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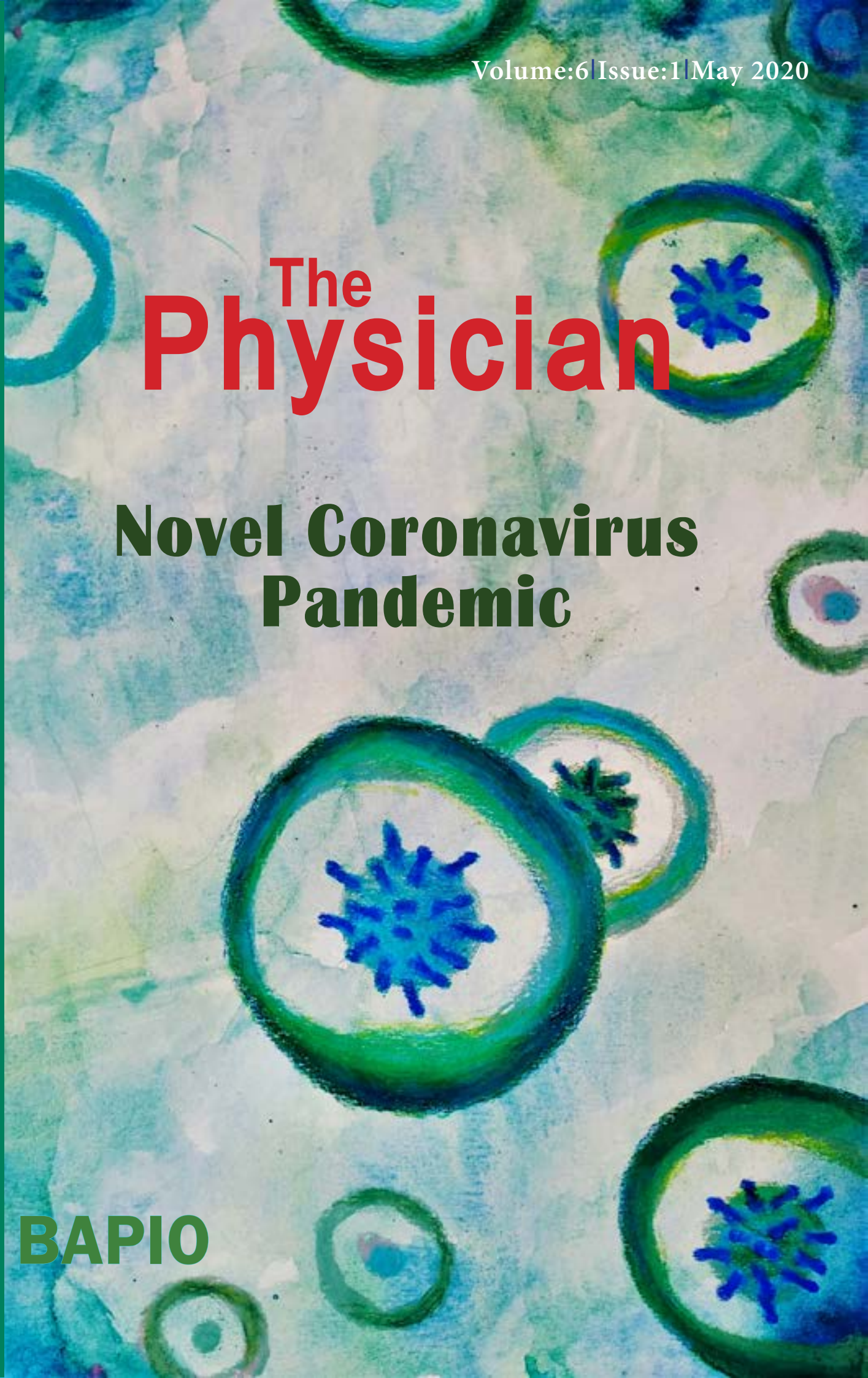
Novel Coronavirus Pandemic



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Editorial

From Snowy White Peaks to Angels of Colour - Ingrained Differential Outcomes of COVID-19 for a Diverse Healthcare Workforce

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The COVID-19 pandemic has profoundly changed the world. In an incredibly short space of time, it has demonstrated the value of international preparedness, the coordination beyond borders from United Nations agencies (such as the World Health Organisation), the politics of leadership and science, with a potential to shape the destiny of billions of people across the world. We see scientists coming together, sharing and collaborating their emerging knowledge, freely, to help nations/communities, who have disparate challenges in combating the virus. As the pandemic ravages through continents, we also see how the variations in the political interpretation of 'science' can affect the destinies of different peoples. Compared to China and South Korea, the experience in societies with large proportions of migrant populations, has revealed a perhaps unpleasant angle to this pandemic, one where there are differential outcomes within cohorts of people. There appears to be overwhelming evidence that patients from certain minority ethnic groups have differential outcomes in disease severity and even death [1,2].

The review by Chakravorty published in this edition, explores the science behind this 'risk' and the rationale for stratification.[3] There are several theories critically explored in this review from biological to demographic and socio-economic variables. This phenomenon of differential outcomes to a similar degree is also seen in healthcare workers, where ethnicity appears to be an independent risk, yet they are so fundamentally different from minority ethnic population groups, in terms of exposure and background.[2] It is therefore inconceivable, that their (healthcare professionals) experience in the face of COVID-19, can be rationalised in the same way.

Although initially thought to be related to the impact of increased prevalence of comorbid conditions,1 it now appears to also include non-biological factors and societal variations in how people are treated differently. This is not surprising to a significant minority, who are aware of deeply ingrained discrimination in many societies, and the impact this has on their lives, livelihood and health outcomes. One hypothesis being considered is that 'structural discrimination' may have contributed to magnifying the adverse impact of COVID-19 in certain populations,[4] and therefore deserves a more centre stage in our public discourse, to help us determine cause and effect.

Why whole communities in different geographical cohorts have differential health outcomes is complicated, and perhaps dependent on multiple factors including biology, education, socio-economic status, culture, ease of access to facilities/ resources, language and organisational or even political attitudes.

This editorial cannot do complete justice to this wider question, but we wish to limit our exploration to the wisdom drawn from a lived-experience of a well-defined cohort of healthcare workers in the United Kingdom who are at the forefront of the COVID-19 pandemic. We have drawn on the experience of a wide range of healthcare professionals through personal contacts, social networks and reported analysis of anonymised surveys from across the healthcare spectrum. [5] The aim of this dialogue is to raise the issues we feel are important in understanding the differential outcomes for healthcare workers and encourage all stakeholders to urgently commission actions which will help to 'save lives and save (all within) the NHS'.

Esmail and Everington described the variation in success in interviews and career progression for Black, Asian and Minority Ethnic (BAME) students and doctors over the last 25 years.[6] In a commentary of their experience over two decades they concluded that raising awareness of such issues is not without its dangers; at one stage they were charged with misconduct by the General Medical Council. [6] Roger Kline, a research fellow at the University of Middlesex Business School, has been persistent in his work raising awareness of the differential access to care for patients, and outcomes for staff from BAME backgrounds in the NHS.[7] In 2015, the Workplace Race Equality Standards (WRES) were established and NHS organisations were required to report on a range of metrics reflecting their culture of equality, diversity and fairness.[8] The most recent report in 2019, shows improvement, but progress remains slow and the issues do not currently occupy enough bandwidth with senior leadership or the commissioners to speed up implementation. [9]

Why is it important to explore differential health outcomes for healthcare workers from BAME backgrounds?

The answer is probably in the emerging evidence of high risk of disease or death among healthcare workers in the UK [10, 2], Southern Europe[11] and USA.[12] Most alarmingly, both within the general population, and in healthcare

workers, the outcomes appear to be disproportionately worse in those from a BAME background. Early reviews of the risk factors from hospital admissions in the UK and USA, indicates that several factors relating to obesity, concurrent chronic diseases, demography and social deprivation may be important. However, in this pandemic upto 20% of healthcare workers appear to be afflicted, a figure much higher than in Middle Eastern Respiratory Syndrome (MERS) or SARS, and have a higher risk of death or severe disease, than those identified in the population.[11] All healthcare workers due to the nature of their roles, naturally face a higher risk of exposure to SARS-CoV-2 in their line of duty. Yet the observed differential outcomes, segregated by ethnicity is difficult to explain by 'the exposure hypothesis' alone. There appears to be another missing factor 'R'. In this pandemic, the letter 'Ro' has seen more popularity than ever before, as politicians and citizens alike, have struggled to make sense of the reproduction number of the 'virus' in understanding transmission prevention strategies, previously an exclusive preserve of epidemiologists.

What then are the potential contributory factors specific to healthcare workers?

The best way to explore this would be to start with healthcare workers and their perceptions of their own environment. Surveys by BAPIO Institute for Health Research[5], British Medical Association[13,14], the Royal College of Physicians [15] and a large study by Goldacre et al [16] all indicate that healthcare workers are facing varying degrees of challenges in availability of personal protection equipment, ability to provide care while complying with social distancing and in their challenge of finding ways to avoid exposure, when vulnerable. [5] While there appears to be an unacceptably high variation in the availability of personal protective equipment (PPE) between clinical settings in hospital, primary care and care homes, this risk appears to be double in those from a BAME background. [17] There are huge variations in the proportions of workers from a BAME background in roles with lower pay and higher exposure, both in clinical and supportive roles. Often these are workers employed by agencies contracted to the NHS and local councils and may not have the infrastructure to provide a comprehensive occupational health risk assessment and support. There is evidence that hospitals were prioritised by the NHS distribution networks for PPE, perhaps erroneously assuming that the risk in care homes or primary care settings was lower. The results of such policy decisions may be manifest in the high rate of overall deaths recorded in the UK and USA due to COVID-19, including care homes[18,] when compared to China, South Korea, Germany, South Africa, New Zealand and Australia.

As the realisation of the higher rate of disease and death among healthcare workers has come, there have been multiple appeals by organisations representing healthcare workers to institute risk assessment and enhanced protection-avoidance strategies. [19]

BAPIO has joined with BMA, Royal Colleges and other bodies to seek urgent action. [20] Public Health England and NHS England/Improvement have been working with public health experts to develop and implement such tools. Many large and progressive NHS organisations with strong BAME liaison networks have been quick to listen to the concerns of their staff and developed tools themselves. [21] A review of such tools undertaken by BIHR researchers as published in this journal and others 3 suggest that the methodology appears to be simply based on biological factors with a composite weightage added for 'ethnicity'.[22] This appears to be a fundamental flaw in the understanding of the vast range of potential issues which unite healthcare workers from a diverse social, professional, educational, cultural and religious backgrounds who are in the 'BAME' category. It is unfathomable why such a diverse group of professionals will have the same experience and what might be the factor uniting them to have the same 'statistical weightage' in the eyes of the novel coronavirus SARS-CoV-2.

Shilpa Ross, writing for the Kings Fund report 'We're here and you're there': lived experiences of ethnic minority staff in the NHS' [23] describes a compilation of stories of microaggressions, exclusion, differential treatment, stunted career progression, anxiety and even fear. There are reports of international healthcare workers from across the world having difficulties in obtaining support for family members, having to pay additional tariff for access to healthcare and restriction to changing their jobs due to Home Office regulations. In all reports of healthcare workers being afflicted by COVID-19 there is no information on their residence/ immigration status, but it is conceivable that a large proportion of healthcare workers in the frontline are facing such personal challenges. What impact does this insecurity have on the choices they make at work? Is it possible that such insecurities may stunt one's ability to raise concerns or challenge unfair treatment. Anecdotes and personal stories from many BAME staff across the country seems to suggest that there is a perceived link between the inequality rife in some organisations and the outcome in the face of COVID-19.

NHS England is committed to meeting the WRES targets and most senior leaders have pledged their support for equality for their patients and staff as well as valuing the richness of diversity. There is much more work to be done to get this message to the middle level of management and to leaders on the frontline. It is time for the scientific community to dissect and explore the multitude of risks emboldened within the 'ethnicity' factor in an objective as well as qualitative way. It is time for BAME leaders to raise awareness of the particular risks to their communities and support their members to come forward to join the BAME liaison committees being formed in different organisations, talk openly about the 'their lived-experience' and help their colleagues and middle-level leaders to take urgent mitigating actions, which are culturally appropriate. Too many lives have been lost perhaps inadvertently, in this pandemic. SARS-CoV-2 has rather dramatically shone the light on the social, health and economic determinants of outcomes in the general population and staff alike. This is a call for action and for ongoing research to explore this area. Science has been underpinning the strategy of many governments during the COVID-19 pandemic and it is imperative that 'science has to show the way' in mitigating the risk for BAME doctors facing adverse health outcomes, simply by the nature of their ethnic background.

Another important issue is the inhomogeneity among the cohorts who constitute the BAME population. For example, the umbrella term. "Asian" includes South East Asian, Chinese, and South Asians. Even among people from the Indian sub-continent, there are significant social, and cultural differences between people originating from India, Pakistan, Bangladesh, and Sri Lanka. These differences and their impact on health outcomes need to be explored in more detail, to be able to understand better, and mitigate the impact of differential outcomes in the BAME population.

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COVID-19 Pandemic - An Update

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In December 2019, a cluster of cases of pneumonia of unknown cause was detected in Wuhan, Hubei Province, China. A novel coronavirus (SARS coronavirus-2 (SARS-CoV-2)) was subsequently identified. The associated disease is now referred to as COVID-19. The source of the outbreak has yet to be determined. A zoonotic source to the outbreak has not been identified yet, but investigations are ongoing.

SARS coronavirus-2 (SARS-CoV-2) is a non-segmented, positive sense RNA virus. It is part of the family of coronaviruses. This contains four corona viruses which are widely distributed and usually cause the common cold but can cause viral pneumonia in patients with comorbidities. SARS and MERS – these caused epidemics with high mortality which are somewhat similar to COVID-19. COVID-19 is most closely related to SARS. It binds via the angiotensin-converting enzyme 2 (ACE2) receptor located on type II alveolar cells and intestinal epithelia (Hamming 2004). This is the same receptor as used by SARS (hence the technical name for the COVID-19, "SARS-CoV-2").

COVID doesn't appear to cause substantially reduced lung compliance (which is generally a hallmark finding of ARDS). The predominant problem might be either atelectasis or by alveolar inflammation. The virus is mutating, and virulence and transmission will shift over time unpredictably. There is evidence of more than one strain, and this may explain the variation in mortality. As of 12 March 2020, over 125,000 cases have been diagnosed in 125 countries and areas with a total of over 4,500 fatalities. Of these totals, over 44,000 cases and more than 1,400 deaths have been reported from countries outside mainland China. Within China, 84% of cases reported to date are in Hubei Province. There is evidence that human-to-human transmission is occurring. Hence, precautions to prevent human-to-human transmission are appropriate for both suspected and confirmed cases. Corona viruses are mainly transmitted by large respiratory droplets and direct or indirect contact with infected secretions. In addition to respiratory secretions, other coronaviruses have been detected in blood, faeces and urine.

For symptomatic, unconfirmed in-patients meeting the COVID-19 case definition, current guidance is use of Personal Protection Equipment (PPE), including, a fluid resistant surgical mask, gloves, apron and eye protection if risk of splashing into the eyes.

For confirmed cases of COVID-19, full PPE is needed with FFP3 respirator, disposable eye protection, preferably visor, long sleeved disposable gown and gloves.

For possible and confirmed cases of COVID-19 requiring an aerosol generating procedure, Full PPE is needed: FFP3 respirator, disposable eye protection, preferably visor, long sleeved disposable gown and gloves.

As corona viruses have a lipid envelope, a wide range of disinfectants are effective. PPE and good infection prevention and control precautions are effective at minimising risk but can never eliminate it.

Emerging information from these experiences has highlighted factors that could increase the risk of nosocomial transmission, such as delayed implementation of appropriate infection prevention and control measures combined persistence of coronavirus in the clinical setting. Under most circumstances, the amount of infectious virus on any contaminated surfaces is likely to have decreased significantly by 72 hours. In the absence of effective drugs or a vaccine, control of this disease relies on the prompt identification, appropriate risk assessment, management and isolation of possible cases, and the investigation and follow up of close contacts to minimise potential onward transmission. It is therefore important that standard precautions to include careful attention to hand hygiene and when handling any clinical waste, which must be placed in leak-proof clinical waste bags or bins and disposed of safely

Hospital Management

Presentation of Covid-19 is that of typical viral pneumonia and management is to do the basics well, delivering supportive care. The majority of cases will present as a mild, self-limiting flu-like illness. The key principle is that those who can be managed at home should be; hospital admission should be avoided wherever possible. The cause of death in Covid-19 is respiratory failure from Acute Respiratory Distress Syndrome (ARDS), or in those with underlying chronic lung disease or other frailty.

