnosis rather than mean to mitigate the high number of outliers evident in the cohort and provide a more accurate central tendency. For patients not diagnosed with lung cancer we subdivided their pathologies into the following categories (i)Other cancers (non-lung), (ii)Pulmonary nodule, (iii)Infectious/Inflammatory (including Bronchiectasis), (iv)Interstitial lung disease, (v)other abnormalities and (vi)Normal CT scan. In addition to the Beaumont Hospital Lung Cancer database we used the HSE National Integrated Medical Imaging System (NIMIS) and the Patient Information Profile Explorer (PIPE) to cross reference the data.

The rate of lung cancer tissue diagnosis in our institution is approximately 75%. Pathologic diagnosis was not pursued in cases of multiple co-morbidities, frailty and according to patient preference and in these cases a clinical diagnosis was made. The median time from CT scanning to histological sampling was 2 calendar days for patients who had a CT prior to RALC and 8 calendar days for patients who had a CT scan post RALC.

Results

Lung Cancer Diagnoses

2,372 patients attended the RALC for the first time between 1st Jan 2012 to 31st May 2018. 866 patients were diagnosed with lung cancer, representing an overall lung cancer case detection rate of 37%. Patients diagnosed through the RALC represented 57% of the total of 1,514 patients who were diagnosed with lung cancer and discussed at Beaumont Hospital MDT over this period (table 1). The remaining 648 patients did not come through the RALC but through other pathways, 15% were emergency department presentations, and 35% were from outside hospitals in one year during the time period studied.

All patients diagnosed with lung cancer underwent a CT Thorax except for one patient in whom it was discovered on post-mortem following unexpected death prior to imaging (Table 1). This highlights the importance of CT Thorax imaging in establishing lung cancer diagnosis. Overall, 1,290 patients or 54% of all clinic attendees underwent CT scanning but were found not to have lung cancer after clinical workup. Only 216 (9.1%) of new referrals to the RALC did not undergo CT thorax in a NIMIS connected institution following initial evaluation. 193 (90.6%) of these had a Chest X-ray only and insufficient information was available in the remaining 23 patients. The median waiting time from RALC to CT scan was 8 calendar days. Reasons patients did not have a CT performed were for clinical reasons, such as frailty, and where a CT would have been inappropriate or was not indicated on the basis of CXR findings or symptoms. All patients who had imaging carried out in other institutions had their CT imaging uploaded onto our system prior to clinic and multidisciplinary team review.

We reviewed the initial CT scan reports in all patients diagnosed with lung cancer (table 1). All were identified as abnormal by the reporting radiologist; in 94% the reporting radiologist suggested lung cancer as the primary differential. In the remainder, other abnormalities were described that subsequently turned out to be a lung malignancy after further investigation (6%) (Figure 1). In this 6%, 'cancer' was not mentioned in the differential of the radiology report. A variety of other abnormalities were described which included pleural effusion without evidence of a primary mass, non-resolving consolidation and atelectasis.

In comparison, 18% of patients subsequently diagnosed with lung cancer had a normal chest X-ray at time of presentation to RALC. This is similar to previous retrospective data published in the UK[12]. The impact of timing of the initial CT scan on time to diagnosis following referral is shown in Table 2.

Table 1: CT findings in Lung Cancer Cases (N=1514).

	N	(%)
Total Lung Cancer Diagnoses RALC Other Pathway	1514 866 648	 57.2 42.8
No CT Performed	1	0.01
CT Performed	1513	99.9
Abnormal CT	1513	99.9
CT Suggestive of Cancer	1427	94
CT Other Abnormality – subsequently cancer	86	6

Table 2: Impact of obtaining CT scan pre-clinic on time to diagnosis.

	No.	(%)	Median Time to Diagnosis from Referral (Days)
CT Pre RALC	569	65.7	21
CT Post RALC	295	34.1	34.5
Unknown	2	0.2	

Non-Lung Cancer Diagnoses

Of the 2372 patients that attended the RALC during this period, 1506 were found not to have lung cancer. 1290 (86%) of these underwent CT evaluation, 193 had chest x-ray only and no radiology was available in 23 patients. The outcomes of patients who underwent CT evaluation is provided in Table 3. 450 patients (35%) had a nodule on CT scan and of these, 371 patients (82%) entered a nodule surveillance programme that required further CT surveillance, emphasising the workload that nodule follow up now requires in modern lung cancer services. Infectious and inflammatory changes, including bronchiectasis, were the next highest finding on scan (364 patients, 28.2%). A further 10% had features of new Interstitial Lung Disease that required follow-up (125 patients, 9.7%). 135 patients (10.5%) had other cancers, these included metastatic breast, melanoma and colorectal cancers as well as other thoracic malignancies such as thymoma. Importantly, only 7% of the entire RALC population had a normal CT scan highlighting both the appropriateness and sensitivity of CT Thorax as a diagnostic tool in in this patient cohort.

Table 3: CT findings in Non-Lung Cancer Cases (N=1290).

	No.	(%)
Other Cancers (Non-Lung)	135	10.5
Pulmonary Nodule	450	34.9
Surveillance recommended	*371*	*28.8*
No Surveillance	*79*	*6.1*
Infective/Inflammatory/Bronchiectasis	364	28.2
Interstitial Lung Disease	125	9.7
Other Abnormalities	63	4.9
Normal CT	153	11.8

Discussion

The results of this study highlight the importance of CT imaging in the rapid access lung clinic pathway, where it is essential in the identification of cancer from non-cancer pathology, as well as its role in tumour staging and biopsy planning. In our centre, one of eight nationally, every patient diagnosed with lung cancer underwent a CT Thorax as part of their evaluation and it was always abnormal in lung cancer cases. The fundamental role of CT highlights the benefit of obtaining a study as early as possible in the diagnostic process. While this is a retrospective study of one clinical site, our findings demonstrate that initial delays in obtaining CT imaging can result in significant delays in overall time to diagnosis and thus lead to delays in treatment initiation. Our service, like others in Ireland, endeavours to acquire CT imaging prior to clinic review to avoid unnecessary delays, however in our experience this is occurring on an ad-hoc basis rather than as part of a national strategy.

NHS initiatives such as the NOLCP and RAPID programme which prioritise early CT scanning and dedicated physician-led triage of GP referrals have eliminated 31-day diagnosis breaches as recommended by the NHS cancer plan for England[13] and resulted in a shortened diagnostic timeframe of 15 days in some institutions[14]. A process similar to that used in the NOPLC where CT same day/within 72 hours is arranged via the reporting radiologist in cases of abnormal CXR, could be followed in this jurisdiction. Adoption of a similar system in Ireland would reduce time to diagnosis, reduce the number of unnecessary clinic appointments and would help to streamline rapid access services. Our experience would suggest that the agreed referral criteria to a RALC are a good "gate-keeper", and as long as they are adhered to, should not result in significant increased in CT demand but rather a shift in the timing of required CTs. In addition, of the patients who were seen in the RALC only 7% of CT scans were normal, highlighting the role of the RALC in case finding other respiratory conditions and non-lung cancer malignancies. A rapid triage and CT evaluation system would also allow re-direction of some of the high volume of non-cancer pathology seen in this study to other specialist services more suited to patients needs than a cancer dedicated clinic.

Lung cancer screening has been shown to increase the number of early stage cases detected and reduce mortality in lung cancer[16,17]. Concerns about efficiency and cost effectiveness of screening, particularly in resource limited settings has prevented their wholesale adoption but is likely to play a major role in future lung cancer care. Through low dose CT scanning in high risk populations, a RALC system that is designed around triaging early CT referrals rather than chest x-ray is therefore likely to complement and improve the efficiency of such programmes if implemented in Ireland[15].

Our retrospective study accounts for only one of the NCCP centres in Ireland and a similar audit of the other centres may be necessary to validate our results. However, these findings, coupled with the improvements seen in other jurisdictions with the adoption of rapid CT evaluation warrant close consideration when devising future national lung cancer policy.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to disclose.

Corresponding Author:
Dr Maeve Hennessy
Medical Oncology Department,
Beaumont Hospital,
Dublin 9.
Email: maeve.hennessy@ucdconnect.ie

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The Role of Endobronchial Ultrasound in Early-Stage Non-Small Cell Lung Cancer

S. Cullivan[1], M. Ahmed[1], R. Weedle[2], J. Bruzzi[3], S. Phelan[4], M. Da Costa[2], A. Soo[2], D. Breen[1]

1. Interventional Respiratory Unit, Department of Respiratory Medicine, Galway University Hospital, Galway, Ireland.
2. Department of Cardiothoracic Surgery, Galway University Hospital – Galway, Ireland.
3. Department of Radiology, Galway University Hospital – Galway, Ireland.
4. Department of Histopathology, Galway University Hospital – Galway, Ireland.

Aim
The aim of this study is to assess the impact of EBUS on the concordance of clinical and pathological NSCLC staging in our center.

Methods
Data was collected retrospectively from the hospital database regarding patients who underwent surgical resection for early stage NSCLC between 2012 and 2017.

Results
A total of 251 patients were included. The mean age was 67 (±9), 55% (n=137) were male and 83% (n=209) were current/former smokers. In group A (n=154, 61%) clinical nodal stage (cN) was established from a combination of CT, PET CT and mediastinoscopy. Group B underwent additional EBUS (n=97, 39%). cN and pathological nodal staging (pN) were concordant in 78% (n=120) in group A versus 62% (n=60) in group B (p=0.009).

Conclusion
This study demonstrated higher rates of nodal discordance in patients who underwent EBUS which contrasts existing data that demonstrates improved concordance with EBUS. We describe these findings and potential explanations further in this study.

Keywords:
Endobronchial ultrasound; Nonsmall cell lung cancer; Mediastinal staging

Introduction

Lung cancer is a devastating illness, that accounted for over 2 million deaths globally in 2018[1]. Due to the frequent lack of symptoms in early stage disease and until recently, the absence of an effective screening program, lung cancer often presents at an advanced stage. Consequently, accurate clinical staging is essential to appropriately select patients for surgical resection.[2] Depending on regional availability and expertise, conventional clinical staging modalities include non-invasive methods such as CT, PET CT and invasive techniques such as EBUS, endoscopic ultrasound (EUS) and mediastinoscopy. Accurate mediastinal nodal staging is essential in early-stage non-small cell lung cancer (NSCLC) to appropriately select patients for surgical resection. The introduction of endobronchial ultrasound (EBUS) has revolutionized mediastinal staging and is now the recommended mode of lymph node

assessment in patients with suspected early stage NSCLC and radiological evidence of lymph node enlargement greater than 10mm, PET avid lymph nodes, central tumors, tumors with low FDG uptake or advanced tumor size.[3-5] Surgical pathological stage is considered the gold standard and guides decisions regarding adjuvant treatment, postoperative surveillance and prognosis. Current evidence suggests that the correlation between clinical and pathological staging remains poor, with an accuracy ranging from 47 to 91%.[6-8] The aim of this study is to assess the impact of EBUS on the concordance of clinical and pathological NSCLC staging in our center.

Methods

This study received ethical approval from Galway University Hospital institutional review board. A retrospective search of the hospital database was performed to identify patients who underwent surgical resection of early stage NSCLC between 2012 and 2017. Data regarding patient demographics, radiological investigations including CT thorax and PET CT and invasive clinical staging techniques including mediastinoscopy and EBUS were collected from the hospital electronic database and electronic patient records. Cases were excluded from further analysis if there was inadequate available data or if patients received neoadjuvant therapy, as this would interfere with the interpretation of pathological nodal staging. Benign disease or malignant disease other than NSCLC were also excluded. Patients who underwent clinical staging using CT, PET CT and/or mediastinoscopy were allocated to Group A. Patients who underwent additional EBUS were designated group B.

EBUS-transbronchial needle aspiration (TBNA) was performed using a convex probe-EBUS bronchoscope (Pentax EB-1970UK; Pentax Medical, Hamburg, Germany). All procedures were performed under conscious sedation using a combination of intravenous midazolam and alfentanyl. EBUS inspection was performed systematically as per ERS guidelines and visible lymph node stations sampled from N3 nodes to N1 to prevent cross contamination.[9] TBNA samples were placed in formalin and sent to the hospital laboratory for examination. The pathologist defined adequacy by the presence of lymphoid tissue or tumor cells.

Intraoperative lymph node sampling techniques included systematic sampling and block lymph node dissection, depending on the surgical procedure and operator preference. Latency was defined as the time from lung cancer multidisciplinary team (MDT) decision for surgical resection, to the operation day. Pathological specimens were classified using the seventh TNM lung cancer staging system.

Statistical analysis was performed using GraphPad online statistical software. Fisher's exact test was employed to assess the statistical significance for categorical variables and t-test was used to calculate significance between means. A value < 0.05 was considered statistically significant ($P < 0.05$).

Results

Patient characteristics

276 cases of early stage NSCLC underwent surgical resection between 2012 and 2017 and were selected for further analysis. A total of 25 cases were excluded; 17 due to inadequate clinical data and 8 due to neoadjuvant therapy. 251 cases were included in the final analysis. The mean age of study participants was 67 (±9), 55% (n=137) were male and 83% (n=209) were current or former smokers. 154 patients underwent clinical staging using a combination of CT, PET CT and mediastinoscopy in Group A and 97 underwent additional EBUS in Group B.

Clinical stage

Table 1 demonstrates results in Group A and Group B. The median age in Group A and B was 67. There was a male preponderance in Group B at 61% (n=61) (p=0.038). Group B demonstrated higher smoking rates at 92% (n=89) compared to 78% (n=120) in Group A (p<0.001). Adenocarcinoma was the predominant histology in both groups at 57% (n=88) in Group A and 43% (n=42) in Group B.

Clinical T and N stage differed between the two groups as illustrated in Table 1. Patients in Group A demonstrated a lower initial clinical T stage, as 54% (n=84) had T1 disease versus 36% (n=35) in Group B (p=0.006), and a lower clinical nodal stage, with 94% (n=145) demonstrating N0 disease versus 78% (n=76) in Group B (p<0.001).

Table 1. includes a detailed breakdown of patient demographics and clinical and pathological staging in Group A and Group B. Information regarding clinical and pathological lymph node concordance in displayed in the two separate Groups.

	Group A n (%)	**Group B** n (%)
Total	154 (100%)	97 (100%)
Age (Mean, SD)	67 (±10)	67 (±8)
Male sex	76 (49%)	61 (63%)
Current or former smoker	120 (78%)	89 (92%)
Pre operative investigations		
CT	154 (100%)	97 (100%)
PET CT	137 (89%)	97 (100%)
Mediastinoscopy	1 (1%)	4 (4%)
EBUS	0	97 (100%)
Clinical tumour stage		
T1a	58 (37%)	24 (25%)
T1b	26 (17%)	11 (11%)
T2a	41 (26%)	29 (30%)
T2b	1 (1%)	10 (10%)
T3	24 (16%)	20 (21%)
T4	3 (2%)	2 (2%)
TX	1 (1%)	1 (1%)
Clinical nodal stage		
cN0	145 (94%)	76 (78%)
cN1	9 (6%)	17 (18%)
cN2	0	4 (4%)
Tumour histology		
Squamous	35 (23%)	35 (36%)
Adenocarcinoma	88 (57%)	42 (43%)
Carcinoid (typical)	8 (5%)	3 (3%)
Carcinoid (atypical)	1 (1%)	0
Large cell neuroendocrine	3 (2%)	1 (1%)
Other	19 (12%)	16 (17%)
Lung cancer surgery		
Lobectomy	135 (88%)	74 (76%)
Bilobectomy	12 (8%)	13 (14%)
Pneumonectomy	7 (4%)	10 (10%)
Pathological tumour stage		
pT1a	38 (25%)	12 (12%)
pT1b	34 (22%)	17 (18%)
pT2a	56 (37%)	36 (37%)
pT2b	8 (5%)	13 (13%)
pT3	16 (10%)	16 (17%)
pT4	2 (1%)	3 (3%)
pTX	0	0
Pathological nodal stage		
pN0	116 (75%)	46 (47%)
pN1	24 (16%)	27 (28%)
pN2	14 (9%)	24 (25%)
Resection margins		
R0	146 (95%)	80 (83%)
R1	3 (2%)	7 (7%)
R2	4 (2%)	9 (9%)
RX	1 (1%)	1 (1%)
Latency (days)		
Mean (**±**SD)	49 (± 26)	45 (±19)
Nodal staging (clinical vs pathological)		
Nodal downstaging		
• One nodal station (-N1)	2 (2%)	0
• Two nodal stations (-N2)	0	0
No change (cN=pN)	120 (78%)	60 (62%)
Nodal upstaging		
• One nodal station (+N1)	19 (12%)	24 (25%)
• Two nodal stations (+N2)	13 (8%)	13 (13%)

EBUS-TBNA adequacy

A total of 97 patients underwent EBUS for mediastinal staging in Group B. The indications for EBUS included lymphadenopathy greater than 10mm (n=50, 52%), FDG avid lymph nodes with a suvMAX ≥2.5 (n=51, 53%), primary tumour size greater than 3cm (n=45, 46%) and central tumours (n=28, 29%). In 7 cases the indications were subcentimeter lymphadenopathy and multiple pulmonary nodules. The indication was not specified in 2 cases. TBNA was performed in 86 of the 97 cases (89%). Regarding lymph node stations sampled, one station was sampled in 38 cases (44%), two lymph node stations in 37 cases (43%) and three stations in the remaining 11 cases (13%). Total EBUS-TBNA adequacy was 87% (Table 2).

Table 2. Describes the adequacy of EBUS-TBNA samples in the 86 cases that underwent EBUS in Group B. This is analyzed per lymph node stations N1, N2 and N3.

EBUS Nodal stations	EBUS-TBNA (n=86):	Adequate n (%)	Inadequate n (%)
N1	52	44 (85%)	8 (15%)
N2	66	57 (86%)	9 (14%)
N3	27	25 (93%)	2 (7%)

Pathological stage

Pathological T and N stages are described in Table 1. The mean waiting time from referral to surgery was not significantly different between groups. (p=0.19).

Lymph node concordance

Clinical nodal stage (cN) and pathological nodal staging (pN) were concordant in 78% (n=120) in Group A versus 62% (n=60) in Group B (p=0.009). Two patients in Group A were downstaged a lymph node station following analysis of surgical specimens. 20% (n=32) in Group A and 38% (n=37) in Group B were upstaged post operatively (p=0.003) (Figure 1).

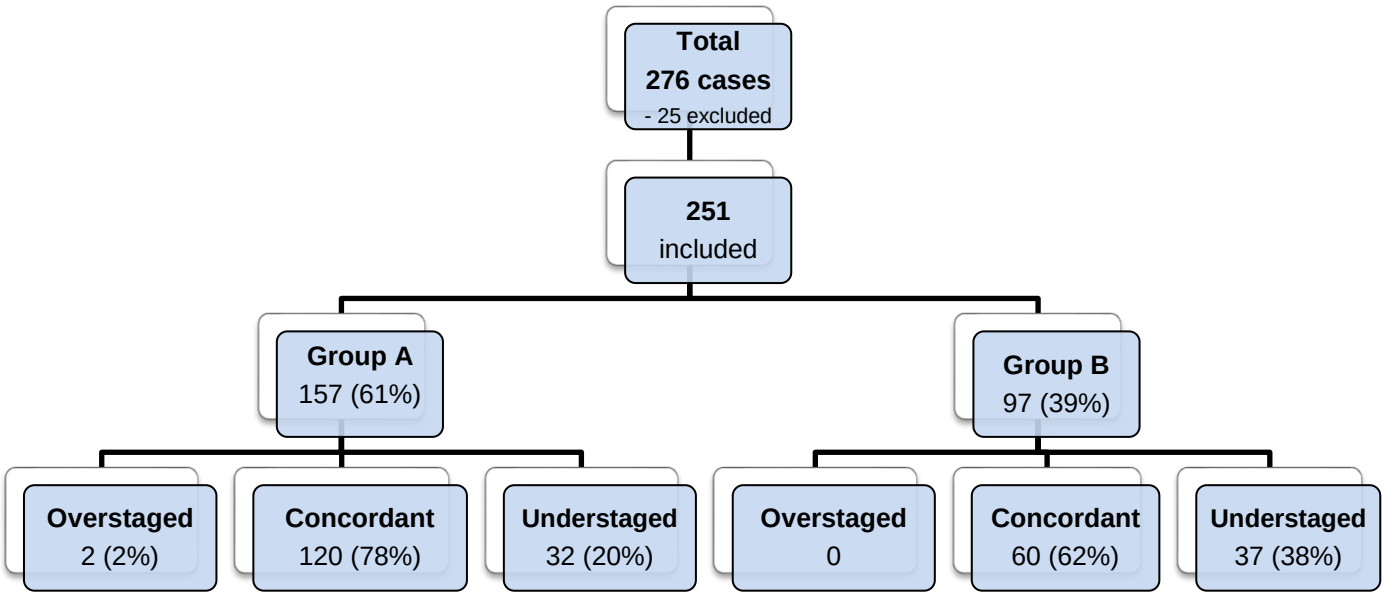

Figure 1. This flowchart illustrates the 276 patients included in the original analysis. 25 cases were subsequently excluded; 17 as there was inadequate available data and 8 as the patients underwent neoadjuvant chemotherapy which would interfere with subsequent nodal station interpretation. 251 cases were included in the final analysis: patients in Group A underwent a combination of CT, PET CT and/or mediastinoscopy, while patients in Group B underwent additional EBUS. 'Overstaged' refers to a situation where clinical lymph node staging indicated a higher lymph node stage when compared to the final pathological lymph node stage, 'Understaged' refers to the opposite situation where pathological nodal staging exceeded original clinical lymph node staging and 'concordant' refers to a situation where clinical and pathological lymph node stages were the same.

In total 37 patients (38%) had evidence of nodal upstaging in Group B post operatively, 19% (n=7) of these cases were not accessible by conventional EBUS; as 11% (n=4) were peribronchial lymph nodes and 8% (n=3) were a combination of stations 5, 8 and 9 respectively. Of these 37 patients, the total number of unexpected N2 disease was 54% (n=20) (Figure 2). Thirty eight percent (n=5) of N2 nodes had no evidence of N1 disease and were defined as 'skip lesions'.