Signs and Symptoms

- Most patients present with constitutional symptoms and lower respiratory symptoms: fever and cough
- Current Criteria for testing for Covid-19 includes (a) clinical/radiological pneumonia OR (b) flu-like

symptoms OR (c) Adult respiratory distress syndrome (ARDS) AND (d) requiring hospital admission

- Patients may develop hypoxaemia and respiratory failure without breathlessness, particularly in the elderly. Up to 10% of patients can present initially with gastrointestinal symptoms (e.g. diarrhoea, nausea), which can precede the development of fever and dyspnoea
- Examination is generally non-specific; crackles may be present on auscultation, but the chest can be clear

Clinical Management

- Management is as for any viral pneumonia and is supportive
- It is vital to make early decisions around appropriate ceilings of care;
- Support hypoxia with oxygen, encourage oral fluid intake, avoid aggressive intravenous fluid resuscitation
- Sepsis is uncommon in primary Covid-19 infections. Where present, additional bacterial infection is probable.
- Wheeze can be treated with bronchodilators
- Assess for and treat complications of bacterial superinfection and for deterioration
- Steroids are not generally helpful and should be avoided unless there is another clear indication

When to contact Respiratory for advice or support

- For escalating oxygen requirements, if patient is for full escalation then early discussion with intensivists will be required
- Early onset of mechanical ventilation may be required in the advent of hypercapnoeic respiratory failure (RF)
- If imaging findings are inconsistent with Covid-19 then consider whether a CT scan of Chest is likely to alter management
- Patients with underlying co-morbidities or chronic respiratory disease are particularly vulnerable

Investigations

- White cell count (WBC) tends to be normal
- Lymphopoenia is common
- Mild thrombocytopenia is common
- C Reactive protein (CRP) correlates to disease severity; respiratory failure with a normal CRP is unlikely to be Covid-19
- High CRP in confirmed Covid-19 is a poor prognostic indicator and may suggest complicated disease
- Procalcitonin tends to be normal

Radiology

- Chest radiograph (CXR)
- May show patchy ground glass changes, peripheral and basal, but may be subtle and are non-specific
- Pleural effusion is uncommon
- Cavitation, lymphadenopathy, masses are uncommon
- Computed Tomography (CT) scan of Chest
- A CT will not add to management unless there are inconsistent findings on the CXR and should therefore be avoided

Management

No antiviral has been proven to be active against COVID-19 but general principles of managing viral pneumonia and ARDS remains. There has been some concern about non-invasive ventilators (NIV) and high flow nasal oxygen (HFNO) in terms of transmission to hospital staff. Recent publications suggest that newer HFNO and NIV systems with good interface fitting do not create widespread dispersion of exhaled air and therefore should be associated with low risk of airborne transmission. Invasive ventilation poses a risk during intubation. Principles of ventilation is as per ARDS protocols (tidal volumes around 6 ml/kg). There is some evidence that prone ventilation is of benefit as is a permissive hypercapnoea.

Prognosis

The vast majority of patients who are infected will have a mild disease and do not get significantly ill or require hospitalisation. About 10-20% of those admitted to hospital will need critical care input. Mortality is reported to be between 2-5%. Risk factors include older age, coronary artery disease, hypertension, diabetes mellitus and Chronic obstructive pulmonary disease

Resources:

//www.cdc.gov/coronavirus/2019-ncov/publications.html
https://www.nhs.uk/conditions/coronavirus-covid-19/

Does Concurrent Existence of Asthma or COPD Affect Susceptibility and Outcomes to Novel Coronavirus Infections?

A Short Review of Evidence and Mechanisms

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Keywords: Asthma, COPD, COVID19, ACE2 receptors

ABSTRACT
The SARS-CoV-2 virus causing COVID-19 pandemic across the world has highlighted the risk of human-to-human transmission, the speed of spread in a globally mobile population and the need for health services to be flexible in their responses to hitherto unknown challenges. One of the hallmarks of COVID-19 is severe acute respiratory syndrome presenting with widespread viral pneumonitis and respiratory failure. It is therefore not unusual for patients with chronic lung diseases such as asthma, COPD and bronchiectasis to be concerned regarding their particular vulnerability. As healthcare professionals responsible for the care of such patients, it is important to understand how the SARS-CoV-2 virus impacts on the respiratory system and the outcomes for patients with chronic lung disease. This review examines the evidence and offers sensible guidance until more is known.

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Background
As the world faces a pandemic with the novel coronavirus "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) causing a spectrum of rapidly spreading illness dubbed COVID-19, one of the key anxieties relates to the susceptibility and outcomes amongst patients with pre-existing lung disease. The typical patients with symptomatic infection present with fever, cough, breathlessness and gastrointestinal symptoms. Profound hypoxia appears to be a typical picture and often patients progress to needing early invasive mechanical ventilation rapidly. The radiological picture is one of bilateral infiltrates typically seen in adult respiratory distress syndrome (ARDS), the full blood count shows lymphopaenia while the inflammatory markers including non-specific C-reactive protein, d-Dimer and procalcitonin are elevated. There is very little data available currently from the analysis of outbreaks in China and South Korea, but patients and physicians are faced with the challenge of giving common sense but evidence-based guidance. The mortality appears to be variable and is reported between 3-10%. Particularly vulnerable are the elderly and those with hypertension, diabetes or kidney disease.[1] There is a presumption that patients with respiratory disease will have negative outcomes when infected with coronavirus. However, the evidence suggests that this may not be the case. This article will attempt to explore the vulnerabilities and draw a quick set of conclusions until more information is available.

Virology
Human coronaviruses are common throughout the world. Coronaviruses are enveloped, non-segmented, single-stranded, positive-sense ribonucleic acid (RNA) viruses named after their corona- or crown-like surface projections observed on electron microscopy that correspond to large surface spike proteins. These viruses are host-specific and can infect humans and a variety of different animals as well. Four distinct genera have been identified: alpha-, beta- gamma-, and delta-coronavirus. SARS and middle eastern respiratory syndrome (MERS) are both in the genus beta-coronavirus.[2] Based on the preliminary information of this novel virus, it is considered that SARS-CoV-2 is the third zoonotic human coronavirus of the century and is transmissible from person to person. Currently, it is still unclear about the origins and possible intermediate animal vectors of SARS-CoV-2 although, in addition to bats, the pangolin species has been highlighted as a natural reservoir of similar coronaviruses, based on analysis at a whole-genome level.3 The exact mechanism of human-to-human transmission is also unclear but it is thought to occur through the inhalation of respiratory droplets or coming in contact with infected surfaces prior to touching the eyes, nose or mouth.[4]

Respiratory Diseases
It is well established that respiratory tract viral infections are associated with asthma exacerbations. Several types of viruses, such as rhinovirus (RVs) and respiratory syncytial

virus (RSV) have been implicated, whereas for coronavirus there is no data yet. There is consensus that a hypersensitivity state, a genetic predisposition, deficient antiviral response, impairment of immune cell function, damage of epithelium, cytokine and chemokine response may all contribute to the synergistic promotion of allergic disease exacerbation by allergen and virus, especially for respiratory tract allergy.[5,6]

The prevalence of chronic obstructive pulmonary disease (COPD) in people ≥40 years old was 13.7% in China and respiratory tract virus infection is a common trigger for acute exacerbations.[7] However, the prevalence of SARS-CoV-2 infection in COPD patients is not clear and the influence of smoking behaviour on the susceptibility to this virus has not been investigated. Huang et al.[8,9] have shown a rate of chronic COPD of approximately 2% and 2.9%, respectively amongst COVID-19 patients in Wuhan.[10] Subsequently, Chen et al. [10] have reported a rate of approximately 1% for respiratory system diseases, different from an estimated COPD prevalence of between 1.2–8.9% in different regions of China. Moreover, interstitial lung disease, bronchiectasis or asthma appear to be under-reported.[8]

In previous coronavirus epidemics, lower respiratory tract infections (LRTI)s with coronavirus in infants and children tended to be mild, unless the infant or child has an infection with a co-viral pathogen, has an underlying pulmonary disorder like asthma or cystic fibrosis, or is immunocompromised (haematological malignancy or solid tumour).[2]

Mechanism

Majority of patients with acute wheezy respiratory illness, (62%-95% of children and 41-78% of adults) have demonstrable infection with respiratory viruses in both hospital and community settings. Rhinoviruses (RVs) are the most frequently detected type of virus at all ages, whose infection could lead to more severe and longer-lasting lower respiratory tract symptoms. In addition to RV, other respiratory tract viruses, such as respiratory syncytial virus (RSV), influenza viruses (IfVs), coronaviruses (CoVs), human metapneumoviruses (HMPVs), parainfluenza viruses (PIVs), adenoviruses (AdVs), and bocaviruses (BoVs), had all been detected in subjects with asthma exacerbations.7

Coronaviruses such as CoV-OC43 and CoV-229E are transmitted primarily during winter have been loosely linked to asthma exacerbations in children and adults. However, in a systematic review the pooled prevalence of CoV infection during asthma exacerbations was only 8%, ranking below RV (42.1%, the highest), RSV, herpes simplex virus (HSV), enterovirus (EnV), and IfV. Overall, CoV seemed to have a minor, if any, contribution to acute asthma exacerbations, and CoV infections were frequently co-infected with other viruses.

Most animal models found no definite association with SARS-CoV and MERS-CoV which could cause severe respiratory disease in humans, and asthma. However, in a retrospective study of children admitted to hospital in Seattle with LRTI with coronavirus, the children who were immunocompromised or were infected by a co-pathogen, i.e RSV or had an underlying pulmonary disorder, were at greater risk for severe LRTI.[9]

Patients experiencing exacerbations of severe COPD usually demonstrate existence of multiple viruses concurrently in their airways suggesting that host response to viral infections may be dysregulated in COPD.[11,12] Human CoV, in particular HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1, were shown to trigger acute respiratory illness in elderly adults with COPD and can result in hospitalisation.[13] Activation of the innate immune axis leads to increased numbers of invariant natural killer T-cells (iNKT-cells) and alternatively activated interleukin IL-13-producing macrophages in the lung. Thus, viruses cause a more severe disease exacerbation with a heightened inflammatory response leading to an accelerated loss of lung function.[14]

Infection Pathways

The epithelial cell is the principal site of viral infection in the airways and plays a central role in viral modulation of airway inflammation by the release of a variety of cytokines, chemokines, and growth factors. Antiviral defence depends at least in part on a network of mucosal epithelial cells and macrophages. When this network is compromised, the host is highly susceptible to infection, but network components can be engineered to provide increased resistance. Development of in vitro experimental models of virus infection has identified interferon IFN-β and nitric oxide (NO) as possible therapeutic targets to augment antiviral immunity, and (nuclear factor kappa-light-chain-enhancer of activated B cells) NFκB as a target for the development of anti-inflammatory therapies.**15**

Viral entry relies on a fine interplay between the virion and the host cell. Infection is initiated by the interaction of the viral particle with specific proteins on the cell surface. After initial binding of the receptor, enveloped viruses need to fuse their envelope with the host cell membrane to deliver their nucleocapsid to the target cell. Coronaviruses use a variety of receptors and triggers to activate fusion, however fundamental aspects that enable this initial step of the viral life cycle to be conserved.[16] The receptor of the SARS-CoV is the angiotensin-converting enzyme 2 (ACE2).[17] ACE2 is a type I integral membrane protein abundantly expressed in lung and gastric tissue; it is a mono-carboxypeptidase that hydrolyses angiotensin II. There is experimental evidence of the likelihood of genetic overexpression or pharmacological activation of the renin angiotensin system by upregulation of the ACE2 in diabetic db/db mice.[18] There is an emerging hypothesis therefore that this upregulation of the RAS may play a role in the observed increased susceptibility of patients with hypertension or cardiovascular disease to coronaviruses. Furthermore, due to the distribution of ACE2 in the body, the lung is one of the main viral entry points.

Transmission by Aerosol

Aerosol-generating procedures (AGPs) are increasingly recognised as important sources for nosocomial transmission of viruses such as MERS-CoV and SARS-CoV, for example, intubation was investigated as a possible cause of Ebola virus (EBoV) transmission among health-care workers in the United States.[19,20] With regards to COVID-19, a study looking at the stability of SARS-CoV-2 found that aerosol and fomite transmission of the virus is plausible because the virus appears to stay viable and infectious in aerosols for hours.[21] The site of deposition after an inhalational event can affect disease kinetics

and pathogenesis, however, the deposition of respiratory pathogens in the lungs will generally result in the more rapid aggressive infection with higher mortality rates. Evidence exists in both animal models and humans for a number of entry/ deposition sites include upper airway lymphoid tissues. lower respiratory tract, the olfactory system, GI tract, and conjunctiva.[22]

Table 1: Potential aerosol-generating medical procedures involved in nosocomial virus transmission. (AGMP How/ Where Aerosols May Be Generated)

Bronchoscopy *	Induced cough, respiratory tract
Cardiopulmonary resuscitation *	Induced cough, respiratory tract
Non-invasive ventilation *	(BiPAP, CPAP, HFOV) Possible mechanical dispersal of aerosols, respiratory tract
Tracheal intubation *	Induced cough, respiratory tract
Manual ventilation *	Possible mechanical dispersal of aerosols, respiratory tract
	Surgery
	Cutting bone and tendon, and irrigation aerosolise blood
Sputum induction -	Induced cough, respiratory tract
Nebuliser treatment -	Possible mechanical dispersal of aerosols, respiratory tract
Suctioning -	Possible mechanical dispersal of aerosols, respiratory tract
Laser plume -	Mechanical dispersal of aerosols

* Possible association with SARs-CoV transmission23

In a meta-analysis, procedures reported to present an increased risk of transmission included tracheal intubation odds ratio 6.6 (confidence interval CI 2.3, 18.9), tracheostomy [OR 4.2 (CI 1.5, 11.5)], non-invasive ventilation [OR 3.1 (1.4, 6.8)], manual ventilation before intubation [OR 2.8 (CI 1.3, 6.4)] and unprotected eye contact with secretions (OR = 7.34, p = .001).[20,24]

Other intubation associated procedures, endotracheal aspiration, suction of body fluids, bronchoscopy, nebuliser treatment, administration of O2, high flow O2, manipulation of O2 mask or BiPAP mask, defibrillation, chest compressions, insertion of a nasogastric tube, and collection of sputum were not statistically significant.[23,24] Theoretically nebulisation also generates droplets and if nebulisation is associated with a productive cough this may expose staff or bystanders by the airborne route to nosocomial infection which is a widely held expert opinion though still remains controversial.[25,26] Use of high-frequency oscillation, high-flow nasal oxygen and continuous positive airway pressure are also highly likely to pose a risk of transmission to healthcare staff. Otolaryngological and dental procedures utilising high-frequency mechanical devices also pose a significant risk. However, there is a scientific debate on how evidence from such studies should be interpreted into national personal protection guidance for frontline healthcare staff. It is Public Health England's view that administering pressurised humidified oxygen and nebulised medication are not thought to carry a significant infection risk because the aerosol is generated from material other than the patient's secretions.[27]

Investigation of small cohorts of nosocomial infection in 2003, showed that staff who used masks, gowns, and handwashing were less likely to develop SARS than those who did not use them, but the association for gloves was not significant. Both surgical and US National Institute for Occupational Safety and Health (N95) masks were significantly associated with protection. The data suggested that precautions against droplets and contact may be adequate for prevention of nosocomial SARS, where no AGPs are undertaken.[28]

Treatment options

Currently, the mainstay of response against the COVID-19 pandemic is based on avoidance of transmission, particularly to the vulnerable populations, social distancing measures, personal protection and hand hygiene.[29] WHO recommends strategies for extensive tracing - testing of all contacts and when community transmission is established moving to a strategy of comprehensive detection by widespread testing.[30] For patients presenting with SARS to hospital, there is a need for the rapid expansion of intensive care capacity as this may determine mortality. Supportive care — including management of organ failure and prevention of complications, especially acute respiratory distress syndrome, organ failure and secondary nosocomial infections — remains the most important management strategy for SARS and MERS, as there is currently no specific antiviral treatment that has been proven to be effective in randomised controlled trials. There are no established treatment regimens, but rapid, open-label trials are underway.

The approach to treatment is based on;

- Virus-based therapies include monoclonal antibodies and antiviral peptides that target the viral spike glycoprotein, viral enzyme inhibitors, viral nucleic acid synthesis inhibitors and inhibitors of other viral structural and accessory proteins.
- Host-based therapies include agents that potentiate the interferon response or affect either host signalling pathways involved in viral replication or host factors utilised by coronaviruses for viral replication.[31]

Inhaled corticosteroids

The inclusion of inhaled corticosteroids in the FDA-requested label change warning physicians that treatment with corticosteroids may place patients with viral infections at increased risk of serious complications does not appear to be warranted. Steroids have been used by some Chinese physicians in the treatment of COVID-19 and it is thought to able to stop the cytokine storm; however, this only appears to occur during a narrow window after the SARS-CoV-2 virus has been eliminated by the human immune response

because otherwise, the virus could replicate faster and exacerbate symptoms.[32] It is also hypothesised that routine use of corticosteroids to treat this virus could result in the exacerbation of COVID-19-related lung injury and in cases of ARDS resulting from COVID-19, it has been suggested that glucocorticoids should be avoided based on the evidence that they can be harmful in viral pneumonia and ARDS caused by influenza.[33,34,35]

However, so far there does not appear to be any evidence linking the daily use of corticosteroid inhalers as a preventer of asthma attacks to poorer outcomes once the patient contracts COVID-19.