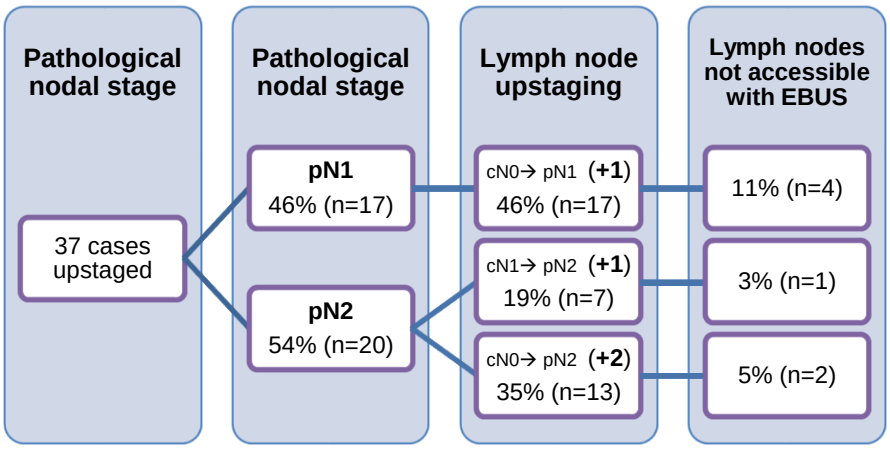

Figure 2. illustrates the 37 cases of nodal upstaging in patients who underwent EBUS in Group B. **pN1** refers to pathological upstaging of one nodal stage and **pN2** refers to pathological upstaging of two nodal stations. Similarly, **+1** indicates a single nodal station upstage and **+2** refers to upstaging of two lymph node stations.

Discussion

Current evidence suggests that the correlation between clinical and pathological staging is poor, with an accuracy that ranges from 47 to 91%.[6-8] Overall clinical and pathological lymph node concordance was 72% (n=180) in this study, reflecting the complex interplay of diagnostic, therapeutic and individual patient factors.

CT and PET CT are important clinical staging modalities; however, the sensitivity is highly dependent on lymph node size. The sensitivity of PET-CT approximates 0.85 for nodes $\geq$ 10 mm in diameter but can drop to 0.32 for nodes less than 10 mm and therefore this modality can potentially miss micrometastases to lymph nodes which do not meet this critical size criteria.[10] Furthermore PET CT can be associated with false positives and though the rates of overstaging were low in this study at 1% (n=2) and occurred in patients who did not undergo invasive mediastinal staging, this should be avoided as it could inappropriately exclude patients from curative treatment.[8]

Convex probe EBUS was developed in 2002 and incorporated into European Society of Thoracic Surgeons (ESTS) and American College of Chest Physicians (ACCP) guidelines for mediastinal staging in 2007.[3,4] EBUS was introduced in our center in 2012 and is currently the recommended initial invasive mode of mediastinal lymph node assessment in patients with suspected early stage NSCLC and suspicion of malignant nodal disease based on aforementioned criteria.[3,5] In this study the rates of nodal discordance were higher in patients who underwent additional EBUS, however interpretation of this finding is difficult in light of potential selection bias, as by definition, patients in group B were inherently more likely to have larger, more central tumors or imaging suggestive of nodal disease. In this study we found that patients in the EBUS cohort were more likely to be male and demonstrated significantly higher smoking rates, initial tumor and nodal stage. Prior studies have reported that a higher cT stage, adenocarcinoma histology and a longer waiting time to surgery are risk factors for upstaging, however they offer inconsistent findings regarding the risk gender poses.[8,10-12]

All EBUS in this study were systematic sampling procedures, performed by an experienced interventional pulmonologist. No formal auditing process exist for EBUS-TBNA in Ireland, however the British Thoracic Society Quality Statement for EBUS-TBNA in 2014 recommend a minimum diagnostic sensitivity of 88% for lung cancer staging.[13] In this study the diagnostic adequacy was 93%, 86% and 85% for N3, N2 and N1 nodes respectively. Sensitivity of N2 and N3 nodes is below the suggested 88% and could reflect numerous factors including increasing patient arousal as the procedure progresses. The limitations of EBUS in mediastinal staging must also be considered when analysing clinical and pathological concordance. EBUS-TBNA typically cannot sample ATS 5, 6, 8 and 9.[10,14] These lymph node stations accounted for 3 (8%) of the 37 cases that were understaged in this study and highlights the utility of EUS guided fine

needle aspirate (FNA) as a complementary mediastinal staging tool, as demonstrated by Zhang et al (2013) and recommended in current guidelines.[15,16]

In this study a total of 2% (n=5) of patients underwent mediastinoscopy as part of their clinical assessment. Surgical mediastinal staging techniques should be considered post EBUS/EUS if suspicion of mediastinal node involvement persists. A recent meta-analysis performed by Bousema et al suggests that the rates of unexpected N2 disease are similar in patients who do and do not undergo confirmatory mediastinoscopy following a negative endosonography, if followed by immediate lung cancer resection, suggesting that local availability and surgical waiting lists should also be factored in to clinical decision making.[17] Authors such as Fujiwara et al and Evison et al have developed risk prediction models that incorporate EBUS lymph node sonographic morphology to predict lymph node metastases.[18,19] These models could also be employed to aid clinical decision-making regarding the need for diagnostic mediastinoscopy.

Latency did not differ significantly between the two groups in this study, indicating that additional EBUS did not significantly alter diagnostic evaluation times or contribute to the higher rates of upstaging in Group B. Current standards recommend treatment to commence within 31 days of MDT clinical decision to treat, and therefore these results are noncompliant with national and international standards, with an average waiting time of 47.5 days. [20]

This study has some limitations, particularly in its retrospective observation nature, however the advantages of such data is that it represents daily practice, rather than selected populations in specialized centers. These findings also highlight the utility of surgical resection as an important staging tool in NSCLC, to provide an accurate final lung cancer stage, guide adjuvant therapy and subsequent prognostication. This is increasingly relevant as alterative curative options such as stereotactic radiation are increasingly utilized in early stage NSCLC.

This study confirms poor concordance between clinical and pathological NSCLC staging, despite advances in mediastinal staging. This is likely multifactorial and reflects a combination of diagnostic, therapeutic and individual patient factors. Additional mediastinal staging modalities, such as EUS and mediasinoscopy, and clinical prediction models based on sonographic features should be considered in a timely fashion following a negative EBUS if persistent clinical suspicion of nodal metastases exists.

Declaration of Conflicts of Interest and funding sources:
None to declare.

Corresponding author:
Dr Sarah Cullivan,
Respiratory SpR,
Galway University Hospital.
Email: sarah.cullivan@ucdconnect.ie

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National Guidelines on the Provision of Outpatient Parenteral Antimicrobial Therapy (OPAT)

E. Sweeney[1], N. Curtin[2], E. de Barra[3], K. Burns[4], E. O'Neill[5], E. Feeney[6], H. Tuite[7], A. Jackson[8], P. Gavin[9], S. Clarke[1], S. O'Connell[10], E. Muldoon[2,11].

On behalf of the National OPAT working Group and the Infectious Diseases Society of Ireland.

1. Department of Genitourinary Medicine and Infectious Diseases (GUIDe), St. James's Hospital, Dublin.
2. National OPAT Programme, Health Service Executive, DR Steeven's Hospital, Dublin.
3. Department of Infectious Diseases, Beaumont Hospital, Dublin.
4. Department of Clinical Microbiology, Beaumont Hospital, Dublin.
5. Department of Clinical Microbiology, Connolly Hospital, Dublin.
6. Department of Infectious Diseases, St Vincent's University Hospital, Dublin.
7. Department of Infectious Diseases, Galway University Hospital, Galway.
8. Department of Infectious Diseases, Mercy University Hospital, Cork.
9. Department of Infectious Diseases, Children's Health Ireland, Crumlin, Dublin.
10. Department of Infectious Diseases, University Hospital Limerick, Limerick.
11. Department of Infectious Diseases, Mater Misericordiae University Hospital, Dublin.

Abstract

Aim

Outpatient parenteral antimicrobial therapy (OPAT) is an option in patients who require parenteral antimicrobial administration and are clinically well enough for hospital discharge. This is an update of the Irish National OPAT guidelines which were last reviewed in 2011.

Methods

The guideline was devised through a collaborative process with the national OPAT Working Group and a review of the literature. It is intended for clinicians who prescribe any intravenous (IV) antimicrobials outside of the inpatient setting in the Republic of Ireland.

Results

Patient care while on OPAT should be provided by a designated OPAT service, with clear managerial and clinical governance lines of responsibility. It should be conducted using a team approach with a clinical lead on each site either as an infection specialist, or a general medical physician with infection specialist input and an OPAT nurse. An antimicrobial pharmacist is also desirable. Several factors must be considered when assessing patient's suitability for OPAT including exclusion criteria, infection-specific factors, and patient specific factors such as physical, social and logistic criteria.

Conclusion

This updated guideline advocates a more individualised OPAT approach, with the recognition that specific antimicrobials and/or specific delivery models may be more appropriate for certain patient groups. Full guidelines are available through www.opat.ie.

Introduction

Outpatient parenteral antimicrobial therapy (OPAT) is a treatment option in patients who require parenteral antimicrobial administration, and are clinically well enough not to require inpatient hospital care[1]. OPAT has consistently been shown to be safe, while decreasing healthcare cost, and maximising patient benefit[1, 2].

Increasingly, OPAT is successfully used to safely treat more complex and serious infections[2-4]. However, despite successes, complications, some serious, may occur, highlighting the need for well-developed protocols and policies for patient selection and follow-up within the context of a formal OPAT service[5].

In 2011, the Infectious Diseases Society of Ireland (IDSI) advocated successfully to the Health Service Executive (HSE) for the establishment of the National OPAT Programme. Since then, a considerable volume of new literature has been published[6, 7]. These publications have informed this update of the Irish National OPAT guidelines.

Methods

This guideline was devised through a collaborative process with the national OPAT Working Group. This group is led by the National Clinical Lead for OPAT and is comprised of Infectious Diseases (ID) Physicians and Clinical Microbiologists engaged in OPAT provision, an OPAT nurse, and the Programme Manager, who is the administrative lead for OPAT within the HSE. The literature review was conducted by E.S, 437 articles were initially identified during a PubMed search for the keyword "OPAT". Of those, 110 articles were deemed relevant, accessed, and read. Overall, 70 articles were included. The evidence appraisal was reviewed by E.M. This guideline is intended for clinicians who intend on prescribing any intravenous (IV) antimicrobials outside of the inpatient setting in the Republic of Ireland (ROI).

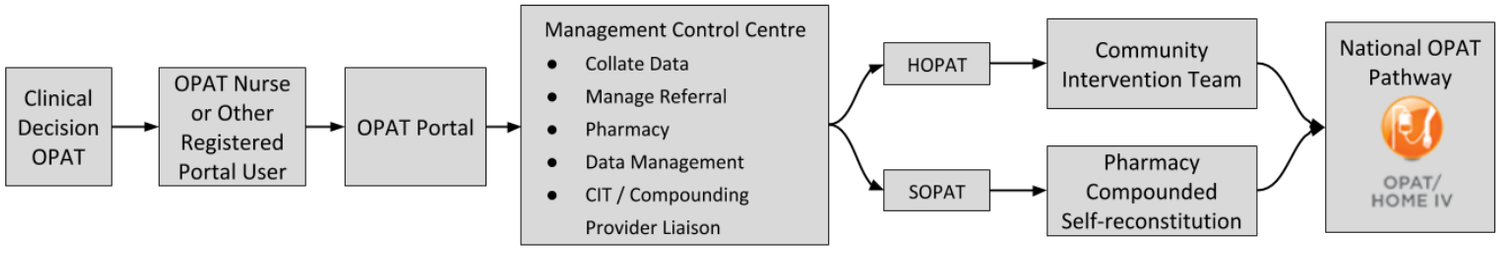
Results

The headings chosen are comparable to previously proposed OPAT "care bundles" which identify the key considerations when planning an OPAT program[8].

OPAT governance

In non-inpatient settings, IV antimicrobials should be delivered within a formal OPAT service with clear governance pathways delineated to ensure patient safety. In the ROI, this service is provided for public patients by the HSE through the National OPAT programme *(Figure 1)*. While other OPAT providers are available and utilise alternative referral pathways, it is expected that all providers will follow these guidelines.

Figure 1. Referral pathway for public patients



OPAT team

OPAT should be conducted using a team approach, with clear managerial and clinical governance lines of responsibility. The team leader should be a consultant infection specialist (ID Physician or Clinical Microbiologist). In hospitals without an ID service, a local clinical lead for OPAT should be identified; a general medical physician with an interest and experience in the provision

of OPAT. In this context, it is recognised that care is provided by the discharging consultant with ongoing infection specialist input from clinical microbiology.

This clinical responsibility is important in ensuring a high-quality service with clear accountability[9]. The OPAT nurse plays a central role, with responsibility for patient assessment, education, consent, training, and monitoring. An antimicrobial pharmacist is desirable for assessing drug interactions, potential adverse events, and monitoring. The OPAT team are responsible for the selection of vascular access, antimicrobial agent, duration of therapy, and coordinating medical evaluations during the entirety of the OPAT course[7]. Each member of the OPAT team is responsible for their own personal continuing professional development.

Management plan

For each patient, the OPAT plan should be agreed between the OPAT and referring team. Clinical responsibility for patients may be shared between the two teams e.g. between discharging consultant and infection specialist or assumed by an infectious diseases service alone. The plan should include choice, dose and frequency of antimicrobial agent, anticipated duration of therapy, along with any requirement for interval imaging[10]. There should be communication between the OPAT team, the referring clinician, the patient's general practitioner and community nursing services (as appropriate).

Data collection

Local data on all referrals to the OPAT service, and OPAT outcomes should be recorded prospectively in a local database which can then contribute to the national database. Audit of individual processes should be undertaken regularly and an annual service review to ensure compliance with national recommendations is advised.

Patient assessment and selection

Studies demonstrate that when infection specialists are consulted for consideration of OPAT, recommendations often include a change in antimicrobial plan or note that OPAT is unnecessary[11]. Possibility of an antimicrobial oral switch should be considered for every patient at time of assessment[6]. All patients must be evaluated by a competent member of the OPAT team, which may be the OPAT nurse, prior to OPAT initiation[6, 7].

Self- OPAT versus Health care professional -OPAT

S-OPAT refers to administration of IV antimicrobials by the patient, or caregiver. H-OPAT refers to administration of IV antimicrobials by a healthcare worker. S-OPAT is preferred and should be considered for all patients, with H-OPAT reserved for those in whom S-OPAT is not appropriate. Most OPAT happens at home, but other settings e.g., day ward or dialysis unit, may be appropriate.

Infection-specific factors

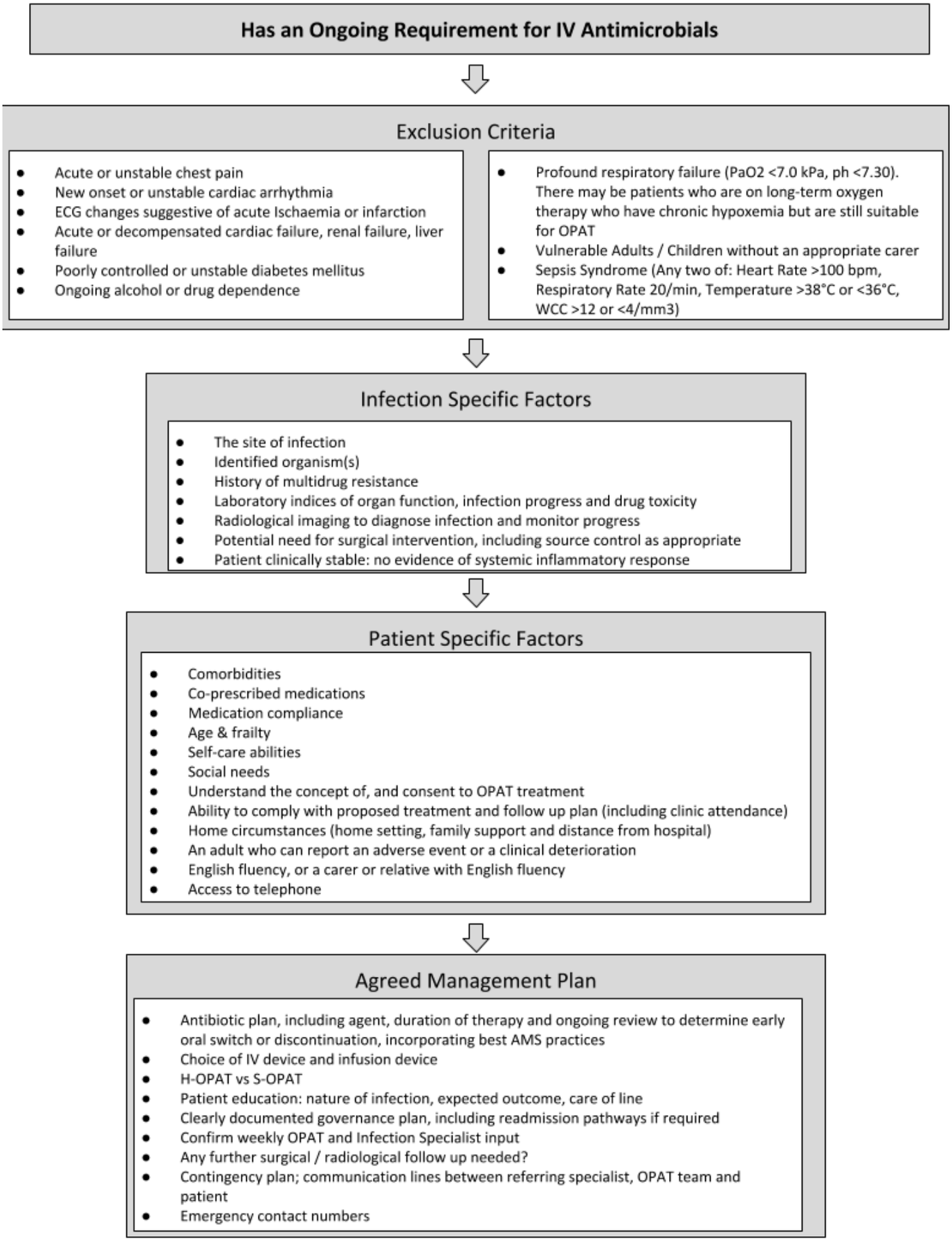
The site of infection, the causative organism(s) and previous microbiology should be considered, with source control achieved and any required surgical intervention performed. The need for interval imaging (e.g., radiology, echocardiography) must be clarified and incorporated into the treatment plan[12].

Patient specific factors

Physical, social and logistic criteria must be considered. The patient must be clinically stable and deemed suitable for discharge on OPAT by a senior clinician, with consideration of inclusion and exclusion criteria *(See figure 2)* for each case. Patients and/or carers must be informed about the nature of OPAT and provide consent[6]. For S-OPAT, either with a compounded agent or one requiring reconstitution, at least one adult should be present who can reliably learn and perform sterile infusion technique and communicate any adverse events with the team[4, 7, 13]. All patients considered at risk of venous thrombosis should be considered

for prophylaxis during OPAT[6]. Although older and frail patients may have greater risks of adverse events and treatment failure, studies demonstrate that OPAT is safe and effective option when patients are appropriately selected and monitored[14].

Figure 2. Inclusion / Exclusion criteria and other factors for consideration



Patient education

Competencies to be covered will be contingent on the S-OPAT versus H-OPAT model; education on IV-line care, troubleshooting on-therapy, monitoring, and provision of contact numbers for OPAT team and infusion nurses is imperative for all patients[15]. Patient information leaflets[16], and standardised teaching should be used to support patient education[13, 17]. Both the nurse and patient/carer must be satisfied that each aspect has been discussed, demonstrated, and practised to ensure competency before sign off, and this should be documented[6].

Antimicrobial selection

OPAT is one of the five key antimicrobial stewardship (AMS) decisions in the Department of Health's antimicrobial stewardship program 'Start Smart — then Focus'[18]. Every decision to discharge a patient with OPAT must have the timely involvement of an infection specialist or be in accordance with clearly defined local pathways endorsed by an infection specialist. OPAT team member representation on local AMS committees is desirable, so that OPAT can be a standing item on the committee meeting agenda[6]. Antimicrobials requiring specific monitoring should only be prescribed when the suitable support is available. Appropriate selection and prescription of antimicrobials during OPAT must be in accordance with the referring hospital's antimicrobial guidelines and incorporate the HSE's national policy on restricted antimicrobial agents[13, 19, 20]. The oral route should always be used in preference to the IV route, where there is equivalent bioavailability or efficacy, unless there are other precluding factors. Recent studies have been published on the use of complex oral antimicrobial regimens for treatment of bone and joint infections[21]. Irrespective of the route of administration, ambulatory management of such infections is complex and requires a well-organized management approach, as exemplified within existing OPAT services. OPAT should remain an important part of a comprehensive bone and joint infection service: complex outpatient antimicrobial therapy—'COpAT'[22]. The first dose of a new antimicrobial should be administered in a supervised setting. Reconstitution and administration of antimicrobials should comply with HSE guidelines, and all administered doses documented on a medication card.

Vascular access

Short peripheral venous catheters are recommended when OPAT is expected to be seven days or less, while a midline or peripherally inserted central catheter (PICC) should be utilised for longer courses[23]. Other patient factors, such as existing vascular access devices (e.g. portacath) or future potential need for vascular access (e.g. dialysis patients) should be considered and decisions individualised.

Infusion devices

IV antimicrobials can be administered via continuous infusion or as a bolus in the outpatient setting; a variety of different delivery systems are available. Choice of device and mode of delivery is dependent on local resources, training and availability of compounding services, and the compatibility and stability of the antimicrobial agent[9].

Safety on discharge & Care transition

Each public patient accepted for OPAT should be entered into the national OPAT registry portal. All patients must have their initial outpatient appointment made prior to hospital discharge; this must be within a week of discharge. The patient should receive written notification of the appointment, along with contact details of the OPAT team should adverse events arise[10].

Follow up, monitoring, discontinuation of therapy and management of readmission

Monitoring whilst on OPAT mandates that the patient have access to weekly outpatient review[4]. OPAT patients whose weekly laboratory values are not available to clinicians have a higher risk (2.53 fold) of readmission than those whose results are monitored weekly[1, 24]. Blood tests should be determined by the antimicrobial agent utilised, and some may require more frequent monitoring[6, 7]. The OPAT team is responsible for monitoring clinical response, tolerability of antimicrobials and coordinating weekly clinic review. If a treatment plan needs revisiting, there should be a mechanism in place for urgent multidisciplinary discussion, review of emergent clinical problems or readmission, as necessary. Regular review of local OPAT

outcomes, including readmission rates (Irish national target < 5%) and reasons for readmission must be recorded. The discontinuation of OPAT should be a clinical decision, based upon the patient's clinical and laboratory response to therapy, and must involve an infection specialist.

Paediatric considerations

Similarly, to adults, more prospective research is required to enable us to predict more accurately which paediatric patients are most likely to have a successful, or unsuccessful, outcome of their OPAT episode. As with caring for adults on OPAT, AMS approaches and oversight is imperative in paediatric OPAT (pOPAT)[25]. In discharging children with pOPAT similar factors should be considered as outlined for adults above. Consultation with paediatric ID services is recommended to ensure the safe and efficacious discharge of children with pOPAT.