Ernst and co-workers used a large health database to identify patients with COPD and to study the frequency of inhaled corticosteroid use in those admitted to hospital because of pneumonia compared with matched control subjects. Current use of inhaled corticosteroids was associated with an increase of 70% in the rate of hospital admission for pneumonia. The admission rate was greatest with the highest doses of corticosteroids used, and a reduction in risk once inhaled corticosteroids were stopped was observed. A 53% increase in pneumonia death within 30 days of admission with inhaled corticosteroids was also found.[36] This has also been shown in large epidemiological association in South Korea with asthma patients.[37] However in a cohort of viral pneumonia patients the inhaled corticosteroid (fluticasone) was associated with a lower risk of pulmonary infiltrates in patients with influenza A (H1N1) infection.[38]

Mortality

The Intensive Care National Critical Care Audit Centre (ICNARC) data from approximately 2,500 admissions to intensive care units in the UK published on 4 April, shows only 1.1% of patients admitted to intensive care units and 1.3% needing advanced ventilatory support had underlying respiratory disease.[39]

Conclusion

SARS-Cov-2 is a severe threat to a huge swathe of the world population. Patients who are older, with co-morbidities such as hypertension, diabetes, kidney disease remain at significantly higher risk of poor outcomes. It is understandable that patients and health care workers with asthma or COPD are likely to be concerned with the potential for being severely affected. However, the data from China and the UK does not indicate that patients with underlying COPD or asthma have an increased incidence of coronavirus infection or are at risk of significant adverse outcomes.

It is well established that these patients are at greater risk of viral infections (not coronavirus) and combination of viruses or secondary bacterial infections are associated with LRTIs and need for hospital treatment. There is a small but real risk of nosocomial infections and transmission by nebuliser therapy of viral fomites/droplets, although the UK PHE guidance does not classify this as such.

Hence, until further robust data is available, here are some common-sense tips;

- Recommend practice of strict transmission avoidance and social distancing
- Recommend vigilance in personal protection by frequent hand washing or use of a surgical mask (against droplet transmission)
- Monitor asthma control and if possible recommend a lower dose of ICS
- Avoid nebuliser use
- If there are signs of exacerbation, treat promptly avoiding prolonged or high dose corticosteroid use and consider early treatment of secondary bacterial infections
- If admitted, consider entry into trials of antivirals, chloroquine or combinations

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Self-reported Occupational Risk for COVID-19 in Hospital Doctors from Black Asian & Minority Ethnic Communities in UK

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Abstract

Emerging data from COVID-19 pandemic shows a trend for increased risk for healthcare workers in the UK, compared to other countries. In addition, there is a disproportionately high risk observed in healthcare workers from Black, Asian & Minority Ethnic backgrounds. This high risk is independent of biological or demographic variables. This paper presents sub-analysis of a larger survey of healthcare workers, particularly describing possible occupational risk of COVID-19 in a subset of doctors in UK hospitals from a BAME background. The results show higher rates of inability to access personal protection or comply with social distancing. The inability to self-isolate was associated with a 1.7x higher risk of COVID-19. The results of this survey suggest further research is needed to explore and understand institutional factors that may explain excess risks to BAME hospital doctors.

Key words: COVID-19, BAME, Healthcare workers, Personal Protective Equipment, Social distancing

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Background

By the nature of their work in caring for patients, healthcare workers (HCWs) remain at the forefront of the risks of acquiring COVID-19. Compared to published data from China, there is a high prevalence of HCWs being infected in France, Italy, Spain and USA during the current pandemic [1-3] Analysis of hospital admission data in the UK, clearly demonstrates a higher risk of COVID-19 severe disease and death in Black, Asian and minority ethnic (BAME) background being affected in the UK and USA [4]. To date the mortality among UK HCWs has surpassed that of UK soldiers in the Iraq war [5]. Further breakdown of data reveals a higher risk of severe COVID-19 disease and death among BAME HCWs than their Caucasian peers [6]. UK National Health Service employers are employing potential strategies to identify and shield staff at risk.

The potential causes of this excess risk of death or disease among UK HCWs remains poorly understood. Population level data analysis suggests that certain inherent or biological variables such as age, sex, body mass index, concurrent cardiovascular, diabetes or kidney disease and previous levels of activity may determine outcomes. However, when such potential biological contributory factors are accounted for in multivariate analysis, BAME background appears to remain an independent risk [7]. Exploring non-biological factors, it is clear that BAME HCWs are a widely diverse group in religious, socio-cultural aspects as well as perceptions and beliefs [8-9]. Yet the observed data demonstrates a unique commonality in the severity of outcomes within this pandemic, which cannot be explained away easily. A deeper exploration of differential experience of BAME HCWs in the UK NHS may be necessary within the context of their shared occupational experience and perceptions.

The British Association of Physicians of Indian Origin, in its 25 years of experience in working with diverse groups of HCWs, predominantly doctors from the Indian subcontinent through engagement with its national membership and their widening social networks provided the perfect vehicle for exploring the risks and perceptions of BAME HCWs. In a national online survey of a wide range of HCWs across different clinical settings, there were clear themes demonstrating perceptions of enhanced risks and behaviours pertaining to profession, clinical exposure, personal protection and even organisational issues [7]. Published mortality figures among HCWs showed that as a group, 95% of doctors who had lost their lives in the current pandemic, were from a BAME background [6]. In addition, within the heterogeneity of the survey respondents, hospital doctors from a BAME background provided a subset with the most common shared experience and a group that was most likely to provide an insight in understanding the excess mortality. Hence, this group was chosen for a subset analysis.

Methods

The components of this survey were conceived through engagement with an active focus group (BAPIO Think Tank)

composed of 67 members of BAPIO. The investigators from the BAPIO Institute of Health Research then designed the survey questions by expert consensus. The anonymised, cross-sectional, online survey was then distributed by email links to all members of BAPIO and through social networks for a period of 2 weeks in April 2020. Results were collected online, using Google forms. Details of the survey components, questions and results are published [7]. A subset of BAME hospital doctors were selected from the survey respondents during this analysis. Non-parametric tests including Chi square tests and multivariate logistic regression analysis was applied to adjust for potential contributory variables in generating odds ratios, using SPSS statistical software (SPSS v26, IBM Inc., USA).

Primary outcome - Self-reported, point prevalence of (i) access to personal protective equipment (PPE), (ii) ability to comply with social distancing guidance during work/ commuting, (iii) ability to self-isolate if at enhanced risk and predicted risk of COVID-19 (defined as positive viral PCR swab test result or self-isolating due to classical symptoms based on published Public Health England and NHS guidance.

Results

There were 1243 BAME hospital doctors in the cohort with a distributed age range **(Figure 1).** Majority of respondents were middle-aged (40-60 years of age) and 33% had one or more comorbidities (cardiovascular, hypertension, cerebrovascular, kidney, diabetes, chronic lung disease and mental health issues **(Figure 2).**

Occupational measures to reduce risk:

Only 22% have reported access to or compliance with recommended / appropriate PPE **(Figure 3)**. Similarly, only 22% of respondents were able to fully comply with social distancing (SD) guidance at work. Around 35% of hospital doctors reported that it was not practical, given the nature of the clinical setting, to comply with SD at work and 36% reported not being able to fully comply with SD guidance **(Figure 4).** There were 23% of respondents who reported inability to self-isolate when they perceived there was a personal / family risk of COVID-19 infection **(Figure 5).**

Figure 1: Histogram showing the age ranges for BME doctors.

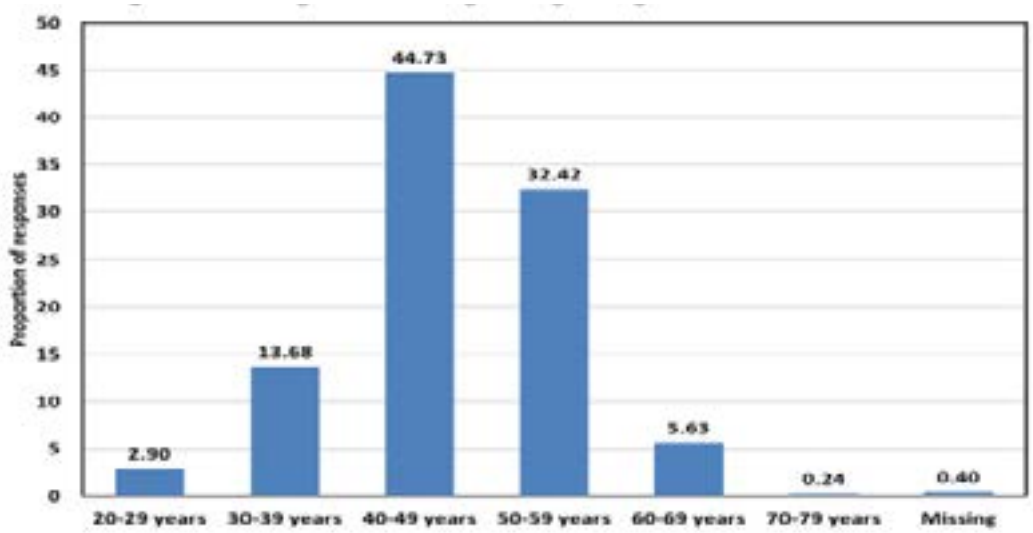


Figure 2: Histogram showing the proportion of BAME doctors with comorbidities.

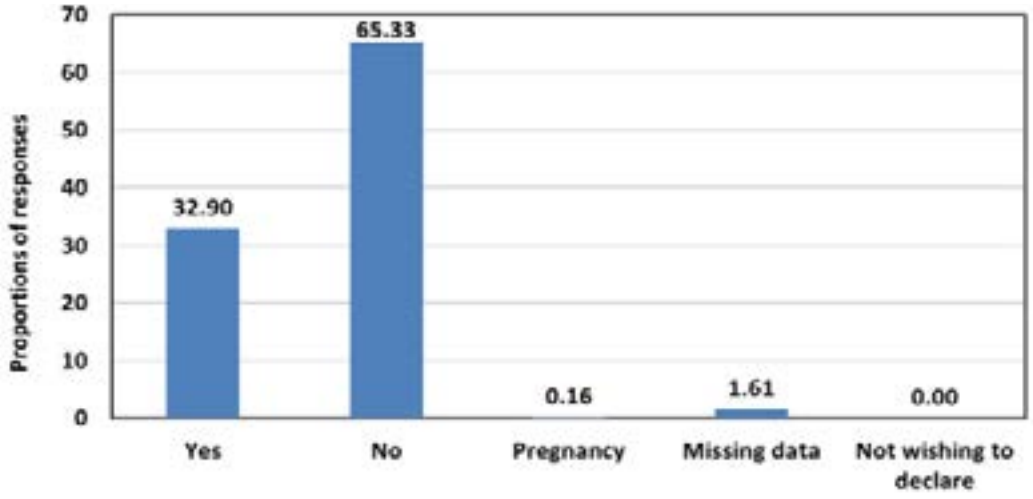


Figure 3: Pie charting showing Personal protective equipment (PPE) at work place

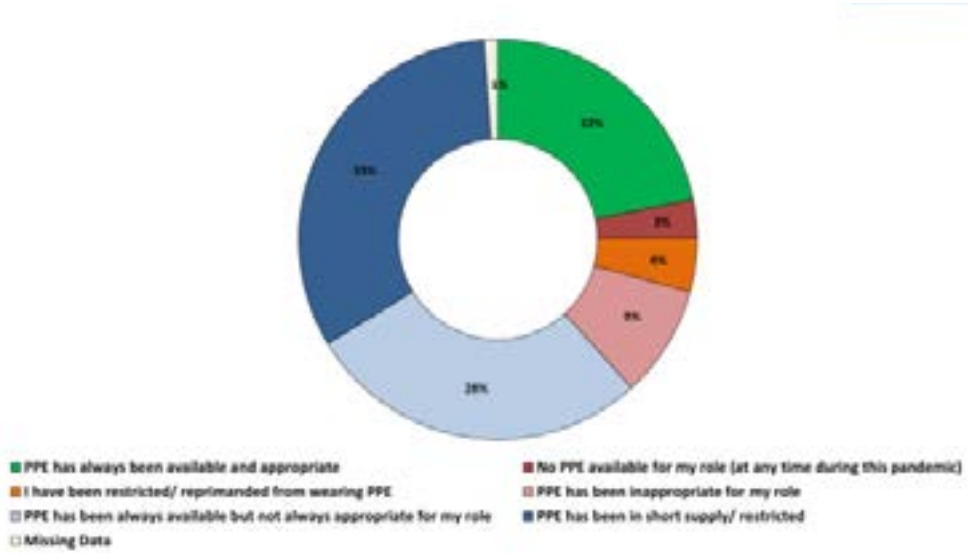


Figure 4: Pie chart showing ability to comply with Social Distancing (SD)

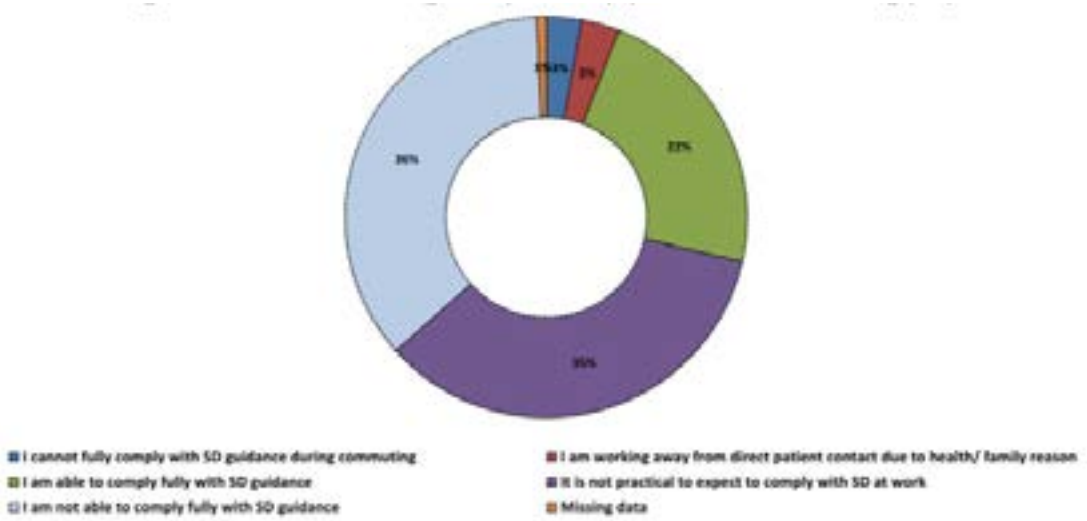
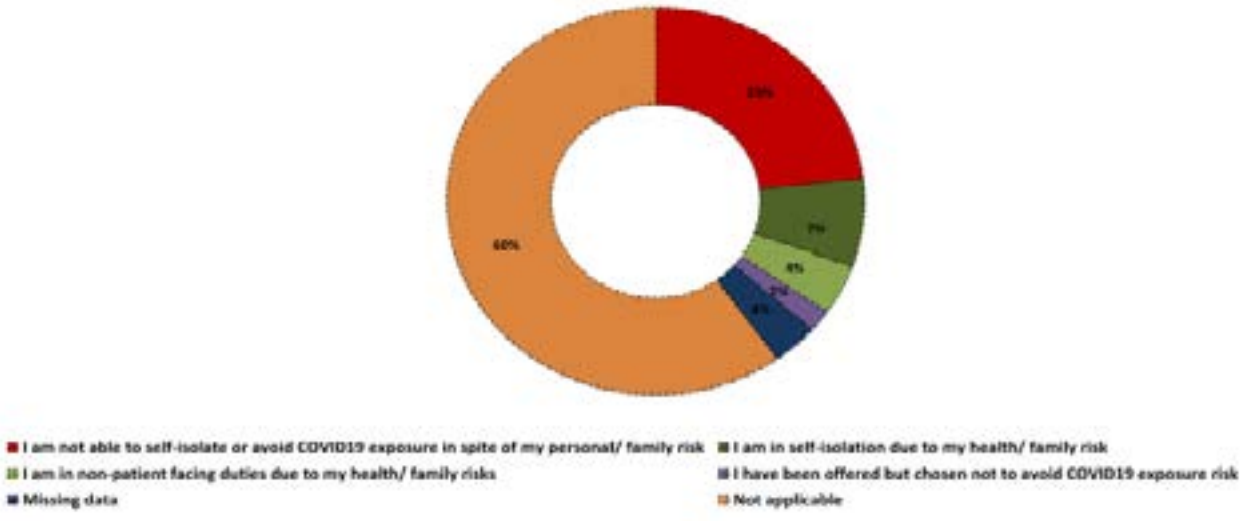


Figure 5: Reported self-isolation and risks to self/family



Self-reported COVID19 illness and risk analysis:

Around 5% of the hospital doctors were in shielding or proactively avoiding exposure to COVID-19 and 18% reported a confirmed positive viral PCR confirming COVID-19 or were self-isolating at home due to symptoms of COVID19 **(Figure 6).** The odds ratio for BAME hospital doctors having COVID-19 diagnosis or symptoms associated with COVID-19 (where testing was not available), when not being able to self-isolate due to personal risk was 1.73 (confidence interval 1.19-2.52, p=0.004) after adjusting for age and comorbidities.

What does the data mean?

The results of this subset analysis of hospital doctors from a BAME background was conducted to explore the likely causes of disproportionate representation of this group in adverse outcomes in almost all recent published data in the UK. The BAPIO online survey of healthcare workers captured an overwhelming majority of hospital doctors from BAME backgrounds, so offered us a unique opportunity to explore the risks and potential vulnerability in this group [7]. Our data showed that nearly 1 out of 5 (18.26%) had COVID-19 or had symptoms requiring quarantine. This figure is higher than that reported for prevalence of infection in HCWs from similar surveys [1, 10-11].

We then explored the potential confounding factors that might explain this risk. Looking at personal protective equipment, we found almost half of BAME hospital doctors did not report that they had access to PPE as per PHE guidance. An overwhelming 3 out 4 reported not being able to comply with social distancing guidance when at work or commuting for work. These proportions appear to be higher than reported in other surveys [10, 11]. What appeared to be most concerning was our analysis suggesting that hospital doctors from a BAME background, who were unable to comply with self-isolation guidance (based on a personal risk characteristic for COVID-19), were 1.7x more likely to have COVID-19; even when adjusted for age and comorbidities.

.

There are potential limitations to the extent of extrapolation of the conclusions drawn from this survey when compared to the population of BAME doctors in the UK health service. As explored in our original paper [7], these include a self-selection bias, the dependence on the accuracy of the respondents' self-declaration of their profession and circumstances, the perception bias for reporting issues with PPE, social distancing and the diagnosis of COVID-19. These limitations are mitigated to an extent by the nature of the distribution of the questionnaire through membership databases and bona-fide professional social networks. Clearly, the results of a survey such as this and its subset analysis must be interpreted with caution, is unlikely to be generalisable beyond the defined group and merely suggests that urgent further well-designed, controlled studies are necessary.

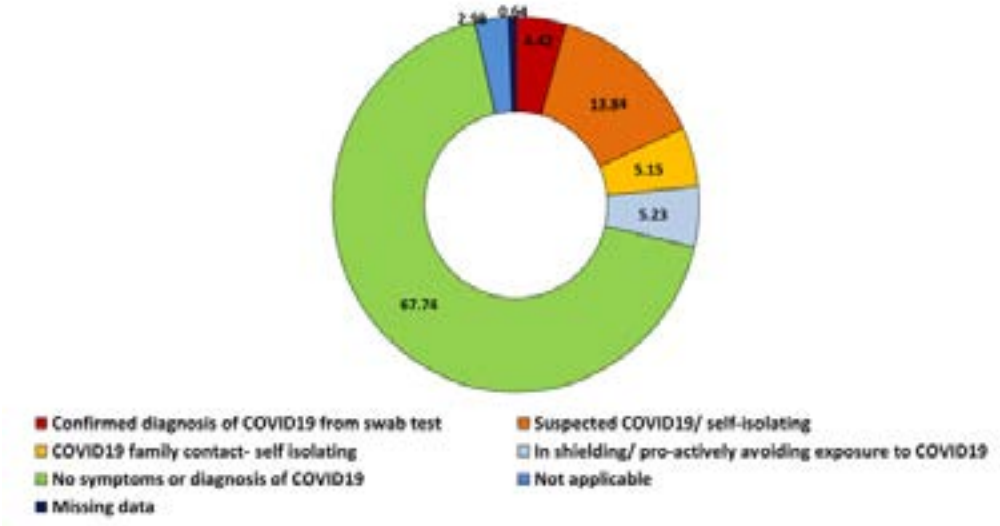
What should be done?

Firstly more studies are needed urgently to confirm the 'vulnerability or health risk' for BAME doctors in the COVID-19 pandemic by comparing a case-control study with non-BAME doctors and perhaps extended to all health care workers who are at the forefront of the COVID-19 response. The scientific exploration of risks must not shy away from examining uncomfortable topics that might constitute independent variables including individual and organisational factors. Discrimination has been linked to poorer health outcomes [12] and this will be a valid variable to examine amongst others.

Secondly, until further robust research results are available, BAME doctors with vulnerability should be offered/ encouraged to comply with strategies for avoidance of exposure. These may be in the form of redeployment away from high risk areas, with limitation to direct patient contact or access to enhanced PPE as available in aerosol generating clinical settings.

And, finally these results pooled with emerging clinical data

Figure 6: Pie chart showing COVID19 related illness in BAME hospital doctors



should be computed to create a risk stratification tool so HCWs with known vulnerability (i.e. ethnicity) can be offered appropriate safety and deployment. It is encouraging to note recent guidance on risk assessments of BAME healthcare workers at workplace in NHS [13], though a validated culturally appropriate risk assessment tool is urgently needed accounting for socio-cultural factors specific for BAME communities.

Author's contribution and conflict of interest statements

The authors have no declared conflict of interest pertaining to this study. Indranil Chakravorty (IC), Sunil Daga (SKD), Geeta Menon (GM), Subodh Dave (SD), Subarna Chakravorty (SC), Neeraj Bhala (NB), Ramesh Mehta (RM) & JS Bamrah (JSB) are honorary members of BAPIO Institute for Health Research, Bedford, UK. BAPIO is a national professional body of multi-professional health care workers in the UK since 1996 (https://www.bapio.co.uk/). Individual contributions are study design (IC, SKD, JSB & SC); analysis (IC & SKD); interpreting the results and writing the manuscript (all).

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CPD - Radiology Quiz

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A 74-year-old man with a recent Covid-19 infection presented to the hospital with new onset of breathlessness and left sided chest pain. His Chest XR is given below.

Risk Stratification in COVID-19: A Review

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Abstract
Following the first few reports of a novel coronavirus affecting a large number of Chinese residents in the city of Wuhan, it was rapidly clear that the disease did not affect everyone to the same degree. Often this is based on socio-political factors, leadership and resilience of the public health infrastructure. The predicted surge in infections due to high viral transmission rates threatened to overwhelm every healthcare system in the world. However it has become clear that the experience of different population groups or subsets with variable characteristics was not the same. This review assesses pre-existing conditions that were identified as pathophysiological or sociodemographic risk factors of COVID-19. This will allow policy makers to decide what mitigation is needed to reduce those risks and protect the public from infections.

Keywords; COVID-19, risk stratification, socio-economic factors

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Introduction

Following the first few reports of a novel coronavirus affecting a large number of Chinese residents in the city of Wuhan, it was rapidly clear that the disease did not affect everyone to the same degree. It emerged that whilst infected children were virtually symptom-free, older male patients with specific underlying co-morbid conditions were more likely to suffer from a severe form of the disease and to die of it as a result. When the disease assumed pandemic proportions, these disparate outcomes were also reflected in clinical data obtained from other parts of the world.

In response to data related to disparate outcomes, it became important for countries to identify groups within the population that were more vulnerable to adverse outcomes of the disease. This was done so that targeted risk mitigation intervention for uninfected persons and treatment escalation for infected persons could be adopted. One group of people at high risk of infection were healthcare and other essential workers who were at continuous risk of occupational exposure to the virus despite widespread restriction in economic activity in other sectors.

Countless reviews and meta analyses have identified a number of risk factors for adverse outcomes due to COVID-19 within the population. With emergence of large-scale population-based data, it became apparent that not all disparities in outcome in some high-income countries could be explained by the well-established risk factors based on gender, age and co-morbidity alone. This review assesses pre-existing conditions that were identified as pathophysiological or sociodemographic risk factors of COVID-19. This will allow policy makers to decide what mitigation is needed to reduce those risks and protect the public from infections. We will have a particular emphasis on risk among healthcare workers and will outline areas where future work is needed to establish causality of some of the identified risk factors. Clinical and laboratory features of patients with confirmed COVID-19 that are associated with high risk of death will not be discussed in this review.

Demographic risk data from China

Early analysis of patient characteristics among 113 deceased patients in China indicated that people who died were more likely to be significantly older, of male gender and with a history of cardiovascular disease including hypertension[1]. Subsequently, two meta-analyses of Chinese studies involving over 1500 patients each identified that hypertension, chronic obstructive pulmonary disease, cardiovascular disease and cerebrovascular disease were significant risk factors for COVID-19 patients[2,3]. A much larger nationwide cohort of >44,000 confirmed cases was reported by the Chinese Centre for Disease Control (CCDC), where co-morbid risk factors for death were age, hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer[4]. Reports from other Chinese groups also identified smoking[5] and obesity[6] as independent risk factors for poor outcome.

Several studies indicated that children were largely unaffected. In the largest population based study from China, children under 10 accounted for 1% of over 72,000 confirmed cases4 and those with co-morbid conditions such as active cancer therapy were at risk**7.**

Analysis of COVID-19 in healthcare workers (HCW) in the large CCDC study showed that HCW infections accounted for 3.8% of >44,000 confirmed cases. Other reports have indicated that 90% of HCW infections in China occurred in the Hubei Province and HCW were infected during the early stages of the pandemic (January to mid-February 2020) when transmission dynamics were not sufficiently understood[8,9]. The greatest risk of dying of COVID-19 among Chinese HCW included working in community hospitals

in the Hubei Province and being of male gender. Several interventions were put in place once HCW death risks were apparent. This included improving shift patterns to allow more rest, improving the availability of personal protective equipment and supporting psychological health of HCW in the community. Incidentally, road traffic accidental deaths among HCWs also reduced following implementation of these measures[9].

Demographic risk data from outside China

Some of the largest population-based data have emerged from the UK, which have mostly mirrored clinical risk of death by COVID-19 that had emerged from the early work in China. UK data have been addressed by the rapid deployment of several large multi-centre observational studies. One such study of hospital admissions with COVID-19 was the ISARIC4C study involving over 16,500 patients [10]. Pre-print data from this study have indicated that male gender, age above 50, presence of chronic cardiovascular, pulmonary or renal disease, obesity and dementia were independent risk factors for death. Surprisingly, data from another multi-centre observational study, the Intensive Care National Audit and Research into COVID-19 study indicated that patients from minority ethnic backgrounds represented over a third of the patients admitted to UK critical care units despite census data from 2011 indicating that minorities constitute about 11% if the total UK population[11]. The proportion of minority ethnic patients admitted to critical care units with COVID-19 were far higher than those admitted in preceding years with seasonal influenza[11]. The reason for this disparity is not known and may become clearer once more prospective data is accrued over time.

Another large dataset obtained from primary care health records of over 17 million UK NHS patients was recently available as pre-print. This showed that ethnic minority status and social deprivation scores were independent risk factors for in-hospital death from COVID-19[12]. Similarly, reports from the US media indicate that disproportionately higher number of people from ethnic minorities and economically deprived communities are dying of COVID-19[13]. Social determinants of health are a much- researched subject, and countless data exist to demonstrate differential health outcomes based on poverty, lack of education and opportunity, poor access to healthcare and health prevention [14]. Inter-racial disparities among minorities have also been reported. For example, UK data indicate that Afro-Caribbean people are at the highest risk of COVID-19 deaths, followed by Asians, mixed racial backgrounds and 'other' non-white races12. The cause for these disparities is not known.

Healthcare Worker deaths in the UK

Several high-profile reports in England during this pandemic highlighted the disproportionately large representation of black African males among those doctors who died after contracting COVID-19. Further media reports, including one from the Health Services Journal[15] reported that over 90% doctors who died were from minority ethnic backgrounds, mainly African and South Asian. Minorities were also over-represented among COVID-19 deaths among nurses and other allied healthcare professions. This raised significant concerns among trade unions, professional groups, charities and others, who highlighted the need for enhanced risk analysis and mitigation.

The role of personal protective equipment (PPE) in protecting essential workers from occupational exposure has been widely discussed. Protection from droplet infections by masks, respirators, eye shield, skin protectors and gloves should ideally be graded according to risk of exposure[16]. Data from China and elsewhere have demonstrated that enhanced PPE use reduces healthcare worker death from COVID-198. However, amidst a worldwide shortage of such PPE equipment, many countries, including England, have resorted to rationing and reuse of equipment[17,] with more enhanced protection offered to those at highest risk of exposure, such as in intensive care18.

It is not entirely clear why a disparate group of minority ethnic professionals is so highly represented among HCW deaths. Whilst population based socio-demographic factors that lead to health inequalities can be explained by poverty, malnutrition, poor housing, large inter-generational households increasing transmission risk, lack of knowledge of English to clearly understand risk reduction guidance from government agencies[19], none of these economic and educational deprivation factors are applicable to HCW with well paid jobs and post graduate professional qualifications. Further research is vital in understanding these risks, so that measures to mitigate these risks can be urgently put in place.

The UK government has advised that NHS trusts implement further occupational risk assessments among HCW in frontline, patient-facing roles. It has recommended that the additional high risk of death among those from minority ethnic backgrounds are taken into consideration when such risk assessments are undertaken. However, due to lack of evidence, this has been difficult to implement in practice. Several individual hospitals have pro-actively initiated mitigation of risk among their staff from minority ethnic backgrounds, with Somerset NHS Foundation Trust being among the first to introduce this[20]. Some early guidance based on available data on COVID-19 hospital deaths are beginning to emerge with proposed risk stratification scores[21]. However, these scoring systems are yet non-validated and requires further prospective work.

It is proposed that other, more systemic factors may contribute to the differential outcome in COVID-19 death among minority ethnic HCW. Among others, these may be due to perceived racial inequalities leading to chronic changes in physiology that may lead to disease susceptibility[22,] inability to address inequalities in access to PPE, lack of ability to speak up against institutional injustices, lack of ethnic minority representation in positions of higher strategic power within organisations[23.] A recent online survey of over 1500 UK HCW indicated that those from minority backgrounds were unable to access PPE or undertake social distancing at work, and the latter was found to have significant association with the risk of COVID-19 among respondents[24]. Future research should focus on validating culturally sensitive and nuanced risk tools that take into

account systemic, personal and organisational factors that compound the known pathophysiological risks. Ultimately, effective pandemic preparedness at national level, adequate availability of PPE, evidence-based use of pandemic control measures will result in lives being saved, as is evidenced in many countries who were able to implement this with more success than others.

The prevalence of COVID-19 deaths among social care workers is not fully known. However, recent data from the UK clearly demonstrate high death rates among care home residents during this pandemic compared to matched data from previous years[25]. It is very likely that care workers in this sector will also be at a high risk of occupational exposure, and further research is needed in this area.

Conclusions

COVID-19 has resulted in a unique set of clinical features which do not mimic any known zoonoses in humans. Many of its pathology remains yet unexplained. For example, it is unclear why children are spared from its severe consequences, males are more affected, some co-morbid conditions are more risk-prone than others. However, this pandemic has also demonstrated disparities that transcend a simple biological premise. Further work is urgently needed to explore those disparities, particularly in the HCW context.

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COVID-19 in Children & Paediatric Multisystem Inflammatory Syndrome

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COVID-19 was first reported in Wuhan China and on 9th January 2020, the Chinese CDC reported a novel coronavirus as the causative agent, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). The World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January, and a pandemic on 11 March.1

Children are less affected by COVID-19 as shown by epidemiological studies. According to the European Surveillance System (TESSy), children (aged 0-14years) accounted for only 2.1% of all confirmed COVID-19 cases[2]. TESSy data suggests a U-shaped pattern in the age distribution of the proportion of asymptomatic cases, with 15% aged less than five years; 17% aged 5-9 years and 17% aged 10-14 years. The most commonly reported symptoms include fever and cough [3]. Data from Italian emergency departments found 21% of SARS-CoV-2 positive children to be asymptomatic4.

Paediatric Multisystem Inflammatory Syndrome
PIM-TS stands for Paediatric Multisystem Inflammatory Syndrome – Temporally Associated with SARS-CoV-2. This stands for the hyperinflammatory state seen in children with exposure to SARS-CoV-2. The first case series was described by Riphagen et al and published on May 7th, 2020 in Lancet[5]. Royal College of Paediatrics and Child Health (RCPCH) developed a case definition for PIM-TS6.

The key features are:

- A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP, and lymphopaenia) with evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki Disease.
- Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus.
- SARS-CoV-2 PCR testing may be positive or negative
- The Centre for Disease Control, America defined it as Multisystem Inflammatory Syndrome in Children (MIS-C).7
- An individual aged <21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological) AND
- No alternative plausible diagnoses AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms.