Outcome measurement

Data on OPAT referrals should be recorded prospectively to evaluate service workload, inform AMS opportunities and identify areas for service improvement. Data should include patient demographics, antimicrobial agent(s) used, duration of treatment, method of OPAT used, type of vascular access and infusion device, bed days saved and all adverse events[6]. Patient-specific aims of therapy outlined in *Figure 3.* should be established in the original management plan and recorded upon completion of IV therapy. Although standardisation of OPAT outcomes are lacking, we have chosen the recent "Updated good practice recommendations for OPAT in adults and children in the UK" outcome proposals[6] *(figure 4).*

Figure 3. Treatment Aims

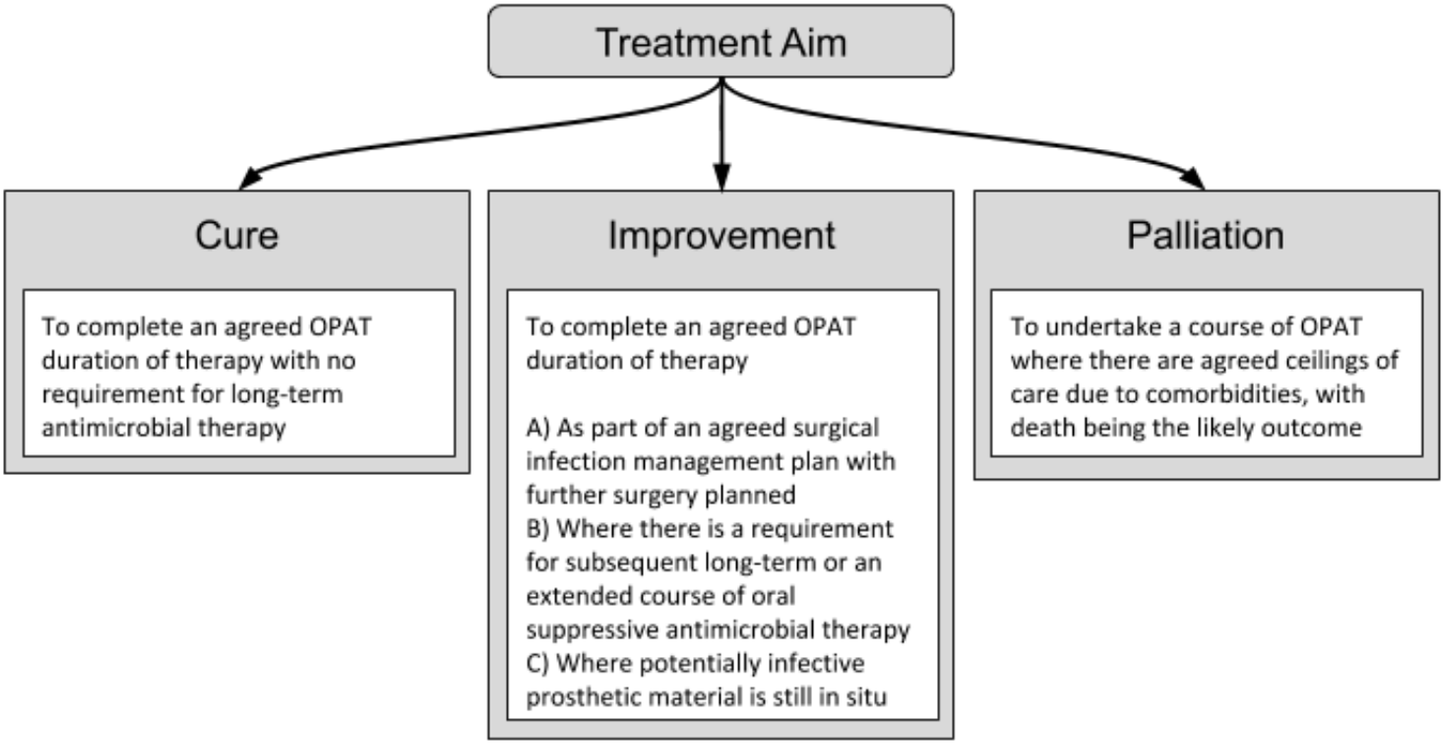
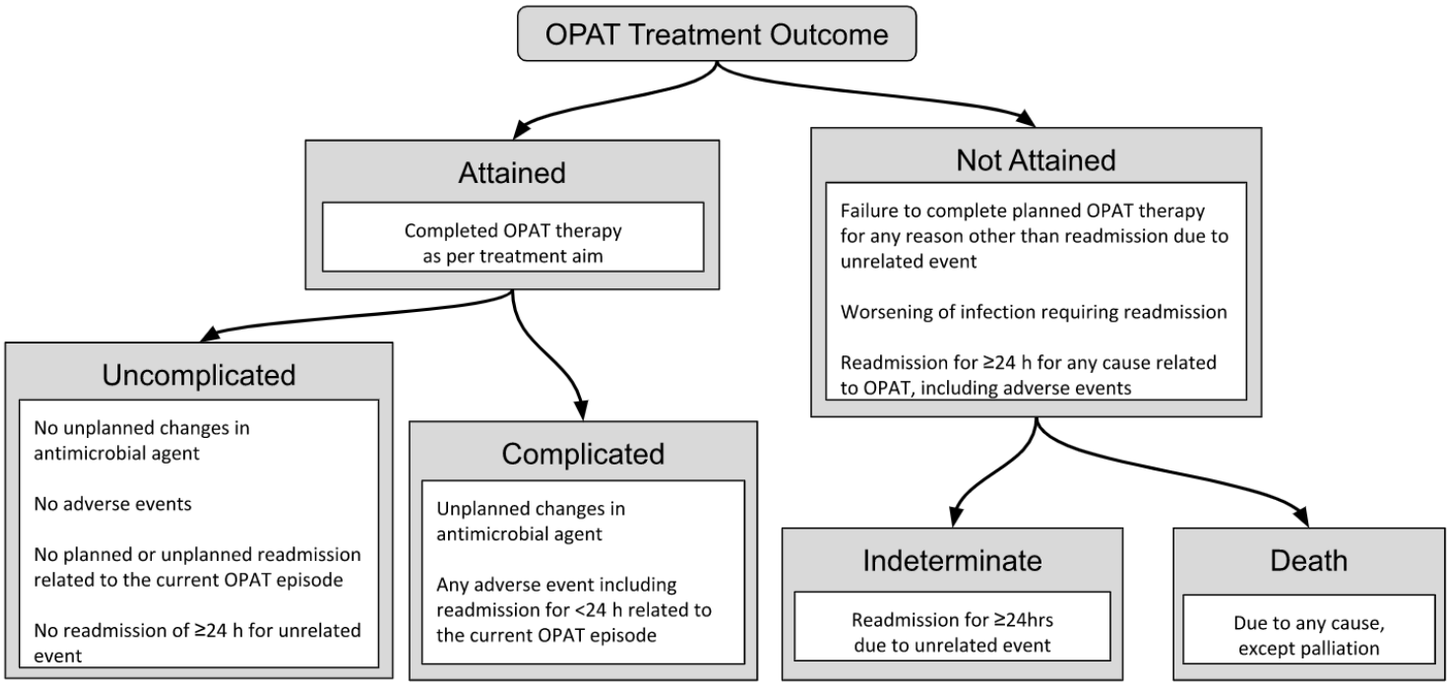


Figure 4. OPAT Treatment Outcomes



Discussion

The number of patients treated through the National OPAT programme continues to increase as the programme expands nationally. These guidelines should inform the safe and efficacious care of patients discharged with OPAT in Ireland and allow further expansion of OPAT services in a structured, safe, and robust fashion. It is not intended to replace clinical judgement in the management of individual patients. Evidence gaps remain within the OPAT literature; prospective research predictive measures on the likelihood of success of a patients OPAT episode, particularly in paediatrics, would be beneficial. More data on antimicrobial stability in infusion devices and the use and monitoring of new antimicrobials, such as the long-acting semi-synthetic glycopeptides is required[6].

Corresponding Author:
Dr Eileen Sweeney
Specialist Registrar (SpR) in Infectious Diseases.
Email: e.sweeney88@gmail.com

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Exploration of Factors Associated with Intention, Initiation and Duration of Breastfeeding

S. Callaghan[1,2], A.A. Geraghty[1], R.L. Moore[1], F.M. McAuliffe[1]

1. UCD Perinatal Research Centre, School of Medicine, University College Dublin, National Maternity Hospital, Dublin, Ireland.
2. UCD School of Nursing, Midwifery and Health Systems, University College Dublin, Dublin, Ireland.

Abstract

Aim
To assess breastfeeding intention, initiation and duration up to three months postnatal and associated factors.

Methods
Secondary data from 131 healthy pregnant women participating in an RCT in a Dublin hospital who recorded intention to breastfeed were included. Demographic and breastfeeding data were collected.

Results
Of the 131 women, 91.6% (n=120) reported intending to breastfeed. 91.7% of those subsequently initiated breastfeeding (n=110/120). Of those intending to breastfeed, 78.9% (n=86/109) and 68.9% (n=73/106) remained breastfeeding at one and three months postnatal respectively. Higher education ($p<0.05$) and lower BMI ($p<0.05$) were significantly associated with initiation and duration of breastfeeding. Ethnicity, age, parity or mode of delivery were not significantly associated with breastfeeding.

Conclusion
Many factors are associated with breastfeeding intention and duration including education and BMI. It is important to develop tailored support measures to encourage initiation and continuation of breastfeeding.

Introduction

Breastfeeding infants from birth has been shown to improve health outcomes both for babies and their mothers[1]. Breastfeeding is important for normal growth and development of infants and has both short and long term health benefits for children[2,3]. Breastfeeding has been associated with decreased risk of neonatal infection, gastrointestinal infection and pneumonia during early childhood, as well as reduced morbidity and mortality from infection[4]. This protective role extends beyond birth and is proven to be important in reducing childhood obesity[5], atopic conditions[1] and chronic diseases such as diabetes[4]. Research also shows that breastfeeding can substantially impact maternal health. Breastfeeding has been demonstrated to decrease women's risk of type-2 diabetes[1], ovarian and breast cancer[4], as well as reducing postpartum weight retention[1]. Several factors have been shown to be associated with both initiation and continuation of breastfeeding, however, including education[4], ethnicity[5], mode of delivery, parity and maternal obesity[6].

The World Health Organisation (WHO) recommends breastfeeding be initiated within the first hour after birth[7], with exclusive breastfeeding recommended for the first six months of life to optimise infant health, growth and development[8].

These international recommendations have been adopted within national recommendations by the Irish Heath Service Executive (HSE). Following these recommendations, the WHO developed global targets to increase exclusive breastfeeding during the first six months to 50% internationally by 2025[9]. In 2018, 41.6% of infants under six months of age were exclusively breastfed internationally, which rose from approximately 37% in 2012[10]. In Ireland, however, breastfeeding rates remain one of the lowest recorded internationally[4]. In 2016, 59.9% of women in Ireland initiated any breastfeeding, with almost 50% exclusively breastfeeding at hospital discharge[11]. Although this is an increase from previous years, rates still remain below the average across Europe and internationally. A report from the HSE in 2015 found that 35% of all babies were receiving some breast milk at three months postnatal[12]. The WHO COSI study (2015/2017) reported 22.6% any breastfeeding and 10.5% exclusive breastfeeding at six months in Ireland [13].

In order to achieve proposed targets to improve breastfeeding in Ireland by 2% annually[14], it is important to examine breastfeeding and associated factors to determine potential avenues for increasing breastfeeding rates[15]. This study aimed to assess mother's intentions to breastfeed from early pregnancy, their subsequent initiation and duration of breastfeeding up to three months postnatal, and potentially associated factors.

Methods

This study involved secondary analysis of observational data collected during a randomised controlled trial conducted in a large maternity hospital between 2017-2019. The trial involved probiotic use in pregnancy, the results of which will be published in due course. 160 healthy pregnant women were recruited in early pregnancy at approximately 12 weeks gestation and followed until three months postpartum.

Data for this analysis were collected at four timepoints; early pregnancy, delivery, one month and three months postnatal. Demographic data were recorded at the time of recruitment through completion of a baseline assessment record. Demographic information included gestation, parity, maternal age, Body Mass Index (BMI), education status and ethnicity. For multiparous women, any history and duration of breastfeeding with previous infants was also recorded. Intention to breastfeed was recorded at this timepoint with the researcher asking each woman their intention regarding breastfeeding following the current pregnancy. Reponses to this included "Yes", "No" and "Maybe". Mode of delivery was also recorded from patient records following birth.

Data regarding initiation of breastfeeding were collected from researcher completed checklists at the time of delivery which recorded infant feeding at this timepoint (exclusive breastfeeding/combined feeding/formula feeding). Participants were then followed up at one and three months postnatal. Data were gathered on continuation and duration of breastfeeding from participant completed lifestyle questionnaires at these timepoints.

Statistical analysis was performed using SPSS Windows's version 24.0. Demographic data were analysed through descriptive analysis to assess frequencies. Some data for ethnicity, education, and parity were dichotomised to increase statistical power as some groups were small and were therefore combined where appropriate. Associations between categorical variables and breastfeeding status were assessed using chi-square tests for independence. Yates' Correction for Continuity and Fisher's exact test were used as appropriate depending on the frequency within each category. Continuous variables including maternal age and BMI were assessed for normality of distribution using the Kolmogorov-Smirnov test. As continuous variables were normally distributed, the mean and standard deviation were calculated. Associations between continuous variables and breastfeeding were analysed using parametric tests (independent samples t-tests). A p value <0.05 was considered statistically significant.

Results

Of the 160 pregnant women participating in the original trial, this analysis included a sample of 131 women with breastfeeding intention data recorded in early pregnancy.

Of the 131 included women, 78.6% (n=103) were Irish, 84.7% (n=111) had achieved third level education and 57.3% (n=75) were primiparous. The mean maternal age was 32.68 years (SD=4.19) and the mean BMI was 25.01kg/m^2 (SD=3.33) (Table 1).

Table 1. Demographic factors of total study sample.

DEMOGRAPHICS		N (%)	
Ethnicity:	**Irish**	103 (78.6)	
	White Other	23 (17.6)	
	Missing	5	
Education	**Completed 3rd level education**	111 (84.7)	
	Second level education	19 (14.5)	
	Missing	1	
Parity	**Primiparous**	75 (57.3)	
	Multiparous	56 (42.7)	
Previously Breastfed	**Yes**	44 (83.0)	
	No	9 (17.0)	
	Missing	3	
Mode of Delivery	**Spontaneous vaginal delivery**	79 (60.3)	
	Instrumental delivery	26 (19.8)	
	Caesarean section[a]	26 (19.8)	
DEMOGRAPHICS		**RANGE**	**MEAN (SD)[b]**
Maternal age (years)		18 – 44	32.68 (SD±4.19)
Body Mass Index (BMI) (kg/m^2)		19.41 – 34.08	25.01 (SD±3.33)

[a]Of those who had a caesarean section, 50% (n=13) had an emergency section and 50% (n=13) had an elective section.
[b]SD=Standard deviation

In early pregnancy, 91.6% (n=120) of women reported intending to breastfeed (Table 2). Upon hospital discharge, 91.7% of those who intended to breastfeed had initiated breastfeeding (n=110/120), of which 77.3% (85/110) were exclusively breastfeeding. At one month postnatal, 78.9% (n=86/109) of remaining participants who had intended to breastfeed remained breastfeeding, of which 70.2% (n=59/84) were known to be exclusively breastfeeding. Continuation of breastfeeding reduced further at three months postnatal, with 68.9% (n=73/106) of those intending to breastfeed continuing breastfeeding. Rates of exclusive breastfeeding were maintained at three months, with 70.8% (n=51/72) of breastfeeding mothers using breast milk exclusively as a source of infant feeding at this timepoint. Some of the 120 participants who had reported intending to breastfeed were lost to follow-up at postnatal timepoints.

Intention to breastfeed from early pregnancy was significantly higher amongst women with third level education (97.3%, n=108/111) compared to those with lower education status (57.9%, n=11/19, p<0.001). Intention to breastfeed did not differ significantly between primiparous and multiparous women (p=0.204). However, women who had breastfed a previous infant were significantly more likely to intend to breastfeed for the subsequent pregnancy (100%, n=44/44) than those who had not breastfed previously (33.3%, n=3/9, p<0.001). There was no significant difference in BMI between women intending to breastfeed (n=119, mean=24.93, SD=3.26) and those who did not (n=11, mean=25.85, SD=4.09, p=0.384). There was also no significant difference in breastfeeding intention with regards to ethnicity (p=0.210) or maternal age (p=0.476).

Table 2. Women's intention to breastfeed in early pregnancy and subsequent initiation and continuation of breastfeeding.

BREASTFEEDING STATUS	YES	NO
	n (%)	n (%)
Intended to breastfeed at booking	120/131 (91.6)	11/131 (8.4)
Of those intending to BF;		
BF at discharge	110/120[a] (91.7)	10/120[a] (8.3)
Exclusive BF at discharge	85/110 (77.3)	25/110 (22.7)
BF at 1 month postnatal	86/109[a] (78.9)	23/109[a] (21.1)
Exclusive BF at 1 month	59/84[b] (70.2)	25/84[b] (29.8)
BF at 3 months postnatal	73/106[a] (68.9)	33/106[a] (31.1)
Exclusive BF at 3 months	51/72[b] (70.8)	21/72[b] (29.2)

BF=Breastfed

[a]These denominators refer to women who intended to breastfeed only. The change in the denominator value is due to the loss of participants to follow-up in the original study at each timepoint.

[b]Denominators refer to women that did breastfeed at each timepoint who intended to breastfeed in early pregnancy. Reduction in the number is due to missing data in relation to whether women were exclusively breastfeeding or combined feeding at each timepoint.

Although not associated with intention to breastfeed, maternal BMI was shown to be a significant factor in the initiation and continuation of breastfeeding at all timepoints (Figure 1). Of those intending to breastfeed, women who did not initiate breastfeeding had a significantly higher BMI (M=27.22, SD=4.55, p=0.02) compared to women who breastfed (M=24.72, SD=3.06). This was also seen in the maintenance of breastfeeding where, of women intending to breastfeed, the average BMI was higher amongst women who did not continue breastfeeding at both one (M=26.59, SD=4.25, p=0.039) and three (M=26.45, SD=3.92, p=0.006) months postnatal, compared to those who remained breastfeeding. Education status was also seen to be associated with initiation and duration of breastfeeding with women with higher education more likely to breastfeed at discharge (94.4% vs 63.6%, p=0.006), one month (82.2% vs 33.3%, p=0.003) and three months postnatal (73.2% vs 12.5%, p=0.001). There was no significant difference regarding feeding status at the three observed timepoints in parity, ethnicity, maternal age, or mode of delivery (Table 3 **(next page)**). There was also no significant association seen between any of the factors examined in this study and exclusive breastfeeding at any of the three timepoints.

Table 3. Factors associated with breastfeeding* intention, initiation and duration

Demographic		Intention		Initiation		1 month		3 months	
		BF	*No BF*	*BF*	*No BF*	*BF*	*No BF*	*BF*	*No BF*
Parity	*Primip*	n=71/75 (94.7%)	n=4/75 (5.3%)	n=65/71 (91.5%)	n=6/71 (8.5%)	n=52/65 (80%)	n=13/65 (20%)	n=48/64 (75%)	n=16/64 (25%)
	Multip	n=49/56 (87.5%)	n=7/56 (12.5%)	n=45/49 (91.8%)	n=4/49 (8.2%)	n=34/44 (77.3%)	n=10/44 (22.7%)	n=25/42 (59.5%)	n=17/42 (40.5%)
	p Value	p=0.204		p=1.000		p=0.812		p=0.133	
Education	*3rd level*	n=108/111 (97.3%)	n=3/111 (2.7%)	n=102/108 (94.4%)	n=6/108 (5.6%)	n=82/99 (82.8%)	n=17/99 (17.2%)	n=71/97 (73.2%)	n=26/97 (26.8%)
	Lower education	n=11/19 (57.9%)	n=8/19 (42.1%)	n=7/11 (63.6%)	n=4/11 (36.4%)	n=3/9 (33.3%)	n=6/9 (66.7%)	n=1/8 (12.5%)	n=7/8 (87.5%)
	p Value	**p<0.001**		**p=0.006**		**p=0.003**		**p=0.001**	
Ethnicity	*Irish*	n=94/103 (91.3%)	n=9/103 (8.7%)	n=86/94 (91.5%)	n=8/94 (8.5%)	n=67/86 (77.9%)	n=19/86 (22.1%)	n=56/83 (67.5%)	n=27/83 (32.5%)
	Other	n=23/23 (100%)	n=0	n=22/23 (95.7%)	n=1/23 (4.3%)	n=17/20 (85%)	n=3/20 (15%)	n=15/20 (75%)	n=5/20 (15%)
	p Value	p=0.210		p=0.686		p=0.760		p=0.599	
Previous BF	*Yes*	n=44/44 (100%)	n=0	n=41/44 (93.2%)	n=3/44 (6.8%)	n=30/39 (76.9%)	n=9/39 (23.1%)	n=23/38 (60.5%)	n=15/38 (39.5%)
	No	n=3/9 (33.3%)	n=6/9 (66.7%)	n=2/3 (66.7%)	n=1/3 (33.3%)	n=2/3 (66.7%)	n=1/3 (33.3%)	n=0/2 0%	n=2/2 100%
	p Value	**p<0.001**		p=0.239		p=1.000		p=0.174	
Delivery	*Vaginal*	-	-	n=92/99 (92.9%)	n=7/99 (7.1%)	n=75/92 (81.5%)	n=17/92 (18.5%)	n=64/89 (71.9%)	n=25/89 (28.1%)
	C-section	-	-	n=17/20 (85%)	n=3/20 (15%)	n=11/16 (68.8%)	n=5/16 (31.2%)	n=9/16 (56.3%)	n=7/16 (43.7%)
	p Value	-		p=0.369		p=0.311		p=0.243	
Age (years)	*Mean SD*	n=120 32.81 3.88	n=11 31.27 6.79	n=110 32.89 3.55	n=10 31.9 6.72	n=86 33.14 3.09	n=23 32.35 5.28	n=73 33.15 2.99	n=33 32.55 4.95
	p Value	p=0.476		p=0.656		p=0.499		p=0.519	
BMI (kg/m^2)	*Mean SD*	n=119 24.93 3.26	n=11 25.85 4.09	n=109 24.72 3.06	n=119 27.22 4.55	n=86 24.52 2.91	n=22 26.59 4.25	n=73 24.23 2.83	n=32 26.45 3.92
	p Value	p=0.384		**p=0.020**		**p=0.039**		**p=0.006**	

BF=Breastfeeding; SD=Standard deviation
**Breastfeeding refers to any breastfeeding and is not limited to exclusive breastfeeding.*

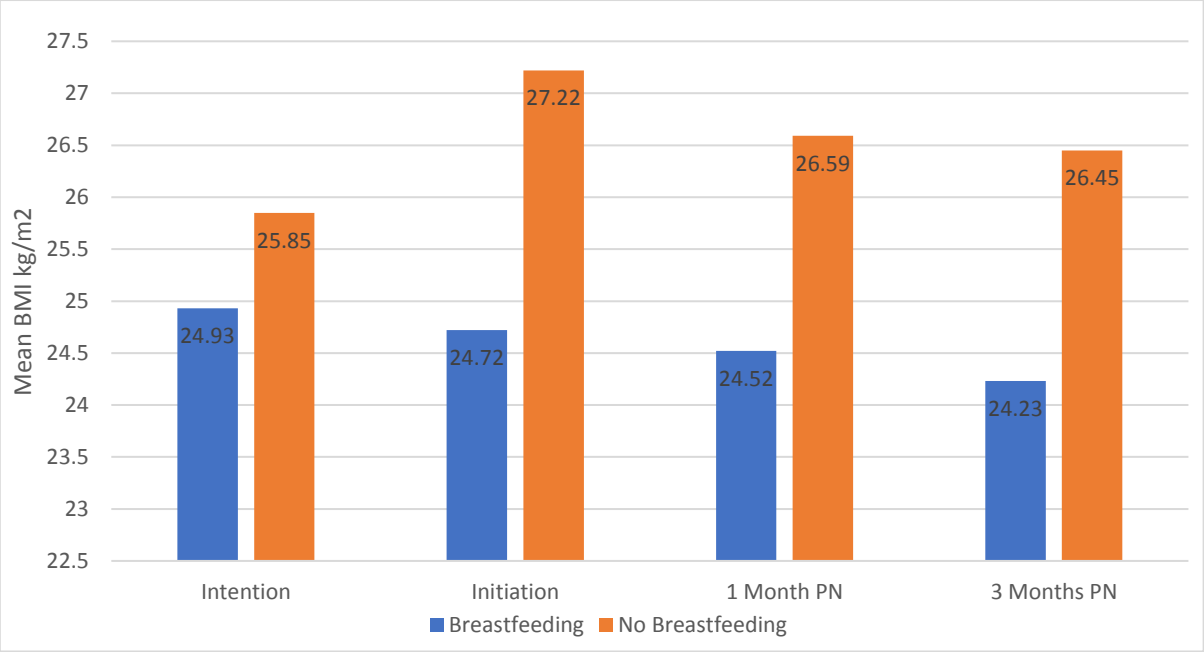

Figure 1. Association of BMI with breastfeeding intention, initiation and duration

Discussion

Of the high number of women who reported intending to breastfeed from early pregnancy in this study, the majority of these went on to initiate breastfeeding at birth, with breastfeeding rates in this sample substantially higher than the hospital and national average of approximately 76% and 59.9%[11] respectively. However, despite these high rates of intention to and initiation of breastfeeding, factors including maternal BMI and education level were still shown to be negatively associated with women maintaining breastfeeding.

Increased maternal BMI was associated with initiation and continuation of breastfeeding in this study. Although BMI was not associated with women's intention to breastfeed in early pregnancy, the average BMI for women who did not breastfeed at all three observed timepoints was classified in the overweight BMI category between 25-29.9kg/m^2[2,16], compared to an average normal BMI amongst those that did breastfeed. Overweight and obesity has been highlighted as a potentially influential factor on breastfeeding initiation and duration in previous studies[17,18]. It is important to examine barriers for breastfeeding amongst women with obesity as breastfeeding has been shown to reduce childhood obesity[13]. This benefit is of particular importance in relation to women with overweight or obesity as children of women with high BMIs are at increased risk of developing overweight or obesity in later life[19,10]. Studies have demonstrated higher incidence of breastfeeding difficulties reported by women with overweight or obesity[18], however; they are also potentially less likely to seek breastfeeding support during the first three months postpartum[21]. This highlights the need for interventions and support services provided by appropriate healthcare professionals to assist and encourage women with overweight and obesity to initiate and continue breastfeeding[22].

Socio-economic status is also proven to be associated with breastfeeding rates in this study, which correlated with previous reports published in Ireland[12,15]. Socioeconomic status was measured in this study by maternal education level. This study cohort had a high education level, with 84.7% having achieved third level education which is higher than the current national average of 47% for adults between 25-64years[23]. However, women with lower education were still shown to be significantly less likely to intend to breastfeed, and to subsequentially initiate and continue breastfeeding compared to higher education women. Maternal education has frequently been highlighted as an associated factor for breastfeeding[6]. Women with higher levels of education may be more aware of the importance of breastfeeding and associated benefits and may have greater access to resources and support. It is therefore important to acknowledge this difference and provide additional education and support for women with lower levels of education to promote breastfeeding.

Potential limitations of this study should be considered. This study involved a relatively small sample of 131 women which limited the statistical analysis that could be undertaken and the low number of women not intending to breastfeed potentially limiting the analysis on factors associated with intention to breastfeed. The study population

had a higher than average breastfeeding rate and education level. This may be due to the nature of participation in trials on a voluntary basis, with women willing to participate in research during pregnancy more likely to be higher educated.

In conclusion, breastfeeding is important for the health and wellbeing of not only the baby and child, but also mothers. Of the high number of women reporting intending to breastfeed from early pregnancy in this study, the majority of these went on to initiate breastfeeding. However, despite this, initiation and maintenance of breastfeeding up to three months postnatal was significantly related to factors including education level and maternal BMI. Further research is needed to explore other potential barriers to breastfeeding and to develop methods for healthcare professionals to support women highlighted in this study to improve overall breastfeeding intention, initiation and continuation to the recommended six months postpartum.

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Corresponding Author:
Professor Fionnuala McAuliffe
UCD Perinatal Research Centre,
65-66 Mount Street,
National Maternity Hospital,
Dublin.
Email: fionnuala.mcauliffe@ucd.ie

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The 100 Citation Classics in the Irish Medical Literature; A Bibliometric Analysis

S.M. Clifford[1], A.M. Akhtar[2], C.E. Redmond[1], Z. Hutchinson[1], H. Al-Sayyed[1], E. Browne[1], G.M. Healy[1], E.J. Heffernan[1]

1. Department of Radiology, St. Vincent's University Hospital, Dublin 4.
2. Faculty of Medicine, Royal College of Surgeons in Ireland, Dublin 2.

Abstract

Identifying citation classics is a valuable metric of research performance. Ireland has a distinguished history of medical research, although Ireland's top-cited articles are unknown. The SCOPUS database identified all medical and surgical articles published by journals in the Republic of Ireland or Northern Ireland. The 100 top-cited articles were analysed. The most cited article received 240 citations. There is an observed trend of increasing number of authors over time ($p<0.05$). General medicine and public health are the most common topics. The majority of works originate from Irish institutions. Collaborative research and non-Irish research are poorly represented among the citation classics. The Irish medical literature contains multiple highly cited and influential articles.

Introduction

Bibliometrics involves the statistical analysis and evaluation of literature and publications. It is a powerful tool for assessing information, citations and measuring activity on publications available from medical databases[1,2]. Scopus is a bibliometric database created by Elsevier which includes all MEDLINE databases and allows comprehensive citation analysis[3]. The number of citations can be used to evaluate the influence of a publication and its potential impact on patient care[4,5]. Exploring the highest cited articles can help scholars become familiar with "classic" landmark studies and can highlight areas for future research[6]. For these reasons, citation classics have been described as the "gold bullion of science"[7,8].

The aim of this study was to include all articles published within Irish medical journals, including all medical and surgical specialities, to determine which articles have received the highest number of citations. To our knowledge, this is the first time that the full scope of Irish medical literature has been analysed to determine the most cited articles. This study is informative to those seeking to discover the "classic" landmark studies published in Ireland and identify particular areas of excellence in the Irish medical literature. Additionally, it serves an instructive role for those currently undertaking research to potentially increase citations by emulating the characteristics of successful articles.

Methods

Articles were obtained by searching the Scopus database on the 10th of July 2019[3]. By using the 'Advanced Search' option, ISSNs of the medical journals based primarily in Republic of Ireland or Northern Ireland were stringed using the 'OR' operator and subsequently searched within the database. This option was comprehensive as it searched for all types of publications within these journals. The journals included in the search and thus comprising 'The Irish Medical Literature' for the purpose of this study were the 'Irish Medical Journal' (formerly the 'Journal of the Irish Medical Association'), the 'Irish Journal of Medical Science', the 'Ulster Medical Journal' and the 'Irish Journal of Psychological Medicine.' Journals only partly associated with Ireland were excluded.

Once all articles published in the medical journals based in Ireland were retrieved, they were sorted in order of descending citation count to determine the top 100 most cited articles. The titles and abstracts of these articles were examined. Information was recorded for each article, including the journal name, year of publication, citation count, names of authors, number of authors, institutions involved, modality and specialty. The variation in number of authors over time was assessed with a one-way ANOVA test using SPSS version 23 (IBM, New York, USA).

Results

A total of 20,152 articles have been published by medical journals in Ireland according to the Scopus database[3]. The 100 articles with the most citations were analysed. A list of the top 10 of these 100 most cited articles are presented in *Table 1*. The number of article citations ranged from 240 to 33 (mean 52.51, St Dev 31.06). Five articles had 100 or more citations.

Table 1. The top 10 most cited publications of Medical Journals based in Ireland.

Rank	Year	Authors & Institution	Title	Journal	Citations
1	2008	Aroori, S., Spence, R.A. Belfast Health and Social Care Trust, Northern Ireland	Carpal tunnel syndrome	Ulster Med J	240
2	1962	Johnston, G.W. Royal Victoria Hospital Belfast, Northern Ireland	A follow-up of one hundred cases of fracture of the head of the radius with a review of the literature	Ulster Med J	211
3	1958	O'Meara, R.A. Trinity College, Dublin, Republic of Ireland	Coagulative properties of cancers	Ir J Med Sci	133
4	1993	MacGowan, S.W., Sidhu, P., Aherne, T., Luke, D., Wood, A.E., Neligan, M.C., McGovern, E. Mater Misericordiae Hospital, Dublin, Republic of Ireland	Atrial myxoma: National incidence, diagnosis and surgical management	Ir J Med Sci	106
5	1954	Allison, R.S., Millar, J.H. Royal Victoria Hospital Belfast and Queens University Belfast, Northern Ireland	Prevalence of disseminated sclerosis in Northern Ireland	Ulster Med J	102
6	1994	O'Hare, J.A., Abuaisha, F., Geoghegan, M. Limerick Regional Hospital, Dooradoyle, Republic of Ireland	Prevalence and forms of neuropathic morbidity in 800 diabetics	Ir J Med Sci	98
7	2011	Dinas, P.C., Koutedakis, Y., Flouris, A.D. University of Thessaly, Greece	Effects of exercise and physical activity on depression	Ir J Med Sci	91
8	2009	Stuckler, D., Basu, S., Suhrcke, M., McKee, M. Oxford University, England	The health implications of financial crisis: A review of the evidence	Ulster Med J	84
9	1990	Ritchie, C.M., Atkinson, A.B., Kennedy, A.L., Lyons, A.R., Gordon, D.S., Fannin, T., Hadden, D.R. Royal Victoria Hospital Belfast, Northern Ireland	Ascertainment and natural history of treated acromegaly in Northern Ireland	Ulster Med J	80
10	2006	Lappin, T.R., Grier, D.G., Thompson, A., Halliday, H.L. Queen's University Belfast, Royal Maternity Hospital Belfast, Northern Ireland	HOX genes: Seductive science, mysterious mechanisms	Ulster Med J	77

The years of publication ranged from 1944 to 2014. The year with the most publications was 2000, which had eight. The 2000s was the decade with the most top 100 publications, numbering 42. The number of authors ranged from 1-10 (mean 3.68, St Dev 2.03). The most frequent number of authors was two, found in 20 articles.
The mean number of authors per article has increased over time; in the 1960s the mean was 1.0, in the 1980s it was 2.4 and in the 2000s it had further increased to 4.4 (p=0.001).

Sixty-nine of the articles were from a single Irish institution, including both the Republic of Ireland and Northern Ireland. Twenty-two of the publications were collaborations involving multiple Irish institutions. Nine articles involved only non-Irish institutions. The Irish Journal of Medical Science published 44 of the top 100 articles, followed by the

Irish Medical Journal with 29 articles, the Ulster Medical Journal with 21 articles and the Irish Journal of Psychological Medicine with six articles. The hospitals with most publications were the Mater Misericordiae Hospital and St. James Hospital, each with 11 publications. The fields of medicine that were represented most frequently were general medicine (16 articles), public health and epidemiology (15 articles), psychology (10 articles) and general surgery (9 articles).

Discussion

This study seeks to identify the most impactful articles in the Irish medical literature. Ireland has a strong history of medical research. Both the Republic of Ireland and Northern Ireland have previously been ranked in the top 20 countries for citations per paper[9] and Ireland has been shown to have one of the highest mean impact factors for surgical publications[10]. Previous bibliometric studies have focused on Ireland's output in a specific medical field, for example in orthopaedic surgery, plastic surgery or radiology[11-13]. These do not adequately demonstrate the broad scope of the multiple medical and surgical specialties published in Ireland. A wide range of topics and medical disciplines are represented among the top 100 most cited articles. General Medicine and Public Health and Epidemiology were the most represented specialties, perhaps unsurprising given the large scope of these fields.

It is striking to observe that a majority, sixty-nine articles (69%), involved single institutions with no collaboration. This may relate to a low rate of completion of collaborative between institutions. For a small country such as Ireland, there would be potential benefits to establishing programmes for formal collaborative research[13,14]. We found nine of the articles were affiliated with non-Irish institutions. As well as increasing collaboration among Irish institutions, collaborations with international institutions could be potentially advantageous.

Over time, the average number of authors per article has increased. This increase has been reflected across the medical literature, with previous studies demonstrating that between 1960-2010 the average authorship increased more than three-fold[15]. This authorship inflation does not appear related to the complexity of the studies; rather, it has been suggested to relate to pressures on funding and promotion[15]. There are ongoing challenges to research in Ireland, including long working hours, limited research funding and limited protected time for research. Aspiring clinicians should take inspiration from researchers who have shown that it is possible to publish highly respected and highly cited work in Ireland.

This study has certain limitations. It does not include articles from Irish authors published in journals based outside of Ireland; however this was not the focus of our research. We made the assumption that articles with higher citations are considered more influential[4], although some older influential articles have been incorporated into common knowledge and therefore are no longer as frequently cited.

In conclusion, medical journals based in Ireland have published many highly cited articles, some of which have over 100 citations. The characteristics and trends of these citation classics will be useful to inform and guide future research.

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The authors declare that they have no conflict of interest.

Corresponding Author:
Dr. Simon M. Clifford
Department of Radiology,
St. Vincent's University Hospital,
Dublin 4,
Ireland.
Email: simonclifford@rcsi.ie

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Airborne Transmission of Covid-19: Implications for Irish Hospitals

H. Humphreys[1,2], F. Fitzpatrick[1,2]

1. Department of Clinical Microbiology, the Royal College of Surgeons in Ireland, Dublin, Ireland.
2. Department of Microbiology, Beaumont Hospital, Dublin, Ireland.

The pandemic spread of COVID-19 raises many questions about its transmissibility. The initial consensus was that spread was primarily by contact with a contaminated surface and by inhalation of droplets. However, airborne transmission is increasingly considered probable. Clarifying COVID-19 transmission is crucial for effective infection prevention and control (IPC) and healthcare worker (HCW) protection.[1] SARS-C0V-2 is more transmissible than influenza, with a mean reproductive number of 2.65, even if not as high as other viruses such as measles.[2] Personal protective equipment (PPE) shortages, IPC lapses, workload intensity and other factors not yet known, may explain significant hospital transmission during the early stages of the pandemic in Ireland and elsewhere.

It is increasingly clear that SARS-CoV-2 can persist in the environment. Under experimental conditions, SARS-CoV-2 remained viable in aerosols for three hours.[3] While these data must be interpreted cautiously in a healthcare context, it is possible that this virus is more persistent than we think and can spread further than by droplets.

In Hong Kong, a number of measures, including isolation in airborne infection isolation rooms (AIIR) were used in caring for confirmed cases of COVID-19, and transmission to patients or to HCW, including following unprotected exposure, was not observed.[4] In Wuhan, SARS-CoV-2 was detected in 14/40 (35%) air samples, and they estimated that the maximum transmission distance might be up to 4m.[5] Liu and colleagues found SARS-Cov-2 containing aerosols of 0.25-1.0u in patient, physician and public areas, and suggest that these are capable of re-suspension from surfaces.[6]

To implement IPC measures, it is easier to classify transmission in the air as either droplet (short range) or airborne (long-range) transmission, even if it may not be as simple as this. Conventional opinion suggest that droplets spread influenza. However, after an investigation of a hospital outbreak, it was concluded that aerosol transmission was possible arising from air flowing from the clinical area of the index patient to areas where other patients acquired influenza.[7] Teller and colleagues suggest that influenza may be transmitted by the airborne route and this may lead to more severe illness.[8]

Many factors are likely to be involved in the transmissibility of SARS-CoV-2, including the stage of illness and the likely viral load, possible differing susceptibilities to infection amongst contacts of cases, airflows, and surfaces,

which vary in their capacity to support viral persistence. However, it seems likely that transmission may include both droplets and aerosols. Full PPE (including respirators or equivalent masks) is required during aerosol generating procedures (AGP). However, it seems biologically plausible that a symptomatic patient may disseminate via both means during coughing, sneezing and even talking. If so, that has implications for IPC practises and for hospital infrastructure.

Some now argue strongly that the transmission of SARS-CoV-2 includes aerosols that may travel 2m or more.[9-12] This is based on experimental and observational data as well as mathematical modelling. Droplets (>5μm) may spread further than many believe, with the distance being influenced by relative humidity, temperature and particulate matter.[10,11]

The inference is that AIIR facilities and full PPE may be required for more patients with COVID-19 than just those during AGP. We also need to consider more the direction of airflows where there are multi-patient facilities, e.g. ward bays, to minimise spread.

After the epidemic of severe acute respiratory syndrome (SARS) due to SARS-CoV-1 in 2003, many countries reviewed their capacity to control epidemics and potential pandemics. In Hong Kong, the government insisted on a minimum distance between beds and the provision of more than 1,400 isolation rooms with negative pressure ventilation in public hospitals.[13] This may partly explain why some Asian countries with prior experience of managing SARS, such as Hong Kong and Singapore, appear to have coped better with this pandemic than countries largely unaffected by SARS.

In Ireland, the Health Information and Quality Authority have published standards for IPC in acute hospitals.[14] However, implementation of best practice IPC is challenging because of sub-optimal infrastructure in many hospitals. In 2009 an expert group recommended that newly built hospital in-patient accommodation should comprise 100% single-patient rooms, existing multiple bedded rooms contain no more than three beds, and that there be at least one AIIR per 150 acute inpatient beds with double that for regional or tertiary referral hospitals.[15] However, little progress was made in implementing these recommendations since then. In a 2011-2012 European hospital study, the country median proportion of single-bed rooms was 24.2%, with Irish hospitals reporting between 10-20%.[16] Of 60 Irish acute hospitals surveyed in May 2017, the average proportion of single patient rooms in public hospitals ranged from 15% to 29% with 52% in private hospitals. The majority (76%) of single rooms were reported to have en suite facilities, however, there were only 1.8 AIIR per 100 beds.[17]

The recent pandemic underscores the need for more single rooms with AIIR capacity in acute hospitals to facilitate appropriate patient placement and to prevent cross-infection. While natural ventilation probably suffices for most patients in hospitals, we need to learn from recent evidence, plan for the future, and improve the environmental conditions for all in acute hospitals. This will help control the next pandemic, reduce nosocomial and HCW acquisition, and better prevent more common infections such as seasonal influenza.

Key words:
SARS-CoV-2, COVID-19, transmission, airborne, droplet

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Corresponding Author:
Prof Hilary Humphreys
Department of Clinical Microbiology,
RCSI Education and Research Centre,
Smurfit Building,
Beaumont Hospital,
Dublin D09 YD60,
Ireland.
Email: hhumphreys@rcsi.ie

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Virtual Clinics in the Covid-19 Pandemic

R. Elhassan, F. Sharif, T.I. Yousif

Paediatrics department, Midlands Regional Hospital, Mullingar, Co. Westmeath.

Introduction

The Covid-19 pandemic crisis has posed great challenges to the health care services worldwide. This crisis necessitated the diversion of all efforts towards providing emergency care to those affected by the disease[1]. The result of this was cancellation of many out-patient clinics and elective services[1]. However, the growing demand for accessing specialized medical advice for non-Covid patients and the urge to enable continuation of patient's care stimulated looking for other feasible alternatives that can be used during this crisis.

Telehealth is defined as the entire spectrum of activities used to deliver care remotely, without direct physical contact with the patient[2]. It could be either provider-to patient or provider-to-provider communications. Telehealth can take place synchronously (telephone and video), asynchronously (patient portal messages, e-consults), and through virtual agents (chatbox) and wearable devices[2]. Tele-health has been utilised to support access to specialized medical advice in remote areas in many countries all over the world. The advantages of Telehealth include cost effectiveness, increased capacity, and improvement in quality of care provided to patients[3]. Virtual appointments were found to reduce the waiting times for consultation between appointments[4]. Use of virtual consultations improved patients' satisfaction and reduced the need for additional tests and investigations[5]. Safety, convenience and effectiveness of virtual clinics (VC) have been reported[6].

Key elements of a VC used include the use of mobile communication devices, mobile health (M-health), videoconferencing (V-health), and communication with patients in an integrated manner, combined with additional online tools to improve accessibility and quality of care[3]. But for this virtual option to operate efficiently, appropriate selection of patients, significant service reorganization and provision of logistical support are important prerequisites[5]. There are still some complex challenges to establish wide virtual consultation services within different routine practices in many sectors[6].

Table 1: Showing requirements, opportunities and limitations of some V.C Platforms. (adapted from wosik et al[2])

Platform	Technology requirements	Opportunities	Limitations
Patient-initiated texting	• High-Tech infrastructure	• Handling clear issues	• Needs staffing • Potential lack of context • No physical exam
Phone calls	• Minimum	• Universally accessible • Cost- effective Easy & quick	• No physical exam
Videoconferencing	• Moderate, Requires WiFi connection, a smart device with good camera and a microphone	• Allows visible inspection • Allows for non-verbal cues	• Could be time consuming and costly
Tele-health Software	• Complex	• Confidential • Allows visual inspection	• Time and high Tech required, Cost
Video-Visit (e.g. for in patients during Covid)	• Complex • Requires Wi-Fi connection, a smart device with good camera and a microphone	• Allows visual and verbal consultation	• May need digital peripherals, e.g Stethoscope. • Needs Infection control re: devices used

Example of Telehealth Platforms - Attendanywhere[R]

Attendanywhere[R] is a platform used to connect clinicians and patients using video. It only requires both patient and healthcare provider to access a smart phone or computer with a webcam and have a good internet connection and a private, well lit area to allow uninterrupted consultation.