Epidemiology
In a case series from London [2], all children were previously well. Clinical presentations included unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral oedema, and generalised extremity pain with significant gastrointestinal symptoms. All progressed to warm, vasoplegic shock; refractory to volume resuscitation and required inotropic support. Majority of them did not have any significant respiratory involvement, though seven required mechanical ventilation for cardiovascular stabilisation. Other features included development of small pleural, pericardial, and ascitic effusions. All children had raised inflammatory markers but tested negative for SARS-CoV-2. Echo-bright coronary vessels was a common echocardiographic finding.
The general picture is of children's persistent high-grade fever, limited or no respiratory compromise, fluid refractory shock, extremely high inflammatory markers and frequent cardiac dysfunction.

Parri et al [4] reported from the Bergamo province, Italy where they noted a 30-fold increased incidence of Kawasaki-like disease. The children were older, had a higher rate of cardiac involvement, and 8 (out of ten) had antibodies against SARS-CoV-2.

Clinical features:
Clinical features include a persistent fever >38.5°C with Oxygen requirement, Hypotension and some of the following symptoms including abdominal pain, confusion, conjunctivitis, cough, diarrhoea, headache, lymphadenopathy, mucus membrane changes ,neck swelling, rash, respiratory symptoms, sore throat, syncope , vomiting and swollen hands and feet.

Investigations
RCPCH 6 and Don't forget the bubbles 8 recommend the following investigations: FBC, U&E, Glucose, VBG, Lactate, Coagulation, D-dimer, LDH, Triglycerides, Ferritin, Troponin, CK, Vitamin D, ASOT and Viral PCRs.
Common findings include [6]:

- Echo and ECG – myocarditis, valvulitis, pericardial effusion, coronary artery dilatation.

- CXR – patchy symmetrical infiltrates, pleural effusion
- Abdo USS – colitis, ileitis, lymphadenopathy, ascites, hepatosplenomegaly
- CT chest may demonstrate coronary artery abnormalities if with contrast

Kawasaki disease:
There are many similarities between the clinical features between PIM-TS and Kawasaki Disease, including fever, rash, conjunctivitis, peripheral oedema and coronary artery involvement on ECHO.8

Kawasaki disease is a medium vessel vasculitis which affects children. American Heart Association criteria (2017) defined it as fever for ≥5 days plus four or more clinical criteria, including bilateral bulbar non-exudative conjunctivitis, changes of lips or oral cavity, polymorphic rash, non-suppurative cervical lymphadenopathy (with at least one node ≥ 1.5 cm in diameter), and changes in the hands or feet (erythema, oedema, induration, desquamation). Incomplete types include fever for ≥5 days plus two or three of clinical criteria and raised erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Blood tests may reveal presence of anaemia, leucocytosis, thrombocytosis (week 2 of fever), hypoalbuminaemia, and raised transaminases. Echocardiogram may show coronary aneurysms or cardiac dysfunction. Complications of KD include aneurysms of mid-sized arteries, giant coronary artery aneurysms, pericarditis and myocarditis. There are no diagnostic tests for KD.

Management:

RCPCH has published recommendations for the management of PMIS-TS. [6]

1. All children should be treated as suspected COVID-19
2. For mild to moderate disease supportive care only is recommended.
3. Close monitoring with hourly PEWS for signs of respiratory or cardiovascular deterioration and clinical signs of worsening inflammation.
4. Standard APLS resuscitation and supportive management.
5. Start empiric antibiotics (as per local sepsis protocols).
6. Consider IVIG and aspirin early if fulfils criteria for Kawasaki Disease and IVIG if fulfils criteria for toxic shock syndrome
7. Immunomodulatory therapy and anti-viral treatment , if needed, after discussion with paediatric ID and/or clinicians with appropriate experience.
8. All stable children should be discussed as soon as possible with specialist services to ensure prompt treatment.
9. There should be a low threshold for referral to Paediatric Intensive Care.

Risk assessment
European Centre for Disease Prevention and Control 2 have summarised that the probability of COVID-19 in children is currently assessed as "low". The impact of such disease is assessed as "moderate", therefore the overall risk of COVID-19 in children is assessed as LOW. In summary, the probability of PIMS-TS in children in the EU/EEA is currently assessed as "very low" and the impact of such disease is assessed as "high", therefore the overall risk of COVID-19-associated PIMS-TS in children is assessed as LOW risk.

Key points:
In the current climate, it is essential that the professionals are aware of PMIS-TS. The children may present to their GPs, Emergency department or Paediatrics with a variety of symptoms. Majority of the children have mild or moderate symptoms, though the small minority may deteriorate quickly.

1. Early recognition and diagnosis of PMIS-TS is important to ensure early treatment and reduce the risk of long-term complications.
2. Clinical features include persistent fever, raised inflammatory markers and with evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder)
3. Awareness and a high level of suspicion in those children presenting with fever, respiratory symptoms and features of Kawasaki disease.
4. Children from BAME backgrounds are more commonly affected.
5. Children with mild to moderate disease require only supportive care. For severe cases, consider retrieval to PICU, antibiotics and immuno-modulatory therapy following discussion with specialists.

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CASE REPORT
Increased Risk Of Venous Thromboembolism In COVID-19

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Abstract:
We report a case of a 61-year-old male who had recently been discharged home after contracting COVID-19 during an extended hospital admission. He presented to the emergency department after episode of sudden onset central chest pain and D-dimer was 390 mcg/L on admission. The patient was initially managed for acute coronary syndrome, however within twenty-four hours of admission the patient desaturated to 74% on room air and required 15L oxygen. CT Pulmonary Angiogram showed right lower lobe segmental pulmonary emboli and extensive COVID-19 lung changes. Subsequently, acute coronary syndrome treatment was stopped, and the patient treated for pulmonary embolus. Following this, his oxygen requirement improved significantly, and the patient stabilised within one week.

Emerging data and clinical evidence suggests an increased risk and prevalence of venous thromboembolic events in COVID-19, particularly in patients with more severe disease. It is currently unclear how long this increased risk persists. This case report highlights the importance of risk stratification of patients on discharge from hospital, to determine who requires extended thromboprophylaxis on discharge. Going forward, clinical trials are needed to evaluate the duration and dose of thromboprophylaxis in high-risk patients, and aid the formation of clearer guidelines for clinicians.

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Background:

The novel coronavirus disease (COVID-19) has spread worldwide, infecting over 3 million people and causing over 230,000 deaths. Patients with COVID-19 may be at an increased risk of developing venous thromboembolic (VTE) diseases, as the infection is associated with increased inflammation, disseminated intravascular coagulation (DIC), hypoxaemia and immobility [1,2]. The incidence of VTE in COVID-19 is not yet established. However emerging data suggests an increased risk and prevalence of venous thromboembolic events in COVID-19, particularly in patients with more severe disease [3]. Klok et al. demonstrated 27% of 184 Dutch ICU patients had CTPA and/or ultrasonography confirmed VTE and 3.7% had arterial thrombotic events. All these patients received at least standard dose thromboprophylaxis [4]. In a French study, Llitjos et al. systematically screened for VTE in anticoagulated COVID-19 patients using complex dual ultrasound (CDU). They found 69% of the 26 ICU patients with COVID-19 had VTE [5]. Given the recent emergence of COVID-19, there is currently no longitudinal data assessing the prevalence of venous thromboembolic events in patients surviving COVID-19 infection.

Case Presentation:
A 61-year-old male presented to the emergency department (ED) after episode of sudden onset central chest pain, which woke him in the night. The patient reported this pain as heavy in nature and 10/10 in severity, with associated nausea. He denied any radiation or exacerbating factors.

Four days prior to ED admission, the patient had been discharged from a two-month hospital stay, during which he had been diagnosed with COVID-19 (36 days prior to this presentation) and required non-invasive ventilation in intensive care. He had been anticoagulated with prophylactic dose LMWH throughout this admission but was not put on anticoagulation therapy post discharge.

His pertinent past medical history includes end-stage renal failure requiring haemodialysis, previous myocardial infarctions with stenting to right coronary artery in 2018, adrenal insufficiency, hypertension and asthma with recurrent chest infections. He is an ex-smoker who gave up 20 years prior.

Upon review, the patient was alert, conscious and not in respiratory distress. His vital signs on presentation were as follows:

- Temperature: 37.3 degrees Celsius,
- Heart rate 84 beats per minute,
- Respiratory rate 18 breaths per minute,
- Blood pressure 162/99 mmHg
- Oxygen saturation 98% on room air.

Physical examination revealed bi-basal crepitations on auscultation and lower limb oedema to the mid-shin level, but no calf tenderness or erythema. Heart sounds were normal, and abdomen was soft and non-tender.

His electrocardiogram showed atrial flutter, with no new

ischaemic changes. Troponin was 72 and 74 ng/mL when repeated 6 hours later, which in the context of end stage renal failure was difficult to interpret (Creatinine was 323 µmol/L, and eGFR was 17 mL/min/1.73m2). His white cells were in normal range and CRP was 62 mg/L. D-dimer was 390 mcg/L on admission.

Diagnosis:
Initially, the primary differential diagnosis was acute coronary syndrome (ACS). Other important differential diagnoses requiring exclusion included aortic dissection, pulmonary embolism, pneumothorax and pneumonia.

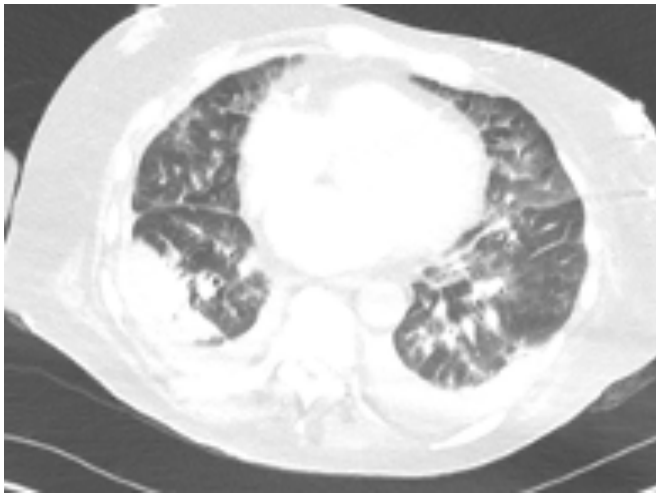
Initial Management and Prognosis:
CT Aortography showed no evidence of aortic dissection. Chest X-Ray showed atelectasis in both bases but no focal consolidation.

Initially, the patient was managed as an ACS patient and was also commenced on unfractionated heparin infusion. However, in light of lack of ischaemic changes on repeat ECGs and stable troponin levels, ACS became a less likely differential diagnosis.

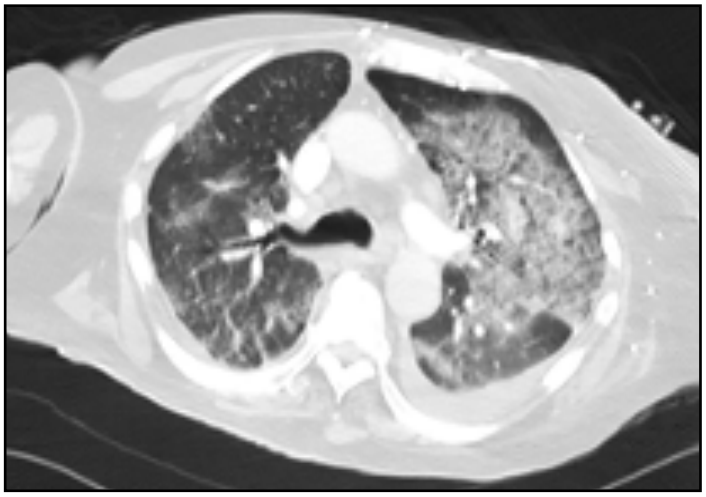
Case Progression and Outcome:
Within twenty-four hours of admission, the patient desaturated to 74% on room air and was requiring up to 15L oxygen to maintain target saturations. Type I respiratory failure was demonstrated on arterial blood gas (pO2 7.11 kPa with FiO2 0.35, pCO2 4.57).

The patient was commenced on IV antibiotics to cover chest sepsis and an urgent CT Pulmonary Angiogram was arranged. Repeat bloods showed a significant rise in inflammatory markers (White Cell Count 12.3 109/L, CRP 410mg/L). The CT Pulmonary Angiogram (CTPA) showed right lower lobe segmental pulmonary emboli and extensive COVID-19 lung changes, with more focal areas of dense consolidation within the right lower lobe (Fig 1).

a) Axial CT, vascular sequence. Reports showed filling defect within right lower lobe segmental arteries in keeping with acute pulmonary embolus.
b) Axial CT, lung sequence



c) Axial CT, lung sequence. Extensive ground glass changes noted within both lungs, worse on the left.
d) Axial CT, lung sequence. Reports highlight some more organised, focal dense consolidation seen at the right lower lobe.



ACS treatment was stopped, and the patient was loaded on unfractionated heparin and commenced on warfarin therapy to treat the pulmonary embolus. During admission, his oxygen requirement improved significantly, and he made good clinical progress. Within five days of admission, he was no longer requiring oxygen and was mobilising short distances.

Discussion:
Emerging data suggests an increased risk and prevalence of venous thromboembolic events in COVID-19, particularly in patients with more severe disease. Using a nationwide Chinese dataset, Wang et al. show that 40% (407) of the 1026 patients that were included were considered as high risk for VTE with a score of 4 or more on the Padua Prediction Score[6]. However, they show that 11% of these 407 patients also had a high risk of bleeding[3]. Thus, risk stratification must balance the risk of VTE with the risk of bleeding.

Whilst there are currently no clear national guidelines, the British Thoracic Society guidance on VTE has stated that on discharge, extended thromboprophylaxis can be considered if the patient is at a high risk of VTE, such as past history of VTE, cancer, significantly reduced mobility or a critical care admission [7]. They suggest that while the nature and duration of thromboprophylaxis is unclear, a standard approach of prophylactic dose of low molecular weight heparin (LMWH) or direct oral anti-coagulant for four weeks might be considered as appropriate.

This case of demonstrates the importance of developing clearer risk stratification for COVID-19 patients who would benefit extended thromboprophylaxis after hospital discharge. To our knowledge, there is currently no evidence in the literature studying excess risk of VTE post COVID-19. Going forward, clinical trials evaluation the dose and duration of LMWH thromboprophylaxis in patients with COVID-19 are critically required to aid risk stratification and clinical management.

Learning Points:
- Recognising increased risk of acute venous thromboembolism in patients who have had recent COVID-19 infection
- Risk stratification of patients on discharge from hospital with COVID-19 in order to determine who requires extended thromboprophylaxis
- A requirement for more data assessing the prevalence of venous thromboembolic events in patients surviving COVID-19 infection
- A requirement for more trials to evaluate the duration and dose of thromboprophylaxis in high-risk patients to aid the formation of clearer guidelines for clinicians

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'Pass it on' - New Organ Donation Law in England May 2020

What Black, Asian or Minority Ethnic (BAME) Communities Should do and Why?

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Editorial Commentary
From 2020, a new legislation comes into force in the UK providing legal status to the concept of presumed consent, extending this from Wales. In essence, consent for organ donation will be assumed unless the donor had actively opted-out. For Black Asian and minority ethnic communities, there is a widening gap between availability of donors and those that are waiting on transplant lists. A particular stumbling block seems to be the denial of consent by next-of-kin, which appears to be disproportionately high. Exploration of the reasons behind such withholding of consent appears to be lack of information, myths, a lack of cultural sensitivity more than any religious decree [1-2]. Hence, this article will explore in depth the current scenario, the causes behind these disproportionate representation and leadership that community leaders need to take to improve the access to this life saving treatment option.

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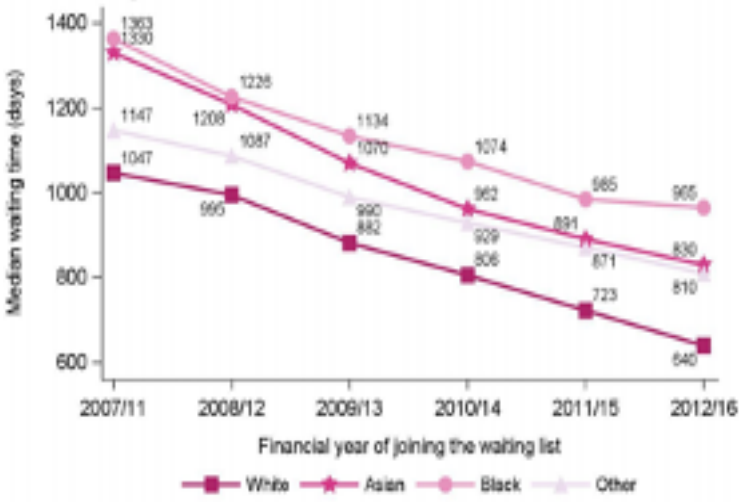
2 Krishnan, N., & Modi, K. (2020). Organ Donation Law & Its Impact on BAME Communities. SUSHRUTA Journal of Health Policy & Opinions, 13(1), 13-15. https://doi.org/10.38192/13.1.4

The New Law
On 20th May 2020, new legislation governing organ donation will come into force in the United Kingdom (UK). Also known as 'Max and Keira's Law' after Max Johnson, a young boy who received a heart transplant from a young girl named Kiera Ball who unfortunately passed away at just 9 years old, Kiera's parents' decision will change the landscape of organ donation forever [1]. In essence – consent for organ donation will be assumed unless the deceased had 'opted-out' or are excluded under the various criteria outlined by the regulation. Nevertheless, the legislation still retains a "soft" opt-out option since the 'family' will be actively involved in decision-making prior to organ retrieval, where objections could still be made.