How it Works

Initially the patient agrees to have their appointment via video. Patients/carers will receive a letter and/or a text message with the link to the virtual waiting room on the website for their appointments. On the day and time of the appointment, patients/carers log to the site through the link. At the start, they will be asked to confirm name, date of birth and contact phone number. The healthcare provider will see them arrive and they will join them in the video room for the consultation. At the end of the appointment, the healthcare provider will disconnect the call and the web page will close. Dictation will be done as usual.

Worldwide Experiences of Virtual Clinics

Advances with internet offered a great opportunity to improve communication at a distance. Telemedicine using videoconferencing allowed valuable direct interaction, but asynchronous telemedicine using e-mail or Websites was considered a cheaper and much more flexible in both time and place[7]. Telemedicine has been used successfully in dermatology consultations avoiding long waiting times for a dermatologist opinion in out-patient clinics when referred by GPs[7]. A study involving two hospitals in London and Shrewsbury and 29 general practices in inner London and Wales showed that conducting virtual outreach clinics was associated with reduced costs to patients and lower losses in productivity compared with conventional outpatients' clinics. However; the costs of virtual outreach consultation was greater for the NHS than the conventional clinics[8]. In Australia telemedicine has been used widely in health care. Since 1996 Tele-health services have been growing steadily, and in 2002 there were over 30,000 Tele-radiology transmissions and 1250 clinical occasions of service via videoconference[9]. Appropriately targeted video consultations have improved the delivery of primary health care in Australia, particularly in rural and remote regions[10]. The same result was noticed in India, where V.Cs are considered a new concept, V.Cs show promise and seem to be of great benefit especially in rural areas where access to specialized medical advice can be difficult[11]. In paediatrics, a Dutch RCT study showed that implementing frequent virtual Asthma clinic improved asthma control and increased symptoms-free days significantly when compared with conventional outpatients' clinics[12]. In Irish setting, using a physician assisted video OPD consultations for some patients who underwent low-risk surgical procedures was proved to be helpful with potential to reduce already increasing pressure on stretched surgical OPD[13].

Examples of Virtual Clinics during the Covid-19 Pandemic

In the US the Covid-19 crisis has presented healthcare service delivery system with hard challenges. To overcome this tough situation rapid adoption of Telehealth was pursued to enable providing health service at a distance. Telehealth has played a vital role in transforming healthcare delivery during the three phases of the US Covid-19 pandemic; Stay-at-Home Outpatient Care, initial Covid-19 Hospital Surge, and post-Pandemic Recovery[2]. Use of telemedicine proved helpful in sustaining the continuity of outpatient care during the pandemic keeping in pace with the Stay at Home orders and physical distancing measures, while limiting community and nosocomial spread[2]. E-consults, remote patient monitoring, telephone calls, video calls and messaging systems have all been used efficiently in triaging and managing patients through the pandemic[2]. These methods have been of great help in reducing the need for face to face interactions[2]. Furthermore, telemedicine proved to be of great benefit not only in outpatient settings but also in inpatient settings reducing the need for PPEs and saving HCWs efforts[2].

Our Experience with V.C in the Covid-19 Pandemic

Virtual phone clinics were implemented in the paediatric department at the midlands regional Hospital, Mullingar at the start of the pandemic even before the regulations generated to minimize patients' risk of contracting Covid-19.

Previously scheduled outpatients' appointments before the pandemic were switched to V.C appointments in the same prescheduled dates. Patients/Carers were contacted and informed regarding date and time of the V.C appointments. They were asked to record the weight and height of the child and have it to hand during the V.C. The doctors in the clinic were asked to call the patients/carers after reviewing their charts. The phone calls start with clinicians identifying their names, purpose of the call, confirming identity of receiver of the call. Clinicians then proceed to take consent for pursuing the call as part of V.C procedure. Limitations of the VCs are then explained. The doctor would start taking relevant history and updates regarding the patient's condition. The weight and height of the child measured are taken and plotted on centile charts in patients' records. Although this needs to be interpreted with caution, it can give a fair idea of the child's growth status. Doctors then address any parents/carers concerns and formulate a plan of action which is discussed with the responsible consultant. This in turn is conveyed to parents/carers. Management plans can involve sending prescriptions by post, ordering investigations, referrals to other specialties or scheduling a ward review appointment where patients can be seen and examined when necessary. We have also used the V.C opportunity to give medical advice to parents /carers regarding keeping healthy during Covid-19 pandemic. While the phone call conversation model is considered accessible and relatively cheap, it also has the advantage of using minimal resources compared with more sophisticated telemedicine measures. However, phone calls based V.C model has the limitation of inability to examine patients and respond to patient's /carer's non-verbal cues.

Conclusion

V.Cs and telemedicine have been used in the past widely in different specialties and proved to be helpful and effective in reducing patients costs ,improving accessibility and reducing need for face to face interactions with HCWs in hospital settings .During the current pandemic of Covid-19, V.Cs have gained more focus. Despite some understandable limitations, V.Cs can represent a feasible alternative to conventional outpatients' clinics during this challenging time of Covid-19 pandemic. V.Cs when used appropriately can allow continuation of patient's care, improve accessibility and reduces the risk of nosocomial transmission.

Corresponding Author:
Dr. Taha I Y Hassan
Paediatric Consultant
Midlands Regional Hospital,
Mullingar,
Co. Westmeath.
Email: Drtaha2002@yahoo.com

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Treatment Modalities for Primary and Secondary Spinal Malignancies

L. Leddy[1], J.M. McDonnell[2], A.W. Phillips[2,3], D.P. Ahern[3,4], J.S. Butler[1,3]

1. School of Medicine, University College Dublin, Dublin, Ireland.
2. Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin, Ireland
3. National Spinal Injuries Unit, Department of Trauma & Orthopaedic Surgery, Mater Misericordiae University Hospital, Dublin, Ireland
4. School of Medicine, Trinity College Dublin, Dublin, Ireland

Introduction

Cancer of the spine is predominantly a metastatic disease as approximately 90% of spinal tumours represent a secondary malignancy. It is associated with an elderly demographic, with incidence rates projected to rise due to advanced treatment modalities for various pathologies[1]. Common primary cancers with bone metastasis to the vertebral column include; breast, lung, gastrointestinal, prostate and myeloma[1]. Treatment strategies for spinal tumours are rarely pan-applicable and must be devised on an individual basis. The purpose of this review is to discuss the individual and multimodal approaches employed in the management of spinal tumours.

Primary Cancers of the Spine

Primary musculoskeletal system sarcomas are ultimately rare in nature and are typically associated with a younger demographic[1]. Osteosarcomas, Ewing's sarcomas, and chondrosarcomas represent the most common primary cancers of the musculoskeletal system, and require multidisciplinary team input with biomechanical imbalance being a major concern.

Osteosarcoma is a high-grade malignant tumour with poor five-year survival rates of approximately 30%-40%[1]. It is characterised by the direct formation of immature bone or osteoid tissue by the tumour cells, and is classically considered a cancer of long bones and infrequently, soft tissue[3]. Ewing's sarcoma belongs to a family of tumours are characterised by chromosomal translocations of the EWS gene on chromosome 22. The cell of origin and the particular pathophysiology remains unclear to date[2]. Similarly, controversy exists regarding the first-line treatment and local management for Ewing's sarcoma of the spine[3]. Chondrosarcomas are a heterogenous group of malignant bone tumours which share the common attribute of chondroid matrix production[4]. Chondrosarcomas can develop de novo or undergo malignant transformation from a benign chondral lesion and can be managed using a variety of approaches[6]. To date, there is a lack of high-quality evidence-based guidance regarding chondrosarcomas treatment strategies due to their inherent rarity.

Several classification systems exist for spinal malignancies, such as; (i) The Enneking system (ii) The Tokuhashi Scoring System (iii) The Tomita Scoring System (iv) The Specialist Neoplastic Score (SNRS)[5]. Regardless of tumour classification and composition, treatment strategies are ultimately a collaborative interpretation of patient and prognostic factors, provided by staging and scoring systems aforementioned, which facilitates deduction of an optimal treatment strategy for each individual patient.

Haematologic Malignancies

Certain haematological malignancies such as plasmacytoma, myeloma, lymphoma can present in vertebrae. The majority of patients diagnosed with solitary bone plasmacytoma (SBP) will progress to develop multiple myeloma. Radical radiotherapy serves as the primary form of treatment[6]. Multiple solitary plasmacytomas may also be treated with radiotherapy (+/- autologous stem cell transplantation) in the absence of systemic disease due to their recurrent nature[8].

Regarding myeloma, first line therapy of the underlying malignancy entails systemic chemotherapy in combination with bisphosphonates and systemic/interventional pain control. In cases of spinal metastases, a variety of interventions may be employed such as; bracing, cement augmentation, radiotherapy, or surgery[7]. Orthotic brace application for a typical two-month period is the preferred form of conservative treatment for spinal instability due to multiple myeloma lesions. The benefits of conservative management is the aversion of potential surgical risks in addition to stabilisation of the vertebral column.

Regarding the management of lymphoma (follicular, MALT, mantle cell, diffuse large B-cell, Burkitt and peripheral T-cell), NICE guidelines suggest a variety of possible approaches to eradication, including; radiotherapy, immunotherapy, chemotherapy, immunochemotherapy and stem cell transplantation with no reference to a role for surgery[8,9]. Management is primarily non-operative, similar to above, with surgery reserved for cases which are refractory to these therapies.

Stereotactic Radiosurgery (SRS) and Intensity-Modulated Radiotherapy (IMRT)

Stereotactic Radiosurgery (SRS) and Intensity-Modulated Radiotherapy (IMRT) are precise measures of delivering radiation therapy in order to reduce injury to normal tissue. Such strategies allow for a non-invasive, highly specific method of efficacious treatment with a high local control rate and low complication rate[10]. SRS combines the principle of stereotactic localisation to achieve accurate targeting with multiple radiation beams of equal intensity to deliver a high dose of radiation to a treatment site while minimizing exposure to normal tissue. IMRT allows for modification of the intensity. It may be utilised as a first-line treatment or in combination to surgery to preoperatively reduce the resection margins[10]. This form of treatment is multidisciplinary in nature and entails extensive imaging of multiple views and modalities to accurately evaluate management strategies[10]. However, evidence for IMRT in the spine is limited, and is currently only employed as an alternative treatment should surgery be contraindicated[10].

Cement Augmentation, Kyphoplasty, Vertebroplasty

Balloon kyphoplasty (BKP) and Percutaneous Vertebroplasty (PV) aid in the management of pain and are also effective in restoring strength to the vertebral bodies[11]. Percutaneous vertebroplasty and kyphoplasty involves the percutaneous placement of one or two trocars into the vertebral bodies either via the pedicles or an extra-pedicular approach, followed by a fluoroscopic-guided injection of polymethyl methacrylate bone cement[12]. The cement stabilises the fracture and preserves spinal stability by providing anterior and middle column support[12]. Potential complications include cement embolus and neurologic dysfunction, albeit rare. Should anatomical defects exist, cement can leak into the intervertebral disc and result in subsequent fractures of other vertebral bodies[12].

Regarding kyphoplasty, the balloon is inflated prior to the injection of cement to restore the vertebral height and is reported to have a lower cement leakage rate[11,12]. BKP is predominantly implemented for back pain and fractures secondary to osteoporosis in addition to pathological vertebral fractures[11]. BKP requires extensive pre-procedural planning which includes; (i) careful clinical assessment to determine the site of pain, (ii) magnetic resonance imaging to evaluate areas of compression, and (iii) computed tomography to assess instability in combination with a SINS score[11].

Separation Surgery

Advances in modern surgical approaches to the spine can ensure circumferential cord decompression when required. Separation surgery is a technique whereby a posterolateral approach is utilised to obtain ventrolateral access to nerve roots, posterior longitudinal ligament, and ventral epidural disease[13].

Rods are fixated postero-laterally and the tumour is then resected circumferentially to allow decompression. Partial vertebrectomy allows dissection of the ventral component of the tumour. Anterior support may be required if a large portion of the vertebral body is removed. Ultrasound can be used intraoperatively to ensure adequate separation.

The primary aim of separation surgery is to completely remove the tumour from the spinal cord to accommodate postoperative delivery of stereotactic radiosurgery (SRS) with maximisation of the biologically effective tumour dose[7]. SRS is often used as a first step in patients with epidural disease too advanced for radiotherapy, as previously mentioned. This combined approach is referred to as 'hybrid therapy'[7]. It merges both modalities, negating the need for aggressive resection and enabling the use of adjuvant radiotherapy.

Decompressive and Stabilization Surgery

Decompression, achieved via laminectomy, is indicated for rapid cord decompression and resolution of any neurological deficit[13]. Depending on tumour location, numerous different approaches can be adopted; (i) anterior (ii) strictly posterior (iii) posterolateral and, (iv) combined anteroposterior. All approaches are associated with an increase in ambulation (60% vs.98%) between pre-operative and post-operative measurements, in addition to significant pain relief reported in 95% of patients[14]. Posterior approaches represent the most commonly employed method as posterior laminectomies can enable multi-level vertebral decompression resulting in a more effective decompression and relief of symptoms[13]. For involvement of the cervical spine, an anterior approach is more frequently engaged. Controversy exists regarding the number of levels for fixation necessary to achieve adequate stability[14,15]. It is generally accepted that at least two levels of fixation above and two levels below the affected vertebrae is required in metastatic disease of the spine.

En Bloc Resection

En bloc resection, described by Tomita is the standard management of solitary spinal metastases confined within the vertebral body. The premise of the procedure is to ensure negative histologic margins[15]. However, multitudes of patients with spinal metastases often present late with multiple metastases, pathologic fractures, and/or cord compression. These patients are no longer candidates for en bloc resection. Thus, there has been a shifting paradigm away from such invasive surgeries as they no longer serve a primary form of treatment for the majority of patients with spinal malignancies[10,12]. Although the benefits of this surgery include better local control and superior functional outcome, it should be reserved for curative therapy as opposed to palliative[15].

Conclusion

Management of primary and secondary spinal malignancies remain a strategic challenge. No pan-applicable treatment approach exists for such pathological states. Surgery is indicated to optimise quality of life and is employed in scenarios of cord compression, vertebral instability and refractory pain. Methods include simple resection, decompressive surgery, radiosurgery, vertebroplasty and kyphoplasty, and radical en bloc resection. Such surgical strategies are incorporated into multi-modal approaches with systemic chemotherapy and targeted radiation to augment effect and ultimately reduce morbidity and mortality rates associated with spinal malignancies.

Declaration of Conflicts of Interest:
None declared.

Corresponding Author:
Jake McDonnell
Royal College of Surgeons in Ireland,
123 St. Stephen's Green, Dublin, Ireland.
Email: jakemcdonnell@rcsi.com

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Leukocyte Adhesion Deficiency Type 1 Due to Novel *ITGB2* Mutation

S. Harvey[1], M. Cremin[1], N. Conlon[2], M. Moore[1], R. Leahy[3], S. Felsenstein[1]

1. Department of Paediatrics, Cork University Hospital, Cork, Republic of Ireland.
2. Department of Immunology, St James' Hospital, Dublin, Republic of Ireland.
3. Department of Paediatric Infectious Diseases and Immunology, Our Lady's Children's Hospital Crumlin, Dublin, Republic of Ireland.

Abstract

Aim
Marked neutrophilia and omphalitis in an infant resulted in the diagnosis of the first case of leukocyte adhesion deficiency type 1 (LAD1) in Ireland.

Diagnosis
LAD1 requires specific molecular diagnostics for its correct identification.

Results
Early identification of this disorder allowed for rapid referral for haemotopoeitic stem cell transplant which has resulted in an excellent outcome for this patient.

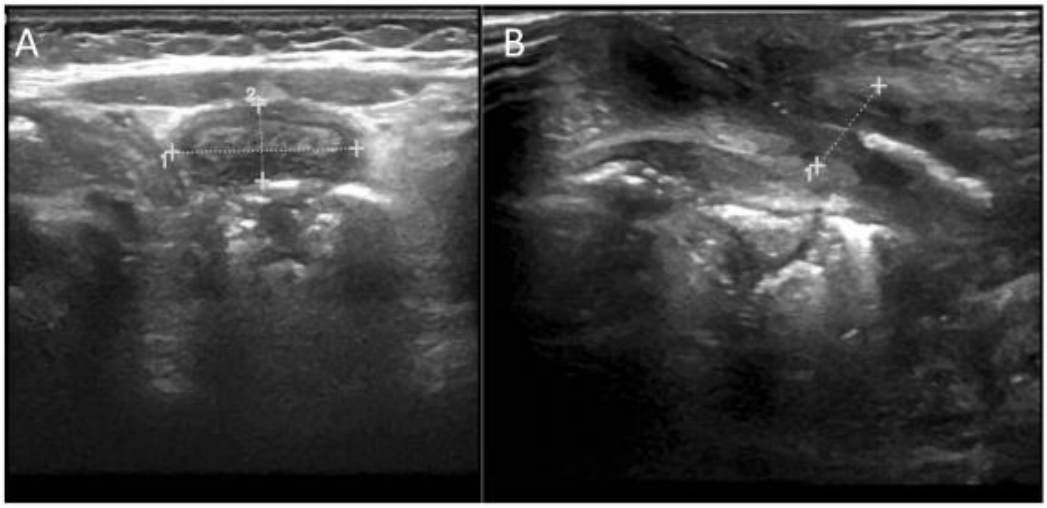
Conclusion
The identification of a previously unknown ITGB2 mutation resulting in LAD1 in Ireland should alert physicians to the diagnostic possibility of this extremely rare disorder.

Introduction

Leukocyte adhesion deficiency is a rare autosomal recessive disorder characterized by recurrent infections as a result of a defective homing response of neutrophils and macrophages. There are three subtypes, Leukocyte adhesion deficiency type 1 (LAD1) being the most common, with 334 cases reported to date[1].

Here, we present a novel *ITGB2* mutation resulting in a severe phenotype of LAD1, and the first reported case of LAD 1 in an Irish child. The patient is the second child to Irish parents. He presented at twenty-nine days of age with a respiratory tract infection and umbilical cellulitis was noted. He received Flucloxacillin intravenously for three days and was discharged on oral antibiotics thereafter. Notably, total white blood cell (TWBC) count was elevated at $52.6x10^9$/L, neutrophils $35.7x10^9$/L, lymphocytes $14.7x10^9$/L and C-reactive protein (CRP) 69.3mg/L (NR<5mg/L). Three weeks later he re-presented with ongoing periumbilical cellulitis and serous discharge. Repeat testing revealed TWBC of $61.5x10^9$/L with neutrophilia ($39.0x10^9$/L), and a CRP of 142mg/L. Abdominal ultrasound identified a 3.5cm long tract extending from the umbilical surface to subcutaneous umbilical tissues (Fig.1A). Surgical exploration revealed a superficial collection which grew pan-susceptible *E. coli*. Postoperative ultrasound showed a tubular structure, resembling an inflamed urachal remnant (Fig.1B).

Figure 1: Collection (dimensions 1x2x1cm) prior to incision and drainage (A); appearance of abdominal wall structures following surgical intervention (B). Note the tubular appearance of deep deated omphalitis extending beyond the abdominal wall structures.



Immunological evaluation was commenced and antibiotic cover was broadened to include piperacillin/tazobactam and fluconazole. Targeted history revealed delayed umbilical cord detachment at 21days of age. CD18 expression on leukocytes was less than 1% (<19 units) of expected, consistent with a diagnosis of a severe phenotype of LAD1. Following further investigation at the Immunology Laboratory at Great Ormond Street Children's Hospital London, he was found to be homozygous for a novel missense mutation in *ITGB2* (c.1034T>C)[5].

The patient completed a course of antibiotics resulting in resolution of the omphalitis and was subsequently commenced on co-trimoxazole and fluconazole prophylaxis before undergoing a fully matched, maternal peripheral blood stem cell transplant at age four and a half months. He had an uncomplicated transplant course, with neutrophil engraftment by day +18, and displays 100% donor chimerism at nine months post-transplant with no graft-versus-host disease.

Discussion

The primary defect in LAD1 lies in expression and function of the Integrin2 subunit-β, or CD18 antigen, which is encoded by *ITGB2* (21q22.3)[1;2] and belongs to the integrin family.

Four integrin-α subunits associate with CD18 to form heterodimers, LFA-1 (CD11a18), Mac-1/CR3 (CD11b18), alphadbeta2 (CD11d18) and p150,95 (CD11c18); expressed on neutrophils, lymphocytes, macrophages, and NK-cells. They are essential for adhesion to antigen-presenting and endothelial cells. Reduced or absent CD18 expression results in impaired homing of immune cells and their ability to extravasate[3]. Clinical presentation of LAD1 depends on the level of CD18 expression and residual function[3]. Patients with severe phenotype present in infancy with delayed umbilical cord separation and life-threatening infections characterized by excessive neutrophilia and lack of pus formation due to the inability of neutrophils to home to infection site, leave the blood stream and attend to tissue injury. The abdominal findings were interpreted in the context of an immune defect once the diagnosis had been established. Similar presentations should caution clinicians to consider LAD1 in neonates with omphalitis and neutrophilia[1].

To date, 323 cases of LAD 1 have been reported worldwide with a mutation identified in only 43% of patients[4]. There are currently 96 identified pathogenic mutations[1]. Our patient was homozygous for a novel, intronic single nucleotide substitution in position c.1034T>C, disease-causing by virtue of resulting in a missense variant and absent Integrin-β2 expression.

Without timely haematopoietic stem cell transplantion (HSCT), LAD1-associated mortality is substantial. However, for the 101 patients having undergone HSCT since 1993, event-free survival rate at 94 months was over 90%[4].

Both parents and the sister are heterozygous for the same mutation. All are healthy and asymptomatic. The parents have remote common ancestors on an island off the coast of the Irish Southwest, which may also serve as explanation for the maternal graft being a full match. The area was severely affected by the Great Irish Famine, as a result of which 1.5 million people emigrated, the vast majority to the United States. It would be of interest to pursue family ancestry should the same mutation be identified in a patient overseas. With our ever-expanding knowledge of genetics in rare conditions such as LAD1, reporting of ethnicity and ancestry in new cases may also allow for targeted genetic re-analysis in those for whom a mutation has not previously been identified.

This case serves as a reminder that frontline clinicians must retain a high index of suspicion for primary immune defects, as early identification and rapid intervention are critical in order to optimize patient outcomes.

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Declaration of Conflicts of Interest:
The authors declare no conflict of interest.