There were 6,170 patients active on the waiting list for a lifesaving or life enhancing organ transplant in the latest UK National Health Service Blood and Transplant (NHSBT) Report [2]. In the year from April 2018 to March 2019, 400 patients died waiting for an organ while being on this list [3]. There are currently 25.8 million people registered under the current opt-in system [2] and donations from these enabled 3,941 recipients to receive a transplant in the same year. These comprised 2,399 kidney, 204 pancreas, 180 heart, 164 lung, 972 liver and 18 intestinal transplants [4]. The overall number of people, who die in circumstances where organ donation is possible, is relatively static at about 6,000 people each year (which is about 1% of deaths in the UK). Finally, despite registering for organ donation, the family of deceased patients is known to only give consent in 68% cases [5].

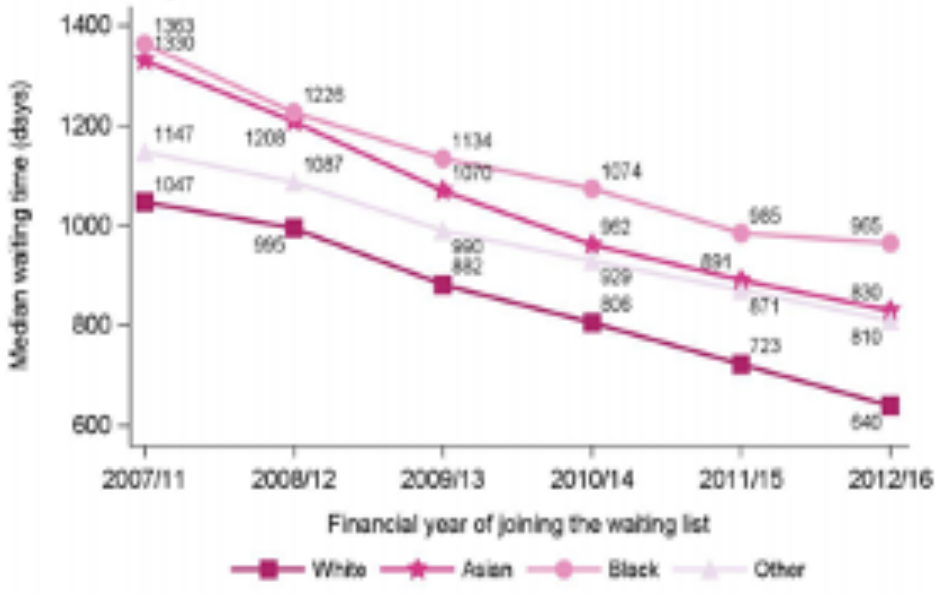
Why black, Asian or minority ethnicity (BAME) communities?
Kidney disease is common in South Asians including a higher proportion of patients from Black, Asian and Minority Ethnic (BAME) communities developing organ failure. Higher progression among BAME patients is attributed to the higher prevalence of concurrent medical conditions such as diabetes mellitus, hypertension and obesity. Mortality rate due to kidney disease is also higher in countries where BAME



patients have emigrated from [6]. The prognosis of kidney disease is also poor in BAME patients since <10% of at-risk patients are actually aware of their kidney disease/kidney function and consequently present late [7, 8]. Approximately 1,800 BAME patients in the UK are currently waiting for organ transplantation. Despite nearly 14% of the UK population being classified as BAME, only 8% are actually registered donors on the Online Donor Registry (ODR) [9]. However, a large proportion of unreported/ unknown ethnicity (67%) on ODR is major limitation to draw definite conclusion. The number of BAME deceased organ donors has increased by 51% over the last 5 years, from 80 in 2014-15 to 121 in 2018-19. In 2018-19, ethnically Asian people represented 4% of deceased donors (DD), 13% of DD transplants and 17% of the transplant waiting list; people of Afro-Caribbean descent represented 1% of DD, 13% of DD transplants and 11% of the list. White ethnicity is significantly over-represented in organ donor register.

There is a real need for more people from BAME communities to donate organs either in life or after death. The compelling reasons include the ethnic variation associated with tissue type and blood group; the disproportionately high number of BAME patients on waiting list; and the longer time BAME patient spend already on the list waiting for an organ. Analysis of waiting list data shows that only 19% of BAME patients receive a kidney transplant within one year of being on the waiting list, compared with 31% of white Caucasian patients [9]. Overall waiting time has improved substantially in last decade (see figure 1) and the new allocation scheme from 2019 is expected to reduce further variation based on ethnicity [10].

Figure 1: Median waiting time for a kidney as per ethnicity in UK (adapted from ref [10])



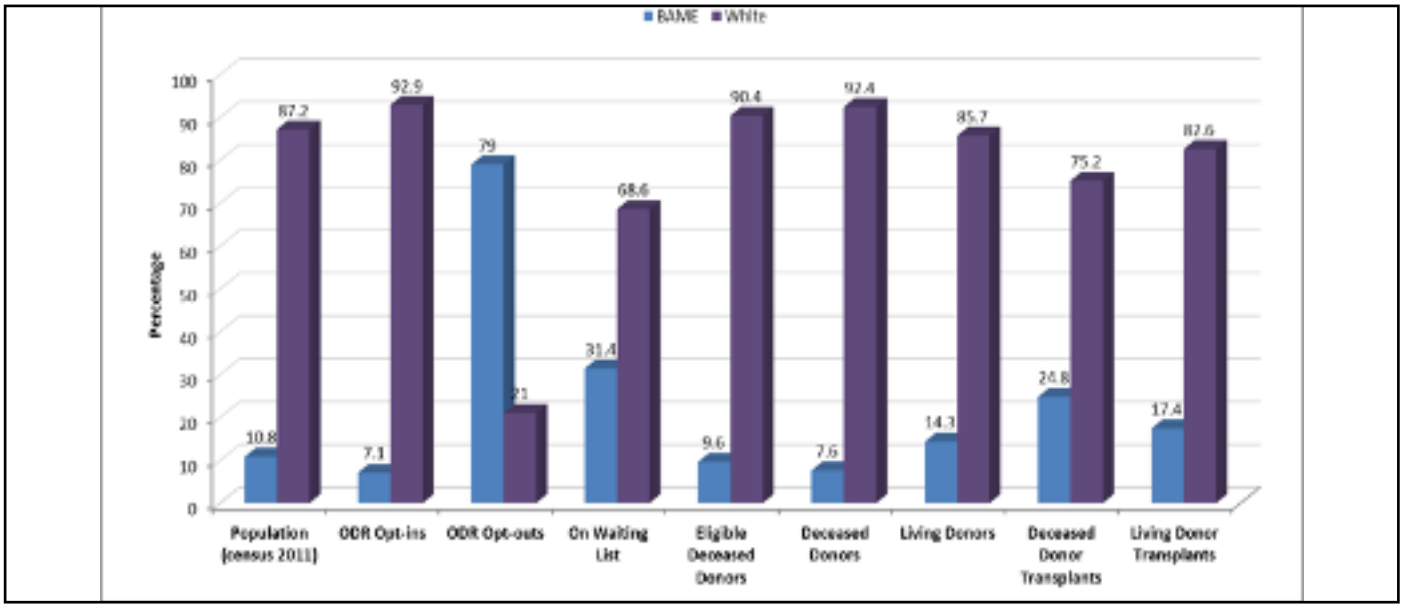
Family consent for donation is much lower within the BAME community - 42% compared with 71% for white potential donors [5]. Although consent rates are increasing from donors of a BAME background, the new opt-out system is expected, along with change in allocation policy, to help a greater proportion of patients from BAME backgrounds.

About 1% of UK population (N=640,435) have opted-out of the organ donation register [5, 10]. Relative to the UK population, there is over-representation (n = 118,000) of opt-outs among traditional BAME communities, in comparison to White and Chinese people. Around 54% of these opt-outs were made by Asian people in 2018-19 (Table 1). While it remains a fundamental right to opt out, the concern is that some individuals are making this decision based on misinformation, misplaced fear or misconceptions about faith beliefs.

Table 1: Ethnicity of Opt-Out ODR by year of registration [5, 10]

Ethnicity	2016/17 (Number (%))	2017/18 (Number (%))	2018/19 (Number (%))
White	18,364 (80.2)	22,942 (8)	23,473 (21)
Black	1178 (5.1)	44631 (15.5)	21812 (19.5)
Asian	2493 (11)	206,454 (72)	60,380 (54)
Indian	585 (2.6)	39,327 (13.7)	7,720 (7)
Pakistani	1018 (4.4)	105,791 (36.8)	31,968 (28.6)
Bangladeshi	371 (1.6)	50,782 (17.7)	17,221 (15.4)

Figure 2: BAME Summary of representations at various aspects of organ donation and transplantation (NHSBT 2020) (Note: data with unknown ethnicity excluded for analysis)



What initiatives can BAME communities take?

Major religions support organ donation. Nevertheless, the most frequent reasons given by family members declining donation was either it was is against a patient's religious or cultural beliefs (20-30%) or uncertainty of the patient's wishes (12-14%) [5, 10] or how the body will be handle during organ retrieval surgery. BAME leaders and organisations now need to work in partnership with the NHS to improve community education, promote faith and cultural engagement including identify key opinion leaders to support awareness-raising campaigns. Less than half

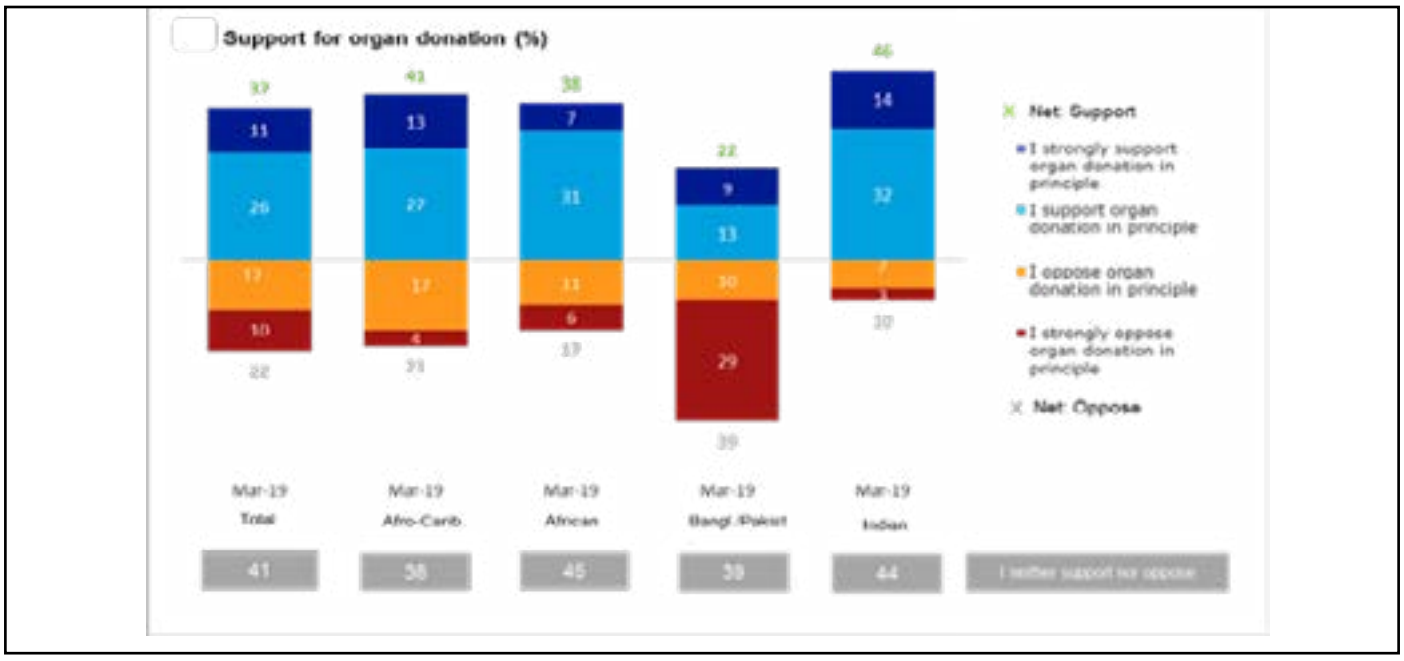
of families agree to organ harvesting when they do not know the deceased's last wishes regarding organ donation. However, rates increase to more than 9 out of 10 families when asked, if the conversation about organ donation had already been discussed with them prior to death. The body is handled with utmost respect and all procedures including analgesia and anaesthesia is performed by experienced surgeon and anaesthetists respectively.

The majority of people opting in are of white ethnicity and elderly [11]. Attitudes towards organ donation among BAME communities vary depending on ethnicity (Figure 3). Recent data suggested an increase from 11 to 15 percent in positive attitude among people who would definitely donate some or all organs after their death [12]. The data also suggests there is a real opportunity to focus on the significant proportion of people who remain undecided, targeting education around clarifying myths and misconceptions.

Funding is available for BAME organisations to promote organ donation. Sources include the Community Investment Scheme Fund from NHSBT [13]. Other available support includes the NHSBT Organ Donor Ambassador programme, the National BAME Transplant Alliance (NBTA) and BAME charities such as South Asian Health Action (SAHA) and African & Caribbean Leukaemia Trust (ACTL). Community specific campaigns and events organised by SAHA have led to signing of many BAME donors. Similarly 'Be the Hero' campaign in Yorkshire has led organ donation promotion by community and public campaign. Individual families have also using social media campaign (such as Hope4Anya).

There are also examples of national steering groups helping to influence outcomes such as Jain Hindu Organ Donation (JHOD) who partnership with NHSBT and Local Assembly in London [14]. Despite 62% of Londoners waiting for an organ transplant being from BAME backgrounds, only 1% of BAME Londoners are registered on ODR [14]. Finally, BAME medical professional bodies such as British Association of Physicians of Indian Origin (BAPIO) and British Islamic Medical Association (BIMA) are now taking on the campaign to increase organ donation from BAME communities. In conclusion, leaders of BAME communities through social events and digital campaigns can demystify the prevalent myths around organ donation and help fellow members with lifesaving organ transplantation. One donor can save up to eight lives and transfer up to 54 lives.

Figure 3: Attitudinal survey of black and Asian adults in England Survey carried out by Agroni Research Ltd 2019 [12].



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Picture sourcemultibriefs.com

Is Vertical Transmission Of Coronavirus (Covid-19) From Mother To Baby Possible?

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ABSTRACT
The coronavirus (COVID-19) pandemic has serious health implications. The potential risk to pregnant women and neonates must be explored. Controversy exists regarding whether Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) can be transmitted vertically via antenatal or intrapartum transmission from an infected mother to her child. Emerging case reports and cohort studies suggest that vertical transmission is likely. However, the data is limited and contradictory, making it difficult to draw definitive conclusions. The continued collection and analysis of data on pregnant women and neonates is necessary.

Key words: COVID19, Pregnancy, direct transmission

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With the number of people infected with coronavirus (COVID-19) globally having reached over one million, it is clear that this pandemic has serious health implications[1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a highly infectious virus with multiple possible routes of transmission. Currently, controversy exists regarding whether SARS-CoV-2 can be transmitted vertically from an infected mother to her unborn child.

Understanding the impact of the virus on pregnant women and the foetus is necessary for generating guidelines for obstetric management regarding COVID-19 infection. This is an important issue to consider, given that changes to the immune system mean that pregnant women, although not necessarily more susceptible to viral illness, may have more severe symptoms, especially in the last trimester[2].In the case of COVID-19, more severe complications include viral pneumonitis, respiratory failure and acute respiratory distress syndrome. These are seen in high risk groups such as older patients, immunosuppressed and those with certain long-term health conditions3. Similar symptoms could occur in pregnant women, making identification and treatment important.

Evidence regarding the possibility of vertical transmission

Emerging case reports and cohort studies from Wuhan, China the epicentre of the pandemic, suggest that vertical transmission is likely[4]. However, results are inconsistent, and studies involve small sample sizes, which may be an unavoidable limitation given the recent emergence of COVID-19.
Chen et al[5] conducted a retrospective analysis of nine pregnant women with COVID-19 pneumonia admitted to Zhongnan Hospital, Wuhan in January 2020. In this cohort, they found no evidence of vertical transmission, which was assessed by testing for the presence of SARS-CoV-2 in amniotic fluid, cord blood and neonatal throat swab samples. However, other case studies suggest that vertical transmission is possible. For example, Zeng et al[6] conducted a cohort study involving 33 neonates born to mothers with COVID-19 in Wuhan Children's Hospital. They found that three neonates (9%) tested positive for COVID-19 and showed symptoms of the viral illness. In this cohort, the neonates were born via caesarean section under strict infection control measures. Based on this, the authors concluded that the three neonates likely contracted the disease in utero. However, it must be noted that the diagnostic test for COVID-19 was not carried out until the second day of life, which raises the possibility that infection occurred after birth cannot be ruled out.