Corresponding Author:
Dr Susanna Felsenstein,
Consultant Paediatrician,
Cork University Hospital,
Wilton,
Cork,
Ireland.
Email: sfelsenstein@protonmail.com

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Quinolone-induced Biceps Tendon Rupture

R. Crawford[1], A. Gallagher[1], C. Devine[2], M. Mijares Zamuner[1]

1. Department of Medicine, Bon Secours Hospital, Glasnevin.
2. Pharmacy Department, Bon Secours Hospital, Glasnevin.

Abstract

Presentation

A 76-year-old man presented with acute left upper limb pain and subsequent large ecchymosis.

Diagnosis
An ultrasound study was performed which showed partial left biceps tendon rupture.

Treatment
He was managed conservatively with Orthopaedic input. The patient was given analgesia and reassured.

Discussion
Tendon rupture is an unusual but serious complication of quinolone exposure. This case highlights that this should be included in the differential for acute limb pain in patients who have been prescribed these drugs.

Introduction

Since being licensed for use in the 1980s, quinolones are frequently prescribed antimicrobials with good gram positive and gram-negative cover. Quinolone-induced tendinopathy is an uncommon adverse effect (affecting around 0.4% of patients overall) but can inflict permanently disabling injury on the patient[1]. In this article we report an unusual presentation of acute upper limb pain in a 76-year-old inpatient with multiple comorbidities; atraumatic biceps tendon rupture following exposure to quinolones.

Case Report

A 76-year-old gentleman was admitted to hospital for recurrence of an infective exacerbation of COPD and commenced a course of IV hydrocortisone and piperacillin-tazobactam. His medical history was significant for recurrent respiratory tract infections, chronic kidney disease, hypogammaglobulinaemia and type 2 diabetes mellitus.

The clinical course was initially uncomplicated. During admission, the patient woke from sleep with sudden onset 8/10 left upper limb pain. There was severe tenderness on palpation of the biceps with minimal surrounding oedema, and there was an absence of erythema or heat. This later evolved to a large ecchymosis extending beyond the biceps and involving the forearm (fig. 1).

Figure 1: Ecchymosis of the left upper arm

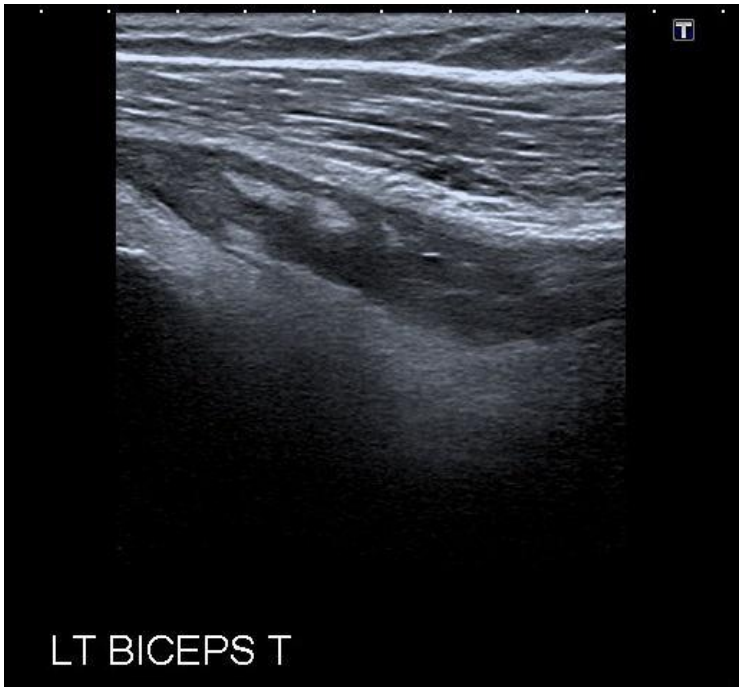

Figure 2: Ultrasound image of ruptured biceps tendon and haematoma.

Our differential diagnosis included an upper limb DVT, thrombophlebitis, cellulitis, infected haematoma and tendon rupture. An US Doppler ruled out a DVT, however a left upper limb haematoma was evident on this study. An ultrasound scan of the left upper limb soft tissues confirmed a biceps brachii tendon rupture (fig. 2). The patient was reviewed by orthopaedics who confirmed an incomplete tendon rupture and recommended conservative management given the patient's age and comorbidities. He was discharged home 10 days later.

Upon diagnosis of this man's atraumatic biceps tendon rupture, we noted that he had received at least six courses of quinolone antibiotics over the last few years, most recently 2 months prior to admission. Of note he had also received many concomitant courses of corticosteroids and had multiple comorbid conditions such as CKD and diabetes mellitus which have been implicated in tendon rupture.

Discussion

It is well established in the literature that quinolones cause tendon injury[2]. Through a variety of cellular mechanisms these agents have toxic and degenerating effects upon the collagen fibres within the tendons[3,4]. The Achilles tendon is known as the classical example however any tendon may be affected.

Multiple systematic reviews show that biceps tendons are not commonly affected by quinolone-associated tendinopathy[2]. However, a 2019 study by the British Society of Clinical Pharmacology looked at quinolone-induced tendinopathy tendon rupture over a 25-year period within the NHS database. It found quinolone-induced biceps tendon rupture accounted for 25% of overall cases[5]. A similar presentation featured in a BMJ case report earlier this year[6].

Gastrointestinal and neurological side-effects are more frequently reported[7]. Overall tendon injury with quinolones is less common affecting around 0.4% of patients exposed[1,3], however the risk is significantly increased for patients with renal impairment and concurrent steroid use[8].

As with the aforementioned clinical case, the patient is at risk of tendinopathy for some time after exposure to the drug. The risk is highest within the first month of exposure, but the risk continues for up to 6 months completing the course[1]. In 2019, the European Medicines Agency published an updated safety warning recommending use of quinolones to be restricted where possible[9]. For patients at high risk of tendinopathy an alternative choice of antimicrobial should be considered in line with local guidelines or following discussion with a clinical microbiologist.

In conclusion, tendinopathy although rare should be considered in the differential for acute onset musculoskeletal pain especially in at-risk groups who have been exposed to quinolones. Clinical suspicion should prompt urgent ultrasonography and orthopaedic input. Where possible use of quinolones should be restricted in patients at risk of adverse effects.

Patient Consent:
Consent received.

Declaration of Conflicts of Interest:
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Corresponding Author:
Ryan Crawford
Bon Secours Hospital,
Glasnevin Hill,
Glasnevin,
Dublin 9.
Email: rcrawford@bonsecours.ie

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Auto-Decompression - Preserved Neurological Function in Bilateral Cervical Facet Dislocations

T. Ó Doinn[1], A.J. Hughes[1], D.P. Ahern[1,2], J. McDonnell[3], E. Kavanagh[4], S. Morris[1], J.S. Butler[1,5]

1. National Spinal Injuries Unit, Department of Trauma & Orthopaedic Surgery, Mater Misericordiae University Hospital, Dublin, Ireland.
2. School of Medicine, Trinity College Dublin, Dublin, Ireland.
3. Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin, Ireland.
4. Radiology Department, Mater Misericordiae University Hospital, Dublin, Ireland.
5. School of Medicine and Medical Science, University College Dublin, Ireland

Abstract

Introduction
Bilateral cervical facet dislocation (BCFD) is an uncommon injury with a high incidence of severe neurological impairment. We describe 4 cases of BCFD with preserved neurological function.

Cases

Case 1: A 78-year-old female who suffered two ground level falls (GLFs). Pre-operative American Spinal Injury Association (ASIA) Score was C5D. Imaging revealed a BCFD at C6/C7 and a C6 laminar fracture.

Case 2: A 63-year-old male suffered a fall down 14 steps. Pre-operative ASIA score was E. Imaging demonstrated a BCFD at C7/T1, and a C6 laminar fracture.

Case 3: A 46-year-old male collided with a tree while descending a hill on a bicycle. Pre-operative ASIA score was C6D. Imaging revealed a BCFD at C7/T1 and a C7 laminar fracture.

Case 4: A 67-year-old male suffered a GLF while exiting a stationary car. Pre-operative ASIA score on admission was E. Imaging revealed a BCFD at C6/C7 with bilateral laminar fractures at C5 and C6.

Outcome
All cases underwent 2-stage surgical fixation. All cases maintained or had an improved ASIA score post-operatively.

Conclusion
In all cases, the presence of concurrent laminar fractures resulted in an auto-decompression of the spinal canal, preserving neurological function

Keywords: Cervical spine, spinal trauma, bilateral cervical facet dislocation, auto-decompression, spinal cord injury, ground level fall

Introduction

Cervical spine fractures account for 19% of all spinal fractures.[1] Of these fractures, bilateral cervical facet dislocation (BCFD) is a uncommon injury accounting for 4% of all acute traumatic cervical spine injuries[2] leading to significant mechanical instability, such as anterolisthesis.[3] This injury pattern typically affects young men in the subaxial region, most commonly at the level of C6/C7.[2-5] BCFDs commonly occur secondary to a high energy force with a hyperflexion component, with or without rotation.[2-5] These injuries typically follow road traffic or diving accidents.[2-4] Unfortunately, these injuries are associated with a high incidence of severe neurological disability [2-5], with the degree of anterior displacement correlating with degree of paralysis.[6]

From August 2018 to June 2019, four consecutive cases of BCFD with minimal or no neurological deficits were treated at the National Spinal Injuries Unit (NSIU) in the Republic of Ireland. These four cases are illustrated below.

Case Reports

Case 1

A 78-year-old woman with Parkinson's disease suffered two unwitnessed ground level falls (GLFs) over 48 hours. The first fall occurred while the patient was turning in the kitchen, which caused her to fall back and hit her head on a countertop. The second fall occurred a day later, while hanging clothes on a washing line. She reported losing balance, falling forward onto outstretched hands and hitting her head on the ground. The second fall precipitated cervical and upper thoracic pain. On reporting her symptoms to relatives 2 days later, an ambulance was called and she was brought to her local emergency department. On arrival, she reported mobilising independently for the previous 2 days and had no loss of consciousness. Her Glasgow Coma Score (GCS) was 14 and she had no neurological deficits. Full spinal precautions were applied, before transfer to the NSIU was arranged for definitive management. Neurological assessment on arrival revealed an American Spinal Injury Association (ASIA) Score of C5D with reduced sensation in a left sided C6 and C7 distribution.

Initial plain film radiographs failed to reveal any spinal injury. Computed tomography (CT) (Figure 1) and magnetic resonance imaging (MRI) demonstrated a BCFD with an Allen and Ferguson Stage 4 dislocation at the level of C6/C7. There was an associated C6 laminar fracture.

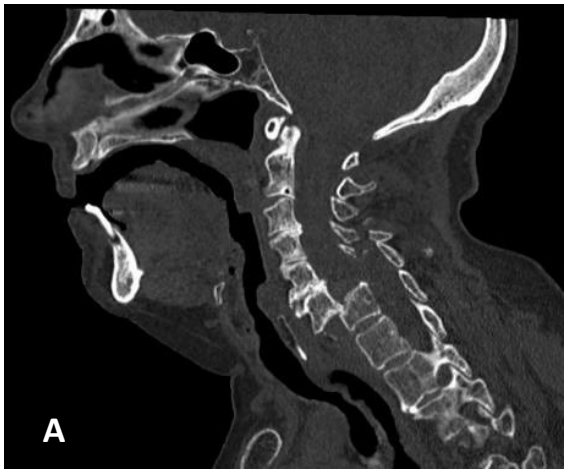

Figure 1: CT imaging for Case 1. A) Sagittal CT demonstrating a fracture-dislocation at C6/C7.

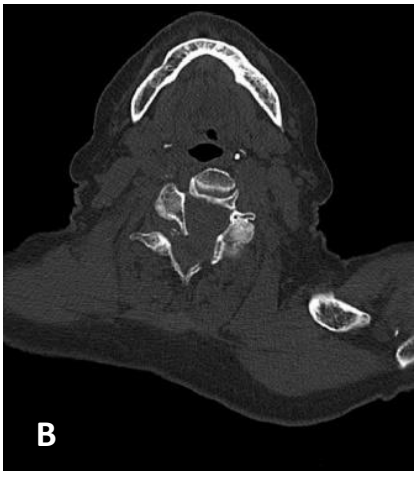

Figure 1: CT imaging for Case 1. B) Axial CT demonstrating overlapping posterior elements due to an associated laminar fracture, resulting in spinal canal enlargement at the site of potential cord compression.

Case 2

A 63-year-old man suffered an unwitnessed fall down approximately 14 steps secondary to alcohol intoxication. Following his fall he stood up independently, walked to his bed and fell asleep. On waking the following morning, he was unable to rise from bed secondary to severe neck pain. He was brought to his local emergency department by ambulance. On arrival he had a GCS of 15, lower cervical spine tenderness and a laceration to his forehead, but no neurological deficits. He was transferred to the NSIU for operative management. Pre- operative examination confirmed no neurological compromise (ASIA E).

Plain film radiographs on presentation yielded inadequate views of the cervical spine. A swimmer's view highlighted discontinuity in the anterior spinal line. Subsequent CT and MRI imaging demonstrated an Allen and Ferguson Stage 4 dislocation at C7/T1. There was significant disruption of the discoligamentous complex with tearing of the anterior and posterior longitudinal ligaments, disc substance, ligamentum flavum and facet joint capsule. There was a concurrent laminar fracture of C6 and spinous process fractures of C6 and C7. The spinal cord was shown to be acutely deviated, however, there was no spinal cord compression.

Case 3

A 46-year-old man lost control of his bicycle while descending a hill at high speed (~50 kph). He collided with a tree with the vertex of his head before falling from his bicycle. He was wearing a helmet and his bike sustained significant damage. He stood up independently and reported an immediate feeling of cervical instability, with neck and interscapular back pain. There was no reported loss of consciousness. He was brought by ambulance to a local emergency department. Initial clinical examinations demonstrated a GCS of 15 and no neurological deficits. He was transferred to our institution for operative management. His neurological injury was classified as C6 ASIA D secondary to decreased sensation in a left sided C7 and C8 distribution.

A CT scan, following non-diagnostic plan film radiographs in an outside institution, and subsequent MRI demonstrated an Allen and Ferguson Stage 3 dislocation at C7/T1, superior endplate fracture of T1 and spinous process fractures of C5-7. There was also a concurrent C7 laminar fracture with a traumatic dural tear, but no identifiable spinal cord injury.

Case 4

A 67-year-old male lost his balance while exiting a stationary car, secondary to alcohol intoxication. He fell forward and struck the frontal aspect of his head on an adjacent concrete windowsill. He denied any loss of consciousness. Following his fall, he continued to mobilise independently and work as a bus driver for a subsequent 17 days before presenting to his General Practitioner (GP) with a new onset of paresthesia in his left second digit. A collateral history from his daughter revealed that he had been mobilising and carrying out activities of daily living in a position of maintained cervical spine flexion. Following examination by his GP, he was transferred by ambulance to a local emergency department. Emergency department examinations revealed a GCS of 15 and no neurological deficits. He was transferred to the NSIU for definitive management. His pre-operative ASIA score was ASIA E.

Plain film radiographs failed to reveal any significant spinal injury. Focused CT and MRI demonstrated a high grade anterolisthesis at C6/C7 with concurrent bilateral laminar fractures at C5 and C6. MRI delineated an acutely deviated course of the spinal cord through the zone of injury, with no evidence of cord oedema. Additional injuries included a burst fracture of the vertebral body of C7, anterior wedge compression fractures at T1 and superior endplate fractures at T2-3. Ligamentous injuries included posterior longitudinal ligament and ligamentum flavum disruption at C6-7.

Results

All cases underwent closed cervical traction and reduction on admission to the NSIU (Figure 2). This was followed by definitive surgical fixation using an anterior and posterior approach (Figure 3). Case 1 and Case 3 had an improved

post-operative ASIA score. ASIA scores for Case 2 and Case 4 did not deteriorate post-operatively. Results are summarised in Table 1.

Figure 2. Lateral plain film cervical spine radiographs for Case 1 with closed cervical traction in situ. Traction magnitude increases from left to right, with progressive reduction of the dislocation.

Figure 3. Post- operative plain film radiographs for Case 1 following C6-T1 ACDF and C4-T2 PCDF.

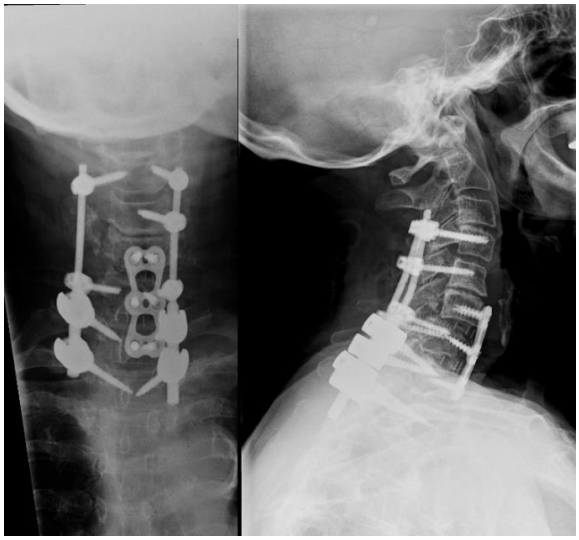

Table 1. Case Series Summary

Case	Sex	Age	Mechanism	Level of BCFD	Pre-op ASIA	Operation (1^{st}/2^{nd} Stage)	Post-op ASIA
1	F	78	GLF	C6/C7	C5 D	C6-T1 ACDF/ C4-T2 PCDF	E
2	M	63	High Energy Trauma	C7/T1	E	C6-T1 ACDF/ C5-T2 PCDF	E
3	M	46	High Energy Trauma	C7/T1	C6 D	C4-T3 PCDF/ C7/T1 ACDF	C8 D
4	M	67	GLF	C6/C7	E	C7 Corpectomy, C6-T1 Anterior Fusion/ C5-T2 Posterior Fixation	E

Abbreviations: BCFD, Bilateral Cervical Facet Dislocation; GLF, Ground Level Fall; ACDF, Anterior Cervical Discectomy and Fusion; PCDF, Posterior Cervical Decompression and Fusion.

Discussion

The cervical spine is the most vulnerable portion of the spine to be injured during trauma, with the cervical spinal cord accounting for 75% of cases of traumatic spinal cord injury (SCI).[7] BCFD typically results in major spinal cord injury due to significant encroachment of the spinal canal. This occurs as the inferior articular facet of the superior vertebrae displaces over the superior facet of the subadjacent vertebrae causing dynamic spinal canal narrowing and resultant cord compression.[8] Previous studies describing BCFD, with or without fractures, have demonstrated that between 52-87% have complete neurological impairment below the affected level.[2, 4, 5, 9] Previously, a limited number of single patient case reports have described BCFDs of the cervical spine with minimal or no neurological deficits.[10-13] In each of these reports there was concurrent posterior element fractures, which was postulated to functionally enlarge the spinal canal preventing SCI. In all four cases presented here, the spinal cord was significantly displaced due to anterolisthesis of the segments at the level of the fracture-dislocation. Despite this displacement, fracture of the posterior elements allowed the spinal canal to be auto-decompressed without any significant SCI.

Weingardt and Rogers[9] specifically addressed the hypothesis that posterior element fractures at the level of a BCFD could auto-decompress the spinal canal, circumventing spinal cord injury. In their cohort no significant correlation was demonstrated between neurological outcomes and associated posterior element fractures during BCFD. However, the cases examined in their retrospective study predated the widespread use of MRI. Additionally, CT was available for less than half of the cases included. Future research should address the correlation between posterior element fractures identified using modern imaging protocols and neurological outcomes in BCFD.

All of our patients underwent cervical spine radiographs during their initial assessment. In each case, these failed to reveal any significant pathology due to inadequate visualisation related to overlying soft tissue shadowing. BCFDs were only revealed on subsequent CT imaging. The poor diagnostic accuracy of radiographs and their poor correlation with CT imaging in the setting of cervical spine trauma is previously well documented.[14-16] Given the catastrophic consequences of missing a cervical spine injury, clinicians should maintain a high index of suspicion of cervical spine insult despite the absence of neurological deficits and identifiable injury on radiographs, in the setting of trauma.

All patients had an uneventful post-operative recovery. Additionally, each of the two patients who had an incomplete spinal cord injury demonstrated an improved post-operative ASIA score. The management of cervical fracture-dislocations at our institution follows a standardised approach, with cervical traction and closed reduction over 24 hours. This is followed by definitive surgical fixation via a two- stage procedure using an anterior and posterior approach. The use of early cervical traction in cervical fracture-dislocations to reduce the injury and decompress the spinal cord, prior to definitive surgical fixation has been demonstrated to be a safe and effective method to achieve closed reduction and improve neurological outcomes[17]. Additionally, a recent systematic review demonstrated that earlier surgical fixation may reduce the incidence of post-operative complications and improve neurological recovery following traumatic spinal fractures[18].

Finally, it is well established that BCFDs most commonly occur secondary to high energy trauma among young males.[2-4]However, the incidence of cervical fractures following ground level falls (GLFs) among the geriatric population is significantly increasing[19]. When specifically examining BCFDs among geriatric patients, Lieberman and Webb[20] demonstrated that 66% of their cohort sustained these injuries following falls in the home. Interestingly, both geriatric patients in this case series (Case 1 and 4) sustained their injuries following a GLF. Despite this innocuous injury mechanism, geriatric patients who sustain cervical spine fractures following GLFs demonstrate relatively high 30-day mortality (13-28%) and readmission rates (31-50%) and have a high rate of dependent discharge (53-55%)[21]. Furthermore, care of the geriatric trauma patient is associated with significantly higher costs[22]. These poorer outcomes and associated costs have significant resource implications, particularly regarding management and preventative strategies. Previously, Matsushima et al.[23] has demonstrated improved outcomes among trauma centres treating a higher volume of geriatric trauma patients. Furthermore, fall prevention interventions can significantly reduce the incidence of GLFs in older adults[24], which may circumvent their associated morbidity and mortality.

In conclusion, these cases illustrate that BCFDs can have a varied mechanism of injury, present within a heterogeneous patient cohort and disclose themselves emergently after relatively benign emergency department presentations. In all cases, the presence of concurrent laminar fractures resulted in an auto-decompression of the spinal canal. Such fracture characteristics and spinal canal enlargement at the zone of injury created space posteriorly for the spinal cord to manoeuvre, preserving neurological function. These findings demonstrate the need to maintain a high index of suspicion for unstable cervical spine injuries following trauma despite the absence of significant neurological deficits.

Declaration of Conflicts of Interest:
The authors have no conflict of interest to declare.