Further evidence for the possibility of vertical transmission is provided by Dong et al[7], who wrote to the Journal of the American Medical Association (JAMA) about a neonate born to a mother with COVID-19 in Renmin Hospital, Wuhan in February 2020. This neonate had elevated SARS-CoV-2 IgM and IgG antibody levels and abnormal cytokine test results two hours after birth. The elevated levels of SARS-CoV-2 IgM antibody present suggests that the neonate was infected in-utero, as IgM antibodies do not cross the placenta, and therefore likely represent a neonatal immune response to in-utero infection[8]. The mother's diagnosis of COVID-19 took place 23 days before delivery, making this the potential time frame for vertical transmission.

Although infection at delivery cannot be ruled out, the precautionary measures taken at the time of birth (including delivery via caesarean section in a negative-pressure isolation room, mother wearing an N95 mask, no mother-neonate contact and immediate quarantine of the neonate in the neonatal intensive care unit) decrease this. Unlike the study conducted by Chen et al, in this case study, the mother's vaginal secretions were tested and found to be negative for SARS-CoV-2, which further supports the possibility that the neonate developed COVID-19 via vertical transmission.

However, it was a single case study, and therefore can only be considered a preliminary observation which warrants further examination of maternal and neonatal samples.

It must be noted that in the case studies mentioned, the women contracted COVID-19 in their third trimester, which means that the possibility of vertical transmission during the first or second trimester remains unexplored. This is an important consideration, since this time period is immunologically significant, as demonstrated by rubella infections that can affect more than 50% of foetuses if maternal infection occurs in the first trimester, whereas the incidence rate halves in cases that maternal infection occurs by the end of the second trimester[9].

Impact of COVID-19 on pregnant women and neonates

The impact of COVID-19 infection on pregnant women and neonates, and whether this differs from the impact of the virus on other population groups is still under consideration. Currently, the proportion of pregnancies affected by COVID-19 is not known[2]. For example, during the 2009 H1N1 influenza pandemic, pregnant women were at an increased risk of complications and were over four times more likely to be admitted to hospital compared to the general population[10]. Furthermore, in a case study of 12 pregnant women infected with SARS-CoV in 2003, the mortality rate was 25%[11], compared to the average global mortality of 10%12. However, in a cohort of nine pregnant women with COVID-19, the clinical characteristics of COVID-19-related pneumonia were similar to those reported for non-pregnant adults[5]. Once again, the lack of large sample sizes makes it difficult to confidently draw any conclusions. Currently, pregnant women are not classed as extremely vulnerable in the Public Health England guidelines[13].

There is currently no evidence to suggest that COVID-19 infection is related to an increased risk of early pregnancy loss[2]. Based on case reports from early pregnancy studies with Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV), maternal viral infection was not associated with an increased risk of miscarriage or second trimester loss[14].

At present, there is limited data regarding the clinical course of COVID-19 in neonates. However, the current consensus is that in children, severe disease from COVID-19 is rare[15]. In the largest review to date of children with COVID-19, only 112 (5%) of 2143 children had severe disease (defined as hypoxia) and 13 (0.6%) of children developed respiratory or multiorgan failure or acute respiratory distress syndrome[16]. In a case study conducted by Zeng et al6, the three infected neonates had fever and pneumonia, which are symptoms typically associated with the virus. For two out of three them, the clinical course of disease was mild. The third neonate required treatment for non-COVID-19-related conditions including bacterial sepsis and prematurity. However, it is not known whether these conditions were impacted by COVID-19 in any way.

Conclusion

Vertical transmission may indeed occur in COVID-19 infection. Due to the limited data available, it is not possible to draw definitive conclusions. However, considering the significance of this ongoing pandemic, it is imperative to continue to collect and analyse data on pregnant women and neonates. For the time-being, screening of pregnant women, close monitoring of at-risk neonates and strict perinatal infection control measures should be carried out in all cases.

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Is Chi Running A Safer Alternative For Those At Increased Cardiovascular Risk?

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ABSTRACT
Cardiovascular disease is a global burden, and exercise is a well-recognised route to reducing the risk. Running is an effective form of exercise; however, its intensive nature leads to an increased risk of injury. ChiRunning is an alternative running programme that uses principles of mindfulness adapted from Tai Chi. It focuses on altering running gait, with the goal to decrease injury risk. Due to ChiRunning's recent emergence, data is limited. However, results suggest that ChiRunning improves running gait and may reduce injury risk when compared to traditional methods. Future research with larger sample sizes is required to assess its effectiveness.

Keywords: ChiRunning, Cardiovascular disease, Alternative running technique

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Introduction

At the beginning of a new year, the minds of many will be on improving health and fitness. It is well known that regular physical activity has several health benefits. Cardiovascular health has been a key focus of biomedical research in the last few decades, and subsequently a substantial body of evidence has emerged linking frequent physical activity with a decrease in cardiovascular mortality and disease (CVD) risk[1].

The benefits of exercise are multifaceted, with evidence showing that physically active individuals have improved cardiovascular performance, a more favourable plasma lipoprotein profile, lower blood pressure and higher insulin sensitivity[2,3]. Blair et al[3] showed in a large scale observational cohort study involving over 32000 individuals, that cardiorespiratory fitness levels are inversely correlated to death rates, even in the presence of other predictors of cardiovascular mortality, such as smoking, hypertension and hyperlipidaemia.

It is clear that the cardiovascular benefits of exercise are vast, and this knowledge is increasingly important when considering that CVD is the leading cause of morbidity and mortality worldwide[1]. For these reasons, frequent exercise should be an essential part of everyone's daily lives. The question remains as to what form of exercise and 'how much' is most beneficial.

Cardiovascular Benefits of Running

Running is a well-known form of exercise that is relatively cost effective, requires little to no equipment and can be performed in a wide variety of locations. Due to its popularity, there are several online applications and programmes that runners can use to improve and track their exercise. Importantly, running is a vigorous and intensive form of exercise, which is associated with higher cardiorespiratory fitness levels compared to less intensive activities[5,6]. Overall, these factors make running a good exercise for beginners and those at a higher CVD risk.

However, the intensive nature of the sport means that there is an increased level of loading on muscles, joints and tendons which leads to increased rate of injury[7]. Exercise related injury is a serious concern, as it has the potential to severely impact how much exercise a person gets. For example, when in a survey of 2000 individuals, Sallis et al[8] found that the most common reason for discontinuation of an exercise regime was an exercise-related injury. In the last few decades, specialised running programmes have emerged that train individuals to change their running gait in order to reduce risk of injury and therefore increase activity levels. 'ChiRunning' is one such programme [9].

Principles of the ChiRunning Programme

ChiRunning is a commercially available running training programme that uses principles of mindfulness adapted from the Chinese martial art Tai Chi[9]. This technique focuses on altering running form to introduce a midfoot strike, decrease stride length and increase cadence[10]. According to the ChiRunning technique, a midfoot strike is characterized as having the runner's heel and ball of the foot touch the ground simultaneously with each foot strike[16]. Cadence is a measure of the number of strides taken per minute, and a lower cadence, along with decreasing stride length is thought to be related to a greater risk of sustaining injuries [13].

There are six guiding principles of ChiRunning;

- Alignment & Relaxation,
- Central Movement,
- Cooperating with Force,
- Gradual Progress,
- Body Sensing and

- A Mindful Approach.

ChiRunning differs from traditional running in several ways. For example, the techniques involved aim to decrease the loading forces that are placed on the body during running. By doing this, ChiRunning claims to decrease the risk of injuries sustained during running and therefore promote a greater amount of running activity[10].

A unique aspect of ChiRunning is the integration of mindfulness[11] into the training programme. Mindfulness and body awareness practices are taught as part of the Chirunning curriculum to both help identify early indicators of injury and increase motivation[12]. This type of running may be particularly important in a subset of the population who have a higher CVD risk and therefore may benefit more from frequent exercise, such as individuals with prehypertension and hypertension. In conjunction with this, the American Heart Association have stated that "alternative" approaches to reducing blood pressure, such as those which increase mindfulness and awareness, may be beneficial adjunctive therapies to prehypertension[13].

When considering how to reduce exercise related injury, ChiRunning provides a novel alternative. If performed correctly, running is a very convenient form of exercise, which may be especially important in individuals who are at an increased risk of CVD. It is of no surprise, therefore, that ChiRunning has been the subject of recent research and investigation.

Impact of ChiRunning

A number of studies have used motion analysis assessment of running biomechanics to investigate whether running using the ChiRunning technique can alter the running gait to reduce the risk of injury in the way that it claims. Kumar et al[13] conducted a randomised controlled trial pilot study comparing the changes in running biomechanics in individuals with pre-hypertension who received ChiRunning training, to those who received traditional training. Although this study was relatively low-powered, the results showed that ChiRunning training for eight weeks led to improvements in strike index and knee adduction. Therefore, ChiRunning may be a beneficial alternative running technique in regard to reducing the risk of injury. These findings were in accordance with another cross-sectional study that showed that ChiRunners had lower average vertical loading rates and less knee extensor work when compared to runners using the traditional rear foot striking technique[14]. Importantly, Kumar et al13 showed with their study that it is possible to train inexperienced individuals the ChiRunning technique in a way that leads to positive results. This has implications for the usefulness of ChiRunning on a larger scale.

In order to investigate the potential impact of ChiRunning on reducing CVD risk in individuals with pre- hypertension (defined as 120-130/80-90 mmHg) who are at a higher risk of CVD, McDermott et al[15] conducted a similar study, which compared a group receiving eight weeks of ChiRunning training to groups carrying out traditional running methods. Whilst they did not find any significant difference in blood pressure between the groups after the intervention, the ChiRunning group did show a reduction in body mass index (BMI) over time. It is possible that changes in blood pressure may only be discerned over a longer time period and with a larger sample number. However, due to the sensitivity of blood pressure to external factors (such as time of day or week), BMI may be a more stable indicator of efficacy overall. It appears that ChiRunning is a feasible and acceptable training technique for people with prehypertension and therefore should be considered when advising individuals about what lifestyle changes to decrease CVD risk.

ChiRunning – A Coach's Perspective

ChiRunning is a personal journey and training can vary greatly depending on individual goals. Initially clients attend a 1:1 session to gain insights into the technique, covering aspects such as posture, alignment and the core principles of ChiRunning. Following this some clients choose to continue with regular individual lessons for a bespoke programme or attend small group sessions.

The ChiRunning technique is developed over time, as regular practice enables the runner to progress and feel more comfortable with changes made to their form. At times a runner may need to slow their pace to body sense and prevent over-using muscle groups, the long-term benefits of this are far superior than developing injury and needing time out to recover. Most runners notice their speed increases with ease once they apply the simple technique without forcing the body. The simplicity of ChiRunning allows

runners to bring mindfulness, enjoyment and a sense of calm to their runs. Over the past twenty years ChiRunning has transformed many runners' technique, enabling them to achieve their goals.

Conclusion

Cardiovascular disease is a global burden, and exercise is a well-recognised route to reducing the risk. ChiRunning is an alternative approach to running that incorporates ancient ideologies with standard running methods. Through adjustments in running gait, this technique may decrease the risk of exercise- related injury. Given that such injuries have the potential to seriously impact how much exercise individuals get, ChiRunning may be a valid alternative, especially in individuals who are at an increased risk of CVD. Due to the relatively recent emergence of this technique, the data surrounding the effectiveness of ChiRunning is limited. However, the results from the handful of studies that do exist are promising, and in the future, larger powered studies with greater sample numbers should be conducted. If the global cardiovascular disease burden continues to follow its current trend, then exploring alternative exercise methods such as ChiRunning may become imperative. it is clear that exercise plans and lifestyle changes can be incredibly hard to stick to. That being considered, ChiRunning may be an alternative exercise method that could motivate people to increase their activity levels in a safe way.

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Chronic Cough - An Approach to Diagnosis and Management

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ABSTRACT

Cough is a common manifestation of many respiratory conditions and mostly is non-specific on its own as a symptom of underlying disease. Most transient coughing episodes tend to settle within 2-3 weeks. Yet cough can herald more sinister disease such as malignancy or progressive respiratory conditions. In epidemiological surveys, cough persisting more than 8 weeks has been shown to have a significant impact on quality of life and is often difficult to diagnose and treat, taking weeks to months. There is consensus that a logical, evidence based, standardised approach is most likely to lead to an efficient diagnosis and provide the highest chance of effective resolution. This paper describes the current evidence and offers a best practice approach for primary care practitioners and general internists.

Keywords: Chronic cough, upper airway cough syndrome, post-nasal drip, gastro-oesophageal reflux

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Background

Cough is a defensive reflex that protects the airways in response to an inhaled foreign body or noxious and harmful environmental irritants. One of the commonest non-acute conditions presenting to a respiratory physician is a chronic, unexplained cough affecting approximately 12% of the population. It is associated with poor quality of life with psychological, social and physical consequences often leading to feeling fed-up and depressed. Patients typically complain of a dry irritating cough, driven by a strong urge to cough and usually associated with a discomfort located in the throat. [1] The severity and frequency of chronic cough is exceptionally difficult to measure or quantify. Traditionally, there is heterogeneity of chronic cough with the recognition of different types of cough which may be due to a variety of underlying aetiologies and therefore require specific approaches to treatment.

There are various definitions of when a cough requires further evaluation. In primary care, a cough lasting more than 3 weeks usually heralds a chest X-ray, a full blood count and if available, a spirometry. Provided there are no warning signs such as haemoptysis, weight loss or chest pain, most patients may receive a trial with an antibiotic, a bronchodilator, a short course of inhaled corticosteroids and sometimes a proton-pump inhibitor, before a specialist referral is warranted. In some cases, investigations may reveal an 'expected cause of cough' such as asthma, gastro-oesophageal reflux, post-nasal drip or rhino-sinusitis but in such cases cough remains refractory to treatment. The American College of Chest Physicians in 2016, published results of a systematic review and guidance where any cough lasting more than 8 weeks without an identifiable cause from systematic investigations was defined by consensus, as 'Unexplained Chronic Cough' [2].

Definition

- Acute Cough (<3w)
- Sub-acute cough (3-8w)
- Chronic cough (>8w)

In population studies the most common cause of acute cough (< 3 weeks) were respiratory infections, (viral), exacerbations of asthma, chronic obstructive pulmonary disease (COPD) and pneumonia. Subacute cough (duration, 3-8 weeks) was most commonly associated with post-infectious cough, exacerbation of underlying diseases such as asthma, COPD, and upper airway cough syndrome (UACS). For chronic cough (> 8 weeks), common causes were UACS from rhino-sinus conditions, asthma, gastro-oesophageal reflux disease (GORD), non-asthmatic eosinophilic bronchitis, any combinations of these four conditions, and, less commonly, a variety of miscellaneous conditions including atopic cough. 3

Aetiology

There are a variety of aetiologies including (i) environmental causes such as cigarette smoke, air pollution (especially particulates), (ii) common respiratory conditions such as asthma, bronchitis and COPD, where the cough is typically related to the pathophysiology of the disease, (eg excessive airway mucus and inhalation of irritants), (iii) other causes include eosinophilic bronchitis, interstitial lung diseases, bronchiectasis, (iv) inadvertent side-effects of drugs (i.e. angiotensin-converting enzyme inhibitors) and (v) extra-pulmonary diseases, such as gastro-oesophageal reflux disease (GORD) and post-nasal drip secondary to rhinosinusitis. Furthermore, up to a quarter of patients may have multiple aetiologies combined.

As cough is ubiquitous in any population presenting to primary care or to general internists, it is most efficacious

if clinicians work systematically towards a clear diagnosis, considering common before rare illnesses. In the past three decades, the diagnostic triad of asthma, GORD or rhinosinusitis in any combination has been suggested to be the likely cause of chronic cough. However, the vast majority of patients with these common conditions do not complain of persistent coughing or have features suggestive of cough hypersensitivity. Treatment of these conditions in patients with chronic cough may improve cough but rarely stops it completely. In some patients, however no clear cause can be identified, leading to the diagnosis of idiopathic cough.

Cough Hypersensitivity

Chronic cough is often associated with an increased response to tussive agents such as capsaicin, a phenomenon identified as cough hypersensitivity. Plastic changes in intrinsic and synaptic excitability in the brainstem, spine, or airway nerves can enhance the cough reflex, and can persist even after resolution of the initiating cough event. Structural and inflammatory airway mucosal changes in non-asthmatic chronic cough could represent the cause or the traumatic response to repetitive coughing. [4]

Recent unravelling of the neurophysiology of cough, suggests that it is likely that neuronal dysfunction may be the primary cause of chronic cough. Indeed, evidence for such has been demonstrated by heightened cough responses to inhaled capsaicin in patients with chronic cough and asthma. In the presence of airway hyper-responsiveness, cough can be triggered by endogenous factors (asthma, GORD, post-nasal drip, even speaking and laughing) or exogenous factors (eg cold air, passive smoking, deodorants etc).