Corresponding Author:
Dr. Tiarnán Ó Doinn
National Spinal Injuries Unit,
Mater Misericordiae University Hospital,
Eccles Street,
Dublin 1,
Ireland.
Email: tiarnanodoinn@rcsi.com

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Enhanced Carbapenemase Producing Enterobacterales (CPE) Screening in a Paediatric Population

D. Broderick[1], C. McNicholas[2], R.J. Drew[3]

1. Department of Microbiology, Children's Health Ireland at Temple Street Children's University Hospital.
2. Department of Infection Control, Children's Health Ireland at Temple Street Children's University Hospital.
3. Department of Microbiology, Children's Health Ireland at Temple Street Children's University Hospital.

Abstract

Aims
The aim of this period of extended screening (to include those being readmitted to TSCUH if they had been an inpatient in the preceding year) was to determine whether any additional CPE positive patients were identified.

Methods
Education was given to Clinical Nurse Managers regarding those requiring screening and reinforced at daily handover meetings.

Results
917 patients were screened during the four-month period; only two positive patients were identified, who would have been screened under the previous local guidelines.

Conclusion
The screening of an additional 314 patients (34% increase compared with the same period in the previous year) yielded no positive results, showing that patients whose only risk factor was admission to TSCUH within the previous year do not currently require screening.

Introduction

CPE are becoming increasingly widespread in Ireland and screening is essential in preventing spread. Various national and international guidelines have addressed appropriate cohorts for screening, informing national policies.[1,2,3,4,5] Introduction and acquisition of multi-drug resistant organisms is a rising concern in Irish healthcare, with 280 cases of CPE seen in 2016.[6] Screening is an integral part of their control, but requires input from nursing staff, laboratory scientists, the Infection Prevention and Control Team and Information Technology support. HSE guidelines published in March 2018 'Guidelines for the Prevention and Control of Multi-drug resistant organisms (MDRO) excluding MRSA in the healthcare setting' detailed groups recommended to undergo CPE screening; this included screening patients on readmission to the same institution if they had been admitted in the previous year.

Other international guidelines include those from the Australian Committee for Quality and Safety in Healthcare and the CPE toolkit (Public Health England), neither of which recommends screening patients on readmission.

Based on the low incidence of CPE in the CHI@TSCUH population, with no acquisitions since the introduction of screening in July 2017, it was decided to evaluate the additional yield of screening re-admissions in addition to others.

Methods

CPE testing was performed on rectal swabs or stool samples. These were cultured on chromogenic agar (CHROMagar™ mSuperCarba™, manufactured by CHROMagar France) and any suspicious isolates underwent further testing using the Xpert Carba-R PCR (Cepheid, USA) testing to determine the presence of the most common target carbapenem resistance genes. Any concerning isolates were also identified to clarify if carbapenem resistance may be an inherent characteristic of the organism or is mediated via mechanisms other than carbapenemase genes. This was done using the VITEK®2 system. Isolates suspicious for carbapenemase production were beaded, sloped and sent to the National CPE Reference Laboratory for confirmation, with further elucidation of the resistance mechanism if necessary.

Results

During the period from October 2018 to March 2019, 917 screening samples were tested; compared to 603 from October 2017 to March 2018 (34% increase), giving an approximate estimation of the increased testing– i.e. the cohort of patients being readmitted to CHI@TSCUH who were admitted in the previous year. There were no other changes to the CPE screening policy during that time. Testing for the period October 2018- March 2019 detected two carbapenemase producing organisms – both *E.coli* carrying OXA-181, a variant of OXA-48. These patients were related and had a history of healthcare contact in an area of high endemnicity; they would have been tested as per the pre-existing local guidelines and were not solely detected due to the increased screening.

Discussion

This period of enhanced screening did not identify any additional CPE, and the 34% increase in screening had implications in terms of both cost and scientist/nursing time. Information relating to epidemiology and risk factors for CPE in the paediatric population is scarce[7] and knowledge is largely based on case reports, case series and one systematic review. Globally resistance rates to meropenem in paediatric populations are as high as 4.4%.[8] The most recent Irish CPE screening guidelines state: 'More limited screening for CPE may be justified where a documented local risk assessment by the IPC team indicates that the risk of CPE colonisation is very low and there is no evidence of CPE transmission in the hospital. Any such risk assessment should be reviewed at least annually'.[9] Our findings may be replicated in other low-risk settings, e.g. other paediatric and maternity services. However, applicability needs to be assessed in the context of local CPE prevalence and patient complexity. CHI@TSCUH does not have patients with an oncological background, for example, who would often have a large burden of antimicrobial exposure, a known risk factor for CPE acquisition. Screening those whose only risk factor was admission to CHI@TSCUH within the previous year did not yield any positive results and therefore we intend to exclude this group of patients from CPE screening, supported by our local risk assessment and the most recent national guidelines.

Declaration of Conflicts of Interest:

The Authors declare that there is no conflict of interest.

Corresponding Author:
Deirdre Broderick
Department of Microbiology,
Children's Health Ireland at
Temple Street Children's University Hospital.
Email: DeBroderick@stjames.ie

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Poem

Coronavirus (Covid-19) - In Praise of the Medical Army

Tell us … about the doctors….
and watch the faithful army.
Fighting a battle… never fought before,
What a formidable enemy, an unseen adversary!
Tell us more…
Tell us about loyalty…
to their cause … honesty and fidelity.
…about a dutiful team, and the lovely theme,
brought to the fore…
No sword in hands but faith in hearts,
Faith is refuge… Faith is shield indeed.
Watch the greatest deed.
Accept the good .. Accept the bad…
with aplomb … and equanimity.
One word they know, shall never creep
into their souls: pusillanimity.
Fortitude in battle, and in fight audacity..
with peace in mind and hope in life..
they show no fear…but all the tenacity.
Astonishing feat…. and at your feet,
vanity is laid ….and rapacity.
You give your hearts so we can live,
in self- denial … What a gallantry..!
With your will…your missions begin,
Keep your golden knowledge in.
Physicians deserve… all the praise..
to them we pay… sincere adulation..
wrapped in love….with commendation.

Author Details:
Zakaria Barsoum
Department of Paediatrics
South West Acute Hospital
Enniskillen
Northern Ireland
Email: Zakaria.barsoum@westerntrust.hscni.net

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Obituary

Sir Peter Froggatt FSS FRCPI FRCP FFOM

(12 June 1928 - 3 May 2020)

It is with great sadness that one of Ireland's foremost medical figures and former President/Vice-Chancellor of Queen's University Belfast and Pro Chancellor of Trinity College Dublin, Sir Peter Froggatt, passed away at the age of 91 on 3 May 2020.

Sir Peter was a distinguished academic with an international reputation. He served as Vice-Chancellor of the Queen's University, Belfast 1976-1986 and Pro Chancellor of Trinity College Dublin 1985-2002. Peter Froggatt was educated at the Royal Belfast Academical Institution, the Royal School, Armagh and Trinity College, Dublin, where he studied medicine. He later worked in Sir Patrick Dun's Hospital, Dublin and as medical officer at Short Brothers and Harland Ltd, Belfast. In 1959 he was appointed lecturer at Queen's University; a personal Chair as Professor of Epidemiology in 1968 and three years later; was appointed Dean of the Faculty of Medicine.

During his career, he produced many papers and articles, including studies on human genetics, occupational medicine, medical history and education, and epidemiology and smoking policies. He received honorary fellowships from a number of learned bodies and was a Foundation Fellow of the Faculty of Occupational Medicine, Royal College of Physicians of Ireland.

A man of many talents with a warm and charming personality, he was a naturally gifted and much sought-after speaker. A former member of Malone and Royal Portrush Golf Clubs, he was an outstanding amateur golfer who played for Ulster and Ireland. Sir Peter Froggatt made a significant impact on academia and the practice of medicine in these islands and beyond. A true Irishman, gentleman and scholar. He will be remembered fondly by all who knew him and condolences are extended to his wife, Norma and their four sons.

Obituary by Professor Ken Addley OBE MD FRCPI FFOM, Past Dean Faculty of Occupational Medicine, Royal College of Physicians of Ireland.

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Cholesterol Pleural Effusion - "Pseudochylothorax" in a Smoker

M. Kooblall, S. Cadogan, J.J. Egan

Department of Respiratory Medicine, Mater Misericordiae University Hospital, Dublin 7.

Dear Sir,

Pseudochylothorax is termed as the presence of high amounts of cholesterol in a pleural effusion. The exact incidence is unknown, with less than 200 cases reported in the literature. The most common aetiology of pseudochylothorax are tuberculosis and rheumatoid arthritis among many other causes. [1]

We present the case of a 37 year old croatian lady, with rheumatoid arthritis, who was referred to hospital by her GP with a 2 day history of pleuritic chest pain and exertional shortness of breath. She denies any arthralgia and was on no medication. She had a history of right sided pleural effusion which required drainage twice in Croatia. She has no significant family history and has no known drug allergy. She is a current smoker of 15 pack year history, rarely drinks alcohol and is independent in her daily activities. On clinical exam, her vitals were normal. She had no arthropathy, no rheumatoid nodules, no ocular symptoms and no muscle weakness. Her heart sounds were normal with no additional sound or murmur. She had decrease air entry on at her right lung base. Her Chest X-ray showed a loculated right sided effusion that was confirmed on thoracic ultrasound. A computed tomography scan of the chest showed the right sided loculated pleural effusion with underlying pleural thickening, likely reactive. There was no evidence of consolidation, nodules or enlarged mediastinal lymph nodes. Her renal profile, liver profile and full blood count and inflammatory markers were normal. Her anti-citrullinated peptide antibodies was elevated consistent with her diagnosis of rheumatoid arthritis. She underwent an ultrasound guided chest tube drain insertion which drained in total 700ml of cloudy fluid. Biochemical pleural fluid analysis revealed an exudate, with fluid cholesterol of 5.8 mmol/L, Triglycerides of 0.73 mmol/L and pH 7.68. Pleural fluid for cytology and microbiology came back negative. A diagnosis of pseudochylothorax was made.

Pseudochylothorax is a rare cause of pleural effusion. The pleural fluid in a pseudochylothorax is a typically milky white exudate, with a high cholesterol content (cholesterol >5.18mmol/L), triglyceride concentration below 1.24mmol/L, and a cholesterol/triglyceride ratio >1.[1]

The exact pathogenesis of cholesterol effusions is uncertain, but it is likely that different mechanisms exist in different clinical settings.[2]

Smoking can increase the oxidative stress in the body. Pryor and Stone reported that there are two phases of cigarette smoke: as a particulate (tar) phase and a gaseous (vapour) phase, both of which contain very high concentrations of free radicals. Cigarette smoke is also known to activate endogenous sources of free radicals. It has been reported that oxidative stress increases in rheumatoid inflammation due to impaired antioxidant systems caused by free radicals, which have a role in the etiology of rheumatoid arthritis. [3,4]

Management of pseudochylothorax includes treatment of the underlying cause.

Reflecting on this case, although the patient had no musculoskeletal symptoms, her smoking history was the only exacerbating factor that we could identified. Patient was therefore referred to smoke cessation service and follow up in the respiratory clinic and by her GP.

Corresponding Author:
Minesh Kooblall
Respiratory Department
Mater Misericordiae University Hospital
Email: mineshkooblall@physicians.ie

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Attitudes Toward Hand Hygiene Among Medical Students on Placement in Primary Care

L.G. Glynn[1,2], R. Cosgrove[1], R. Halls[1], M. Casey[1,2], C.P. Dunne[1,2,3]

1. School of Medicine, University of Limerick, Limerick, Ireland.
2. Health Research Institute, University of Limerick, Limerick, Ireland.
3. Centre for Interventions in Infection, Inflammation & Immunity (4i), University of Limerick, Limerick, Ireland.

Dear Editor,

Many studies outline the beneficial role that effective hand hygiene has in preventing healthcare acquired infections in clinical settings [1 2]. Healthcare workers and the general public have become increasingly aware of the importance of hand hygiene since the emergence of SARS-CoV-2 in December 2019. There is a paucity of research on this topic in primary care where approximately 90% of health contacts occur.

We have conducted the first study to determine the attitudes and knowledge of medical students towards hand hygiene in primary care in Ireland. This study was carried out prior to the emergence of SARS-CoV-2. A 37-question on-line survey was circulated to all year three medical students in the University of Limerick School of Medicine examining attitudes and knowledge towards hand hygiene. Out of a total of 138 students, 64 students responded (46%). Overall, the students surveyed had awareness of the evidence base, relevance and benefits of hand hygiene.

Attitudes towards hand hygiene were predominately positive with 72% (n=46) of students claiming hand hygiene is important in their area of practice and 86% (n=55) agreeing that hand hygiene policy is relevant to their work. The study found that the majority (83%, n=53) of medical students were compliant with current recommendations on hand hygiene. In spite of positive attitudes, over a quarter (27%, n=17) of students had not implemented the recommendations of their practices' hand hygiene policy. In addition, although the survey response shows students are compliant with hand hygiene in certain settings, over 50% of medical students are not familiar with the National SARI guidelines for hand hygiene.

Alcohol based hand rub was viewed as a practical and accessible method of performing hand hygiene. Students expressed uncertainty in regard to the expectations of GP tutors around hand hygiene. The role of GP tutors in hand hygiene practices was not well defined and there may be a need for further training in hand hygiene for medical students prior to primary care placement. This study provides insight into hand hygiene practices among medical students in primary care placement in Ireland.

In essence, students placed in primary care have positive attitudes towards hand hygiene. They are open to change and willing to incorporate change into their clinical practice in relation to hand hygiene on placement. However, it appears some students perceived low expectations in terms of hand hygiene in primary care, so the integration of primary care physicians into hand hygiene training may be beneficial. Overall, the results of this study, consistent with previous studies, suggest the need for further training of medical students regarding optimal hand hygiene practices[3,4].

Gaining an insight into the attitudes of medical students towards hand hygiene is vital as they will become the future of healthcare and play a vital role in preventing the spread of infection. We plan to repeat this survey with medical students to explore differences that may have emerged as a result of the experience of the SARS-CoV-2 pandemic.

Keywords:
Alcohol-based hand rub, Attitudes, Hand hygiene, Hand rubbing, Infection prevention and control, Medical students

Ethical approval and consent to participate:
Ethical approval was obtained from the Research Ethics Committee of the University of Limerick Faculty of Education and Health Sciences (Reference number 2014_12_04_ EHS).

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Corresponding Author:
Liam G. Glynn,
School of Medicine,
University of Limerick,
Limerick,
Ireland
Email: liam.glynn@ul.ie

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Palliative Care Within Neonatology

R. Egan[1], A. Smith[1], F. McElligott[1,2]

1. Department of Neonatology, The Rotunda Hospital, Dublin.
2. Department of Palliative Care, Children's Health Ireland at Temple Street, Dublin.

Dear Sir,

The National Perinatal Epidemiology Centre (NPEC) recently published its 7th annual report on perinatal mortality in Ireland. Stillbirth accounted for 61.7% (n=235) and neonatal death 38.3% (n-146) [1] End of life care decisions can be divided into two categories. Firstly, where it is known before delivery that the infant cannot survive and therefore initiating resuscitation is not appropriate, and secondly, in the redirection of care following a period of neonatal intensive care as it is deemed inappropriate, or ineffective, to continue. The main reasons for redirecting care are lethal congenital anomalies (45%); extreme prematurity (35%); and severe birth asphyxia & other causes (20%) [2].

The advances in antenatal care have led to an increase in prenatal identification of those who will require palliative care after delivery. Education & training of staff is stated as the fourth standard of the National Standards for Bereavement Care Following Pregnancy Loss and Perinatal Death [3]. Despite this there is currently no dedicated training for neonatal NCHD's on providing care & symptom management during such situations [3]. Instead, we rely on accruing knowledge under the guidance of experienced practitioners over time. Low case numbers and considerable variability in individual patients' needs results in an underdeveloped skill set amongst NCHD's.

We performed a survey on paediatric doctors (n=25) working in the Rotunda in October 2019 consisting of 18 NCHD's and 7 consultants. Thirty-three per cent of NCHDs and 86% of consultants had received specific palliative care training. Twenty-two percent of NCHDs and 14% of consultants had received this training as part of their BST/HST schemes. Forty-four percent of NCHDs felt comfortable to provide palliative care however, none of the NCHDs considered the current training approach sufficient. Thirty-nine percent of NCHDs and 86% of consultants felt comfortable prescribing pain medications and sedation. When asked about the challenges of palliative care, 78% of NCHD's stated communication with parents. For consultants the biggest perceived challenge was management of nutrition & hydration at 57%. While 60% stated reliance on the BNF & local medication guidelines for prescribing, only 1 responder utilised of the APPM formulary highlighting a lack of awareness of available resources. The main barriers perceived to providing quality care were training & education (28%), communication deficits (28%) and hospital infrastructure (44%), notably doctor to patient ratios and suitable spaces to provide care and family privacy. Strikingly, only 14% of consultants felt that trainees received enough support and opportunities for debriefing following the death of a patient.

In summary, our results highlight that on the whole NCHDs are not fully comfortable in palliative care situations. Our study has demonstrated that NCHDs are keen to receive more palliative care training in order to ensure that they are well prepared to handle such momentous and difficult situations in a caring and sensitive manner. This may be achieved by including palliative care education in induction programs of individual hospitals, attendance of NCHD's at palliative care team meetings and the development of a specific BST & HST palliative care curriculum with the allocation of specific scheme training days.

Corresponding Author:
Dr. Roisin Egan
The Rotunda Hospital,
Parnell Square,
Dublin,
Ireland.
Email: egan.roisin@gmail.com

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Spontaneous Uterine Inversion

A. Javaid, R. Langhe, A. Munir, S. Selvamani

Department of Obstetrics & Gynaecology, Our Lady of Lourdes Hospital, Drogheda, Co Louth, Ireland.

We report a case of acute uterine inversion which occurred in a young primigravida after forceps delivery for prolonged second stage of labour.

A 19-year old primigravida was admitted to the hospital for induction of labour due to postdates. Her pregnancy was categorised as low risk. She had a forceps delivery due to a prolonged second stage and maternal exhaustion. Placenta was delivered by controlled cord traction 10 minutes after delivery of the baby. Following placental delivery, the woman had a primary postpartum haemorrhage (PPH). After initial medical management for primary PPH the woman was transferred to theatre for examination under anaesthesia in view of persistent heavy bleeding, severe lower abdominal pain and hypovolemia shock. Following induction of general anaesthesia, an immediate diagnosis of acute complete uterine inversion was made and the uterotonics was stopped instantaneously. Management involved multidisciplinary team including obstetricians, anaesthetists, midwives and blood bank services. Manual replacement of uterus was done followed by insertion of Bakri ballon and syntocinon infusion. Postnatal recovery was unremarkable, and the woman discharged 4 days after the delivery.

Uterine inversion is one of the rare and serious obstetrics emergencies. Based on timing of occurrence, it can be classified into acute (within 24 hours of delivery), subacute (> 24 hours but < 4 weeks) or chronic (>1 month postpartum)[1,2]. If not immediately identified will lead to massive and often underestimated blood loss which may results in hypovolemic shock and maternal death that can reach 15% in some cases[1]. Risk factors include mismanagement of 3rd stage of labour, primiparity, fatal macrosomia, excessive fundal pressure, abnormal placenta localization uterine hypotonia, short umbilical cord and ligament laxity[1]. The initial approach of the management of uterine inversion is to try to reverse the uterus with manual pressure on the fundus through the vagina called Johnson manoeuvre. Hydrostatic pressure is another method used if manual reduction failed, which involves inserting a balloon vaginally to increase the pressure on the uterine fundus to push the uterus to its initial position[4]. There are two main surgical techniques described as Huntington and Haultaim. In the Huntington technique, the round ligament is grasped by clamps, near to its insertion in the uterus, and slowly pulling up repeatedly until uterus is re-inverted[3]. In Haultaim technique an incision is made in the posterior part of the ring formed by the cervix in order to increase the size of the cervical ring and thus reposition the uterus[3].

Corresponding Author:
Amina Javaid
Registrar Obstetrics & Gynaecology
Our Lady of Lourdes Hospital,
Drogheda,
Co Louth,
Ireland.
Email: draminaj@gmail.com

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Minimum Alcohol Pricing

On behalf of The Faculty of Public Health Medicine RCPI and Faculty of Public Health in Northern Ireland

L. Holcroft[1], D. O'Donovan[2], D. O'Hagan[3]

1. Foundation 2 trainee, Belfast.
2. Global Health, Queens University Belfast.
3. Public Health Agency, 182 Galgorm Road, Ballymena BT42 1QB, United Kingdom.

Dear Sir,

Over the past few months, we have seen that there is nothing like a pandemic to focus the mind both personal and political and to use this focus to implement radical change. The collective aim has been to protect the vulnerable, ensure our health services are not overwhelmed and ultimately to save lives. As we emerge from a period of restrictions there is an opportunity to implement a measure which could, albeit in a less dramatic and inconvenient fashion, fulfil those aims. Now is the time to act to introduce minimum unit pricing (MUP) for alcohol on an all island basis.

Alcohol related illness and injury places a considerable burden on our healthcare system every year. There were over 17,000 alcohol related discharges from Irish hospitals in 2013[1] and with reports of 5.9 % of ED presentations being alcohol related, the impact alcohol has on our healthcare systems is undeniable [2]. In its pre-budget submission for 2020, Alcohol Action Ireland estimated that alcohol related illness and harm would cost the Irish exchequer over €2.35 billion and strongly advocated for the immediate introduction of MUP. Modelling on the introduction of MUP for Ireland conducted in 2014 showed that the introduction of a 90c MUP would lead to an estimated reduction of 139 deaths and 4,102 fewer hospital admissions a year[3].

Alcohol is associated with domestic violence, mental ill health, self–harm and suicide.[1] A worrying feature of the "new normal" is a reported rise in levels of alcohol consumption. Prior to the pandemic it was reported that 1 in 6 children's lives were negatively impacted by parental drinking. Higher alcohol consumption coupled with the increased dependence of children on their parents and less outside support during the pandemic has the potential to further exacerbate this. The myriad other negative effects which alcohol has on health and wellbeing are likely to be compounded by the effects of the containment measures.

Previously objections to MUP have been raised regarding its impact on moderate drinkers, the concept of "the nanny state", the potential for cross border trade and its resultant economic impact. Modelling suggests that the introduction of MUP would have a negligible impact on alcohol expenditure amongst those who drink moderately but could have a more significant impact on harmful drinkers and those who consume large quantities of cheap alcohol[4]. MUP is unlikely to have any effect on the pub and restaurant trade as the majority don't currently engage in below cost selling and have advocated for the introduction of MUP.

The changes we have seen introduced in response to the risks of SARS-CoV-2 have presented opportunities to address these objections and point towards a level of tolerance for actions which aim to protect the health and well-being of citizens. Introduction of MUP is a feature of the 2018 Public Health (Alcohol) Act in Ireland and the Alcohol Strategy for Northern Ireland.

There is now a functioning executive in Northern Ireland and communication between the two parts of the island has strengthened with the aim of managing the response to SARS-CoV-2. Surely this is an opportune time to advance the introduction of MUP on an all Island basis to continue our efforts towards saving lives and protecting our health services.

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Delayed Access and Uptake of Care for Children During Covid-19

C. Sloane, P. Mallett, K. Ferris, C. Bennison, P. Moriarty

Royal Belfast Hospital for Sick Children (RBHSC), Belfast, N. Ireland.

Dear Editor,

We are writing to discuss some anecdotal evidence that is emerging in Northern Ireland's paediatric population during the COVID-19 pandemic, regarding recognition of potentially delayed presentations of children to paediatric services.

To date, there has been over five million confirmed cases of SARS-CoV-2 globally, including nearly 350,000 deaths.[1] It has emerged that children have been significantly less affected, comprising <2% of all cases reported.[2] This is also illustrated in disease severity with small numbers of children requiring hospitalisation and critical illness reportedly occurring in <1% of all affected children.[2]

Northern Ireland has a population of almost 2 million people, with 20% aged under 16.[3] There were substantial concerns about our specific group of vulnerable patients including those with chronic cardio-respiratory conditions, neuro-disabilities and underlying genetic conditions. Particular concern was raised at extrapolating information from diverse paediatric patient populations from China and Italy, two of the country's initially most severely affected and where much of the initial evidence originated.

In response to this now global crisis, a UK-wide national lockdown, including school closures began on 23rd March 2020. Soon the UK government began disseminating the now well-recognised slogan of 'stay home, protect the NHS, save lives'. The Royal Belfast Hospital for Sick Children (RBHSC) had begun postponement of elective surgical procedures, and any routine outpatient clinics.

The marked decrease in the number of paediatric patients presenting to hospital began to raise concerns among paediatricians here. RBHSC emergency department attendances fell by over 30% in March, and over 50% in April compared to the corresponding periods of 2019. This prompted a Public Health Agency announcement on 15th April, urging parents to remain 'vigilant of other childhood illnesses', and to seek help if their 'child is unwell and needs medical attention'.[4]

We began to see some cases of children presenting, in our opinion, later than usual with a variety of treatable conditions. This includes infants and children with a number of medical and surgical conditions, both newly diagnosed and exacerbations of known chronic conditions. Our difficulty lies in accurately quantifying this; what constitutes a delayed presentation for each of these illnesses, how can direct case comparisons be made, how do we screen for delayed cases? There are also cases of delayed presentation to hospital that occur throughout the year, pandemic or not.

The perception amongst our group, discussed at regular clinical meetings, is that these included cases of late onset neonatal sepsis, new and known patients with diabetes mellitus presenting with severe diabetic ketoacidosis, some requiring prolonged intensive care stays. In addition, we have experienced infants and children with perceived delayed presentations of readily treatable surgical conditions such as pyloric stenosis and appendicitis; some of whom experienced significant derangement in electrolyte profiles, inflammatory markers, and clinical instability. These surgical presentations have particularly led to more complicated operative management, resulting in challenging post-operative sequalae and prolonged hospital admission.

After eight weeks of strict lockdown measures, the RBHSC has seen very few patients with COVID-19 related illness. As these measures have begun to gently ease, we are seeing increasing numbers of emergency department attendances and hospital admissions, and this is very reassuring. During this and the anticipated future phases, it is our collective role as healthcare professionals to actively encourage and promote parents and carers to seek healthcare appropriately.

Corresponding Author:
Dr Charlotte Sloane,
Royal Belfast Hospital for Sick Children (RBHSC),
Belfast,
N. Ireland.
E-mail charlotte.sloane@belfasttrust.hscni.net

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Issue: Ir Med J; Vol 113; No. 7; P141

Pulmonary Rehabilitation Programme: A Transcendence During Covid-19 Pandemic

M. O'Reilly, C. Gillen, Celine Meehan, I. Counihan, T. Hassan

Our Lady of Lourdes Hospital, Drogheda, RCSI Hospital Group.

Dear Editor,

The Covid-19 pandemic has caused disrupted scheduled care including rehabilitation services which are a key intervention for chronic disease management including respiratory diseases. Pulmonary rehabilitation (PR) has established itself as one of the most cost-effective interventions for chronic obstructive pulmonary disease (COPD) after smoking cessation and flu vaccine[1], and as effective as inhaler therapy in improving exercise capacity and reducing exacerbations as well as hospital admissions.

PR traditionally entails an exercise programme in which patients attend a hospital/community setting twice weekly classes for at least 6 weeks. However, international surveys reported that this programme is only available to a small fraction of COPD patients[2]. In addition, many countries like Germany offer a limited 3-weekly programme due to lack of funding sourced by national health insurances.

Alternative approaches to deliver PR are much sought after to offer a cost-effective intervention and improve accessibility. However, in PR programmes, sustained effort of professionals is key to motivate and support symptomatic patients and therefore, real-time or live interaction as well as supervision are emphasized to ensure clinical effectiveness. Although further research is needed to confirm this theory, a passive PR programmes using readily available videos are unlikely to be as beneficial for patients whose sedentary behavior relates to perceived fear of respiratory symptoms, specifically shortness of breath. Recent studies reported non-inferior clinical benefits of virtual real-time PR compared to traditional PR, in addition to a decrease in the need for staffing and less travelling time for patients[3].

In November 2019, an innovative virtual PR project was launched in Ireland for the first time. Based in Our Lady of Lourdes Hospital, Drogheda, a real-time and interactive 7-week PR programme was offered to patients with chronic respiratory diseases. This project utilized both resources from the Health Service Executive and the patients, in the comfort of their own home. There was 100% completion rate and all patients reporting improvement in COPD-related health indicators while 80% had an improvement in their exercise tolerance. For the first round of the programme, an estimated 1900km and 42 hours in travel expenditure was saved.

Since the Covid-19 pandemic, this innovative, award nominated initiative has gained interest nationwide leading to adaptation of a National guideline[4]. There is also international interest in the Irish National Guideline from other countries including the United Kingdom, Canada and Brazil. Continued provision of PR for chronic respiratory patients is essential to continue a scientifically proven and safe intervention to alleviate the high clinical workload on primary and secondary care at a time of social distancing and enhanced infection control in the health care system.

This virtual programme also facilitate a transcendent platform, beyond the Covid-19 pandemic, as Ireland contemplate to deliver a better health system that will incorporate telemedicine integrated with personalised care as the basis of Ireland's e-health strategy, published in 2013.

Corresponding Author:
Tidi Hassan, MBBCh BAO, PhD
Consultant in Respiratory Medicine,
Our Lady of Lourdes Hospital,
Drogheda,
Co. Louth.
Email: tidi.hassan@hse.ie

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The Feel in PPE: "Sous le Sunlight des Tropiques!"

M. Kooblall, S. Cadogan, C. Hopkins, D. Casserly

Department of Respiratory/ General internal Medicine Mater Misericordiae University Hospital, Dublin 7.

Dear Sir,

Personal Protective Equipment (PPE) is now being used daily by all healthcare workers (HCWs). Since the start COVID-19 pandemic, guidelines and training were provided about donning (putting on) and doffing (taking off) of PPE. At the Mater Misericordiae University hospital, the COVID-19 medical team on call has been experiencing symptoms and signs of dehydration during their shifts.

We surveyed 40 Non-Consultant Hospital Doctors (NCHDs) at the Mater Misericordiae University hospital who were on call and asked them whether they experienced symptoms and signs of dehydration during their 12-hour shift. Out of the 40 questionnaires sent between March and June 2020, 32 (80%) responded. Out of the 32 who responded, 19(59.38%) were female and 13(40.62%) were male. 3(9.38%) were aged between 18 and 24 years, 27(84.38%) were aged between 25 to 34 years and 2(6.25%) were aged between 35 to 44 years. 32(100%) complained of sweating, 21(67.74%) complained of fatigue, 26(83.87%) complained of thirst, 2(6.45%) complained of muscle cramps, 7(22.58%) complained of dizziness, 18(58.06%) complained of headache, 1(3.23%) fainted and 10(32.26) had increased body temperature. Between donning and doffing, 10(31.25%) stayed in PPE for over 2 hours and 22(68.75%) doctors stayed less than 2 hours in PPE on average during their shift. On average 28 out the 32 NCHDs took less than 1L of fluid during their busy on call shift.

Normal adults are considered to have a minimal obligatory water intake or generation of approximately 1600 mL per day, are of composed ingested water (500 mL), water in food (800 mL) and water from oxidation (300 mL). On the other hand, the sources of obligatory water output in normal adults are composed of urine (500 mL), skin (500 mL), respiratory tract (400 mL) and Stool (200 mL).[1]

Although sweat production is low in the basal state, it can exceed 1 to 2 L/h in a subject working in a hot environment.[2] During a busy medical on call, it is crucial that our NCHDs are adequately hydrated to ensure them doing their job properly. One of the main problems identified was that because of their heavy workload, they always postponed the idea of getting a glass of water because the water dispenser was not nearby.

The Royal College of Physician of Ireland is putting lots of emphasis on the well-being of NCHDs during this COVID-19 crisis.[3] The problem of dehydration among NCHDs wearing PPE could have been be properly addressed if there was adequate communication between the management and NCHDs.

NCHDs among many other HCWs coping with the pandemic have been working round the clock. The emergence and rapid spread of SARS-CoV-2 still represents a major threat. Reflecting on our findings, we concluded that systems must be placed for effective and coordinated communication that supports the delivery of continuous and safe care of NCHDs to optimise a better clinical governance.

Corresponding Author:
Minesh Kooblall
Department of Respiratory/ General Internal Medicine,
Mater Misericordiae University Hospital.
Email: mineshkooblall@physicians.ie

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Our vCreate Experience

P.B.J. Sanneerappa, C. Fitzpatrick, Y. Fennell, M. Tariq

Department of Paediatrics, Midland Regional Hospital, Portlaoise.

The Corona Virus Disease in 2019 (Covid-19) is a pandemic that has changed priorities in the world. Even though few businesses can operate from home, services like healthcare still needs to function in a hospital setting, which can cause a lot of stress among the frontline healthcare staff prompting many countries to adopt new strategies to combat this. In the UK a digital learning package using Agile methodology was introduced within the first three weeks of the outbreak[1], serving as a tool to help health care staff.

The physical distancing guidelines by Health Service Executive (HSE) allows only one parent are allowed to visit a child/baby in a hospital. This means newborn babies cannot see their dads, which could have a very strong impact on mental health. To overcome this many hospitals in the Republic of Ireland have adopted video messaging applications like Skype, WhatsApp, face time, Facebook calling and vCreate to connect everyone. After tremendous success in the Rotunda Hospital, Cork University Hospital, Coombe Women's Hospital, we at Midland regional hospital in Portlaoise used the vCreate application. Due to this initiative we were able to receive highly valuable contributions from the general public and friends of the hospital funds, which in turn enabled us to both buy the tablets and also to buy the subscription plans.

vCreate[2] is a secure video messaging service that allows our clinical team in the Special Care Baby Unit to send video updates to parents when they're unable to be with their baby. Mothers only are allowed access to the Unit and their baby. Dads and extended family are not allowed to visit. This is a way to minimise separation anxiety among dads. It shows that we as a unit care for the psychological and emotional needs of all the family and are willing to change and adapt to meet these needs, building trusting relationships with parents and families. It is very important to note that these videos and images can be downloaded and shared with extended family members, which means they can have these memories forever.

vCreate also has an important role to play in breastfeeding support. It helps mothers to continue breastfeeding during this pandemic which can further reduce stress and to give provide good quality milk to their babies[3]. It is very important to help her to promote good levels of oxytocin and reduce stress. Having a secure video and picture messaging service can help parents to build up a diary of events and images will help mothers emotionally and psychologically during their breastfeeding journey.

Many parents have given very highly valuable positive feedback regarding this new initiative. Last week, one of the SCBU nurses got a feedback from mum that vCreate images and videos really motivate her to keep pumping her breast milk when separated from her baby. It was lovely to hear these positive feedbacks and we strongly think that vCreate can really lift up the spirits of many mothers' who are at risk of post partum depression.

In conclusion, we think that vCreate is a fantastic application to connects dads' and extended families to spend very important virtual time with their babies remotely and we encourage other units across the country to adapt this application.

Corresponding Author:
P.B.J. Sanneerappa,
Department of Paediatrics,
Midland Regional Hospital,
Portlaoise.
Email: phanibhushan2005@gmail.com

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Worldwide Asthma Societies' Recommendations During the Covid-19 Pandemic

M. Mohamedsaeed, P.B.J. Sanneerappa, M. Tariq

Department of Paediatrics, Midland Regional Hospital, Portlaoise.

There have been many pandemics in the world which were worse than the current COVID-19 pandemic. But due to the emergence of widespread digital technology through mobile phones, this pandemic seems to have caused more panic, especially in people who have co morbid chronic conditions like cardiac, respiratory illnesses and immune compromised individuals. In children the stress could be compounded by added stress of parents and grandparents. Even though WHO has plenty of information on COVID -19, there is no specific guidelines on treating children with asthma during this pandemic. Children who become acutely ill and need hospital intervention will be taken care of in our acute hospital setting. However, children at home will need more guidance on how to prevent and how to be prepared with this pandemic. In this letter, we explore some of the guidelines laid by important asthma societies around the world with regards to the proper management of Asthma in the paediatric population within the setting of the COVID-19 pandemic, and the important messages they send to healthcare professionals and the general public.

After reviewing recommendation from various important Asthma societies worldwide like American Academy of Allergy Asthma Immunology, National Asthma Council Australia, Asthma Society of Ireland, NICE guidelines and Asthma UK guidelines, we observed the following advice. We found that all these societies shared common pathways regarding management of asthma during the COVID 19 pandemic, these recommendations included : following hand hygiene measures, maintaining social distancing, making sure the patient has an updated asthma action plan, continuing asthma medications as normal including inhaled corticosteroids and bronchodilators, to ensure patients have at least a month's supply of medication, to avoid stockpiling medications and to be prepared for the flu season. Most of the societies suggest avoiding aerosol generating procedures as much as possible (including nebulisers). While some of these societies like NICE guidelines and Asthma UK advised patients and carers to continue using nebulisers at home because the aerosol comes from the fluid in the nebuliser chamber and does not transmit the virus particle among patients. The Irish Asthma Society and NICE guidelines also advised the patients to continue their biological therapy as there is no evidence that it suppresses immunity. NICE guidelines were also unique in advising physicians to start biologic therapies on appropriate patients even during the COVID-19 restricted service.

In conclusion, most of the asthma societies recommended focusing on prevention of the spread of the virus. Importance was given to minimise exposure among vulnerable groups through promoting hygienic practices, social distancing. They also emphasised the need for good communication with patients and their carers to support mental wellbeing and mitigate their anxiety. They also advised to provide management options at home to minimise hospital admission and thus prevent virus exposure.

We hope this information will be very useful to decrease stress among many families in Ireland and reassure them that by following simple routine advices, they can maintain good health during this restricted health service.

Corresponding Author:
P.B.J. Sanneerappa,
Department of Paediatrics, Midland Regional Hospital, Portlaoise.
Email: phanibhushan2005@gmail.com

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Incorrect and Misleading Claims Regarding Vitamin D

M.J. Bolland,[1] A. Avenell[2]

1. Department of Medicine, University of Auckland, Auckland, New Zealand.
2. Health Services Research Unit, University of Aberdeen, Aberdeen, Scotland.

In Response to Article Entitled:
'Optimisation of Vitamin D Status for Enhanced Immuno-Protection against Covid-19' by D.M McCartney et al – Ir Med J; Vol 113; No. 4; P58

McCartney and Byrne claim[1] we misrepresented the findings of Martineau[2] in our BMJ editorial.[3] They are wrong. The absolute risk reduction is the difference between the absolute risks in the control and intervention groups. In the meta-analysis by Martineau[2] this is 42%-40% = 2%. McCartney and Byrne divide this figure by the baseline absolute risk to get 4.8%, which is the relative risk reduction.

Unfortunately, they compound their error by equating an odds ratio of 0.88 with a 12% reduction in risk. The odds ratio only approximates the relative risk when the absolute risk is small. In the Martineau meta-analysis,[2] the absolute risk (42%) was not small, and thus the odds ratio substantially overestimates the relative risk.[4] The relative risk was actually about 0.93,[4] fairly close to the estimate of 4.8% by McCartney and Byrne.[1]

McCartney and Byrne then suggest that a 70% reduction in risk in those with baseline 25OHD <25 nmol/L from the Martineau meta-analysis could apply to Irish nursing home residents.[1] Notwithstanding the fact that they mean a 70% reduction in the odds (the relative risk reduction is about 48%), this finding is not generalizable. In the subgroup analysis McCartney and Byrne quote, there are 234 individuals with baseline 25OHD <25 nmol/L treated with daily or weekly vitamin D.[2] However, Table 1 shows that 225/243 individuals treated with daily/weekly vitamin D and 25OHD <25 nmol/L were infants or children (or all but 18).[2]

192/225 children were from a single study in school children in Mongolia which showed an extremely positive effect of 7 weeks of milk fortified with vitamin D compared to milk alone on parent-reported chest infections or colds occurring within the previous 3 months.[5] These results should be interpreted with extreme caution. The trial was cluster randomized by classroom with an undescribed (but small) number of clusters per treatment arm. In the Martineau meta-analysis, the study appears to have been analyzed as though children were individually randomized.[2] The data on colds or chest infections were not collected prospectively, instead gathered from parental recall for the preceding 3 months, of which the children were not taking vitamin D for 6 weeks.[5] The analysis was post-hoc and data for only 1 of the 5 different vitamin D arms have been reported.[5]

The claim that vitamin D supplementation prevents respiratory tract infections in the Martineau analysis, overall or in subgroups with 25OHD <25nmol/L, is largely or entirely dependent on this study. Applying fragile, post-hoc, selectively reported results from a cluster randomized trial of school children in Mongolia (or meta-analyses dependent on it) to Irish nursing home residents is both misleading and unwise.

Corresponding Author:
Mark Bolland
Bone and Joint Research Group
Department of Medicine,
Faculty of Medical and Health Sciences,
University of Auckland
Private Bag 92019,
Auckland,
New Zealand.
Email: m.bolland@auckland.ac.nz

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Authors of Article **'Optimisation of Vitamin D Status for Enhanced Immuno-Protection against Covid-19'** by McCartney et al (Ir Med J; Vol 113; No. 4; P58) *comment on response letter* **'Incorrect and Misleading Claims Regarding Vitamin D'** by Bolland et al (Ir Med J; Vol 113; No. 7; P145)

D.M. McCartney[1], D.G. Byrne[2,3]

1. School of Biological and Health Sciences, College of Sciences & Health, Technological University Dublin - City Campus, Kevin Street, Dublin D08 NF82, Ireland.
2. Department of Internal Medicine, St. James's Hospital, James's Street, Dublin 8, Ireland.
3. Dept. of Clinical Medicine, School of Medicine, Trinity College Dublin, Dublin 2, Ireland.

Dear Editor,

In response to Bolland and Avenell's comments on our recent response letter in the *IMJ*, we are very happy to clarify our reference to *relative* risk rather than absolute risk reduction. We view relative risk to be a meaningful representation of risk reduction which significantly augments that shown by absolute risk reduction alone, particularly in interventions with a binary outcome (respiratory infection versus no respiratory infection in this case). For example, in a study of 200 individuals where the treatment group's risk of an adverse outcome was 17% (i.e. 34/200) versus 20% in the control population (i.e. 40/200), it would be helpful to report this difference between the two groups as a 15% reduction in relative risk (i.e. 1-(34/40) x 100) rather than just reporting a 3% absolute risk reduction in isolation, as the latter may appear inconsequential and be overlooked in clinical decision making. In other words, the use of relative risk takes account of the background incidence of the adverse outcome, as well as the reduction in incidence associated with the intervention. In the same way, a 7% reduction in relative risk of respiratory infection amongst a treatment group will augment the interpretation of a 2% absolute risk reduction presented in isolation[1]. This has significant implications for healthcare utilisation projections and resource planning where the prospective value of initiating any treatment regimen needs to be clearly understood. So while we are happy to clarify our point from a methodological perspective, we would suggest that the best approach is to report both the relative risk and absolute risk reduction in evaluating studies of this nature. It is notable that Bolland & Avenell do report this relative risk in their subsequent *BMJ* rapid response[2], but that this larger relative risk reduction figure was not cited by Rabbitte & Slattery[3].

We are also happy to clarify the 70% reduction in the *odds* of respiratory infection rather than relative risk in the sub-group analysis of those with baseline 25(OH)D levels below 25nmol/l in Martineau et al[4]. The key finding from this meta-analysis however, is that there is a very substantial reduction (~48%) in relative risk for those with low baseline serum 25(OH)D receiving vitamin D supplementation. In their disaggregation of the <25nmol/l sub-group analysis, Bolland & Avenell have opined that the analyses in Camargo et al. were *post hoc* – this is not the case; as stated directly in the publication: "This comparison was determined *a priori."* Also in the study by Camargo et al., the reason why the comparison between group 1 and group 6 was reported was because the goal of the study was to compare daily vitamin D vs. placebo. Arms 2-5 of this study comprised different regimens (with the same overall vitamin D dose), but only group 6 facilitated a direct comparison where the vehicle (Mongolian milk), and the dosing regimen (daily) were exactly the same as that used in the vitamin D intervention group.

It is also noteworthy that in Martineau et al.[4], the data used to estimate relative risk reduction in those with baseline serum 25(OH)D <25nmol/l were also derived from five other studies where bolus supplementation was not used, albeit with lower participant numbers than the Camargo study.

Age was not identified as a covariate influencing this relative risk reduction in the overall fourteen studies with baseline 25(OH)D <25nmol/l, although dosing regimen and baseline 25(OH)D were, suggesting that the applicability of these findings to other age groups should not be discounted.

There is biological plausibility[5] as well as meta-analysis data to suggest an association between vitamin D status and risk of respiratory tract infection. These data have recently been augmented by experimental data which specifically demonstrate a direct suppressive effect of calcitriol (the active metabolite of vitamin D), on Covid-19 viral replication in cultured human nasal epithelial cells *in vitro*[6]. Further RCTs and meta-analyses will be required to fully articulate the effects of vitamin D supplementation on Covid-19 risk and severity. Until such data are available for measured consideration, we are self-evidently reliant on the existing peer-reviewed data in this area and we are compelled, in a manner redolent of Tennyson's Ulysses, 'To follow knowledge like a sinking star, Beyond the utmost bound of human thought.'[7]

Yours sincerely,

Dr. D.M. McCartney, Dr. D.G. Byrne

Corresponding Author:
Dr Daniel McCartney,
School of Biological and Health Sciences,
Technological University of Dublin - City Campus,
Kevin Street,
Dublin D08 NF82,
Ireland.
Email: Daniel.McCartney@TUDublin.ie

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