Neurophysiology

Activated sensory airway nerves transmit information via the vagus nerve to first synapse in the brainstem, which rapidly initiates the motor cough response [1]. The cough reflex is thought to involve two main subtypes of sensory vagal afferent nerves. The first subtype is c-fibres; these form networks of unmyelinated nerves throughout the airways and are characteristically sensitive to capsaicin (chilli pepper extract) through activation of the transient receptor potential vanilloid type 1 (TRPV1) receptor and other irritant chemicals. They can also respond to other stimuli such as heat, acidity and inflammatory mediators. The second type, myelinated sub-epithelial Aδ fibres, are found in the proximal airways and respond to mechanical stimuli, osmolarity and acidity but do not typically express TRPV1, and are normally insensitive to capsaicin and inflammatory mediators. The morphology of these airway nerves has been delineated in human airway tissue and shows similarity to that seen in animal models (Fig 1).5 The transient receptor potential (TRP) ion channels are found abundantly in the airways, present in primary airway sensory neurons, and also in airway smooth muscle and epithelial cells. They have important functions in airway chemo-sensation and reflex control regarding temperature, osmolarity and oxidant stress. Reactive oxygen species that are induced by exposure to air pollutants can activate TRPV1 and TRPA1 to induce cough and could underlie air pollutant-induced cough. Increased expression of TRPV1 ion channels has been reported in airway epithelial nerves of patients with chronic cough.

P2X3 receptor antagonist, AF-219 ATP is known to activate and sensitise signal transmission at sensory sites including primary afferent neurons such as airway vagal afferent nerves via its P2X and P2Y receptors and P2X3-containing trimers. P2X3 antagonists have been shown to be active in many inflammatory and visceral pain models, by inhibiting inappropriate chronic signals and decreasing peripheral and central hypersensitivity.

Stimulating these airway nerves generates action potentials that synapse in the nucleus tractus solitarius (NTS) and paratrigeminal nucleus of the brainstem. These afferent nerves then activate complex neural networks, projecting to cortical and sub-cortical areas responsible for sensations of airway irritation and the urge to cough and ultimately, if the stimulus is sufficient, results in coughing via activation of spinal motor nerves to the diaphragm, intercostal muscles and larynx (Fig 2). Importantly, coughing can also be initiated voluntarily without any peripheral stimulus or precipitating sensations, and in some cases voluntarily suppressed. [6] Thus, the potential drivers of excessive cough could originate either in the peripheral nerves or central nervous system, including the brainstem.

Hypersensitive or hyper-responsive cough?

Recent consensus suggests that 'Cough Hypersensitivity Syndrome' (CHS) be used to describe patients with chronic cough.[7] However, evidence from experimentally evoked cough suggests that the neuronal pathways exhibit hyper-responsiveness rather than hypersensitivity. Patients complain of an inability to stop coughing and quality of life is most severely impacted by the length and severity of coughing bouts.

The concept of CHS is that there is a stage of peripheral sensitisation induced by inflammatory factors setting up the scene for a central component that can be visualised by functional magnetic resonance imaging (fMRI).[8] One of the potential mechanisms underlying CHS is that this may be triggered by an inflammatory process that impacts on the nerve endings that increases the sensitivity of these nerves leading to peripheral sensitisation. There is already some evidence that in idiopathic cough, there is inflammation measured in terms of inflammatory cells such as mast cells and of inflammatory cytokines in the upper and lower airways. In addition, in conditions where chronic cough could be a predominant symptom such as asthma, COPD and pulmonary fibrosis, there is a characteristic inflammatory changes for that disease that could interact with cough sensory nerves.

Measuring Cough Hypersensitivity

Measurement of cough hypersensitivity with citric acid or capsaicin indicate that patients with chronic cough usually demonstrate an excessive cough response to inhaled tussigens, with correlation obtained between the level of the neuroinflammatory mediators and the degree of the cough tussive response, supporting the value of cough provocation tests in the diagnosis of CHS. The larynx is an area where the cough hypersensitivity may originate, manifest as inappropriate vocal cord adduction (associated with difficulty in breathing and dyspnoea), globus pharyngeus,

impaired phonation (associated with paradoxical vocal fold motion) and muscle tension. This hypersensitivity has been described in athletes who develop cough and dyspnoea during usually with intense exercise.

Imaging of the brain using fMRI physiological sensory circuits, Mazzone et al have shown that sensory hypersensitivity is represented by both an enhanced activity of the brain regions encoding sensation as well as abnormal responses in brain circuits that usually have descending control on primary afferent processing [8]. Patients with chronic cough demonstrating CHS, had increased activity in the midbrain regions that are involved in nociceptive control.

Cough associated with respiratory conditions
Cough is often dissociated from other symptoms usually attributable to asthma such as wheeze and shortness of breath. In COPD, cough is reported in 70% of patients, and many consider it to be extremely severe contributing to impaired quality of life. Current smokers with COPD tend to have the highest cough rates, almost double that of COPD + ex-smokers or healthy smokers.

Investigations

Assessment of cough may include a simple visual analogue scale (VAS), cough symptom score, quality of life questionnaire, cough frequency monitoring, and cough provocation test. These tests are used to monitor disease status and treatment efficacy.

In the VAS scoring system, patients mark a point on a straight line corresponding to their perception of the severity of cough. The score ranges from 0–10 cm (0–100 mm), with 0 representing minimal severity and 10 representing extreme severity. Compared with the cough symptoms score, the intervals between grades with the VAS are smaller, which is helpful for longitudinal comparison before and after treatment.

The Coughing Score is a quantitative scoring system used to assess the severity of cough and efficacy of treatment. Daytime and night-time scoring is done, however it may be difficult to discriminate between grades [9]. Appreciation of the impact of cough on health-related quality of life has led to the development of three validated, cough-specific, health-related quality-of-life questionnaires that assess cough severity: Leicester Cough Questionnaire (LCQ)[10], Cough-specific Quality of Life Questionnaire (CQLQ)[11], and Chronic Cough Impact Questionnaire (CCIQ)[12]. These tools capture additional information not measured with objective tools and can be used to assess therapy. They should be used in conjunction with other cough severity measures such as cough frequency monitors to obtain a more complete assessment of cough severity.[13]

Investigation for causes of chronic cough are commonly chest radiography, bronchial hyper-responsiveness (BHR) and sinus imaging. Specialised investigations of GORD by using oesophageal pH probe monitoring, a chest CT scan or induced sputum (for eosinophilic bronchitis) are uncommon. Fractional exhaled nitric oxide (FeNO) and maximum mid-expiratory flow (MMEF) might have value as negative parameters for differentiating cough variant asthma (CVA) from chronic cough. [14]

Differential Diagnosis
The common causes of chronic cough are as follows:

- Cough variant asthma (46%)
- pper airway cough syndrome/postnasal drip syndrome (32%)
- Eosinophilic bronchitis (9%
- Gastroesophageal reflux-related chronic cough (9%)
- Postinfectious cough (6%)
- Angiotensin-converting enzyme inhibitors-induced cough (5%) {Yu et al}

In addition to respiratory disease, cough may be a manifestation of cardiovascular, autonomic or neurological disease.

Chronic cough is difficult to manage, and many patients self-medicate with 'over the counter' cough therapies despite lack of evidence supporting their efficacy. A survey of of chronic cough in general practice estimated that 87% of patients could have been managed solely in primary care using a simple guide and that most cases of chronic cough referred to secondary care could be managed with a simple systematic approach. This indicates that efforts need to be made to improve the management of such patients in general practice.

Stage I
Most patients who develop a cough will see their general practitioner first, who will exclude any obvious cause of cough and will most likely order a chest radiograph to exclude any gross pathology in the airways. Asthma and GORD are usually considered and may be excluded with a trial of inhaled corticosteroid therapy and proton pump inhibitor.

Stage II
The next stage is a referral to the hospital respiratory clinic, usually to a chest specialist, although referrals can be made to an otorhinolaryngologist for exclusion of upper airway nasal/laryngeal causes, or to a gastroenterology specialist for exclusion of GORD. Under hospital care, certain additional investigations are usually organised including a lung function test, bronchial hyper-responsiveness, a CT scan of sinuses and thorax and a bronchoscopy may be available.

Stage III
When all known causes of chronic cough have been excluded, and cough is still persistent, the skills of a highly specialised chronic cough may be required. These clinics should provide a multidisciplinary approach to diagnosis and management, and should have access to various facilities for assessment of oesophageal function, nasal and laryngeal hypersensitivity measurements, sleep studies, computed tomography of upper airways and lungs, and have access to otorhinolaryngology facilities such as the visualisation and assessment of the postnasal space and larynx and nasal passages. A speech and language therapist should be part of the team. An important role for specialist cough centres is in educating and training primary and secondary care in the management of chronic cough.

Management of Chronic Cough

Non-pharmacological Measures

This non-pharmacological approach consists of education, cough suppression strategies, vocal hygiene training, and psychoeducational counselling. This has the goal of improving voluntary control over the cough, by teaching patients to identify the causes and sensations that precipitate the cough and to replace the cough response with another response such as a breathing or swallowing exercise, and to alter behaviour that contribute to laryngeal irritation. This method likely acts on both peripheral and central parts of the cough pathway.

(a) Cough control measures such as Buteyko breathing control techniques 14 have been shown to improve quality of life and inhaled corticosteroid use by reducing the perception of breathlessness. Although the 'physiology' suggested is of reducing shear stress that leads to mast cell activation 15, several studies have failed to show any change in physiological measures of asthma. [16]

(b) Yoga- Tai Chi [17] [18] have been found to be more effective than usual care in COPD with clinically meaningful improvements in 6-min walk distance, lung function and health-related quality of life. They have also been found to be comparable to pulmonary rehabilitation interventions in improving breathing control, reduced perception of breathlessness and cough. Mindfulness techniques have been shown to improve perceptions of breathlessness and symptoms in patients with chronic lung disease and may have a role in the management of cough. [19]

(c) Behavioural - Speech therapy may be underutilised in practice and could lead to improvement of otherwise recalcitrant cough.[20] A multi-dimensional speech pathology treatment programme (used to treat hyper-functional voice disorders and paradoxical vocal fold movement) included education, vocal hygiene training, cough suppression strategies and psycho-educational counselling. Participants demonstrated a significant reduction in cough, breathing, voice and upper airway symptoms following intervention. [21] [22]. However the availability of specialist behavioural-speech therapy services is usually restricted to tertiary units and the usual waiting time is over 2 years in the UK.

Pharmacological Measures

(a) Macrolide antibiotic treatment has beneficial effects on lung function in non-asthmatic, productive, chronic cough patients with normal chest X-ray findings. The improvement of chronic rhinosinusitis may have some role in the lung condition.[23] Patients demonstrated neutrophilic or pauci-granulocytic airway inflammation, whereas subjects with eosinophilic airways inflammation do not appear to respond symptomatically.[24] The agreed consensus suggests at least a prolonged therapy of up to 3 months to assess benefit.

(b) Proton-pump inhibitors (PPI) – PPIs are ineffective as single agents in the absence of significant acid GORD. A cohort of GORD patients may present with more proximal reflux, non-acid reflux, and gas reflux, and get better efficacy with neuromodulators (gabapentin or baclofen) used as an add-on therapy with a proton-pump inhibitor. [25] Although gabapentin and morphine exhibit positive effects on cough-related quality of life, only gabapentin is currently supported as a treatment recommendation.

(c) Inhaled corticosteroids (ICS) were found to be ineffective for chronic cough except in the presence of asthma or eosinophilic bronchitis. 2

(d) Neuromodulatory therapies are believed to act on the enhanced neural sensitization that is a key component of unexplained cough. Each of the centrally acting neuromodulators (amitriptyline, pregabalin and gabapentin) have been shown to have positive effects on cough-specific quality of life. Adverse effects can be significant and limit the maximum tolerable dose of these agents. Recommendations suggest that reassessment of the risk-benefit profile be performed at 6 months.

(e) Codeine & Morphine could be used when all other therapeutic options have failed to improve cough and there was close follow-up at 1 week and then monthly.

New targets for chronic cough

(i) Transient Receptor Potential ion channel antagonists - There are TRPV1 and TRPA1 channel blockers in development but it is currently unclear whether they are of benefit in management of chronic cough.

(ii) AF-219 is a P2X3 receptor antagonist - holds promise as a potentially new neuromodulator drug for chronic idiopathic cough, and also for chronic cough associated with chronic respiratory diseases such as asthma, COPD and pulmonary fibrosis. [26] However all patients had taste disturbances (hypogeusia or dysgeusia)

(iii) Central neuromodulators - Central targets that selectively disrupt specific encoding mechanisms of cough may present new therapeutic approaches such as the acid-sensing Ion channels (ASIC). N-methyl-d-aspartate (NMDA) receptors are involved in these acid-evoked reflexes. Memantine, an NMDA channel blocker, has been shown to suppress citric-acid induced cough. [8]

Conclusion

Cough is a common presentation to primary care and to internists and may have a significant impact on quality of life and often lead to social and psychological consequences. Once, acute or sinister causes of cough have been excluded in primary or secondary care, a systematic approach is warranted. Even in chronic cough (>8 weeks), the triad of cough variant asthma, rhinosinusitis – postnasal drip and GORD may be the cause of majority of presentations and often in combination. Therefore, a combined therapeutic approach with objective cough intensity and impact measures (Leicester Cough Questionnaire + cough counters) are beneficial. If these commoner conditions have been excluded, a specialist multi-disciplinary approach is recommended. This will involve specialised investigations, provocation testing, and a comprehensive approach with education, physiotherapy, cough suppression and neuro-modulators. Careful and close monitoring of the benefits of this treatment is essential with objective measures and psychological support may also be needed. There are newer agents being tested approaching the cough reflex from a neuro-biology and inflammatory aspects.

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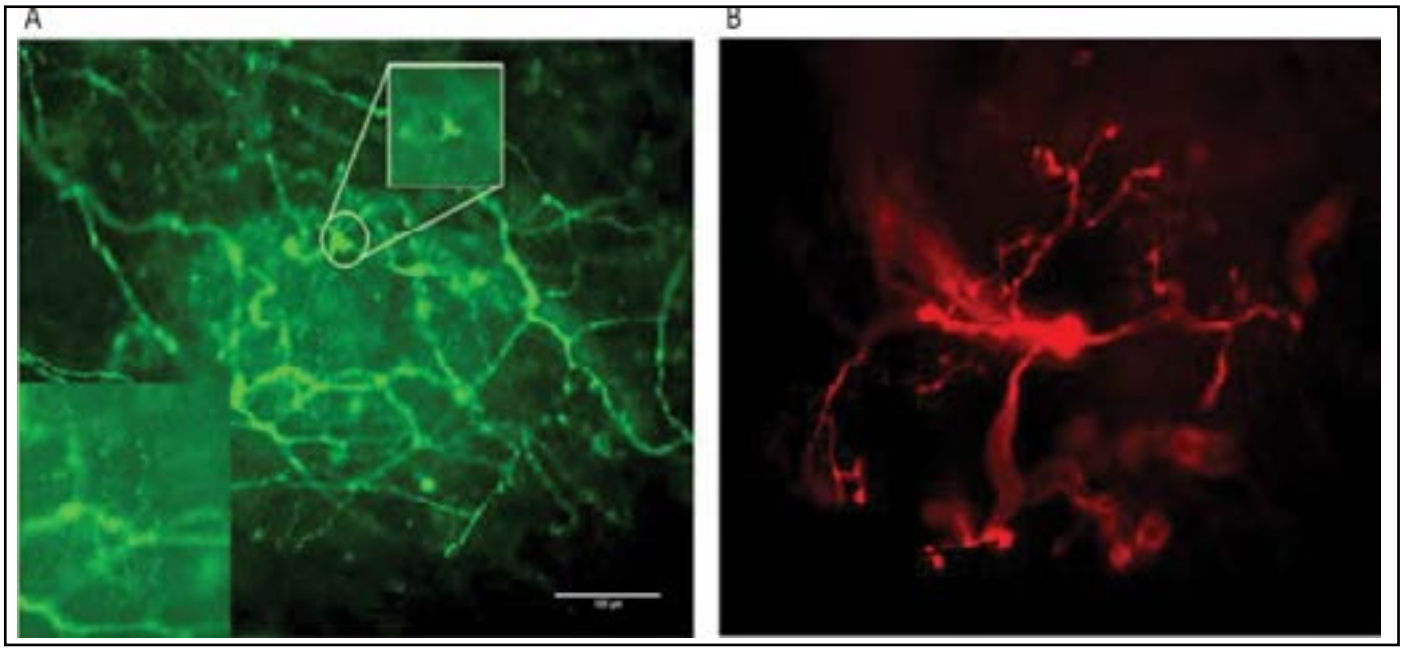


Fig 1.
Structure of human airway nerves. A – thin unmyelinated c-fibres located near the ¬epithelial membrane; B – sub-epithelial ¬myelinated Aδ fibres. Reprinted with permission of the American Thoracic Society.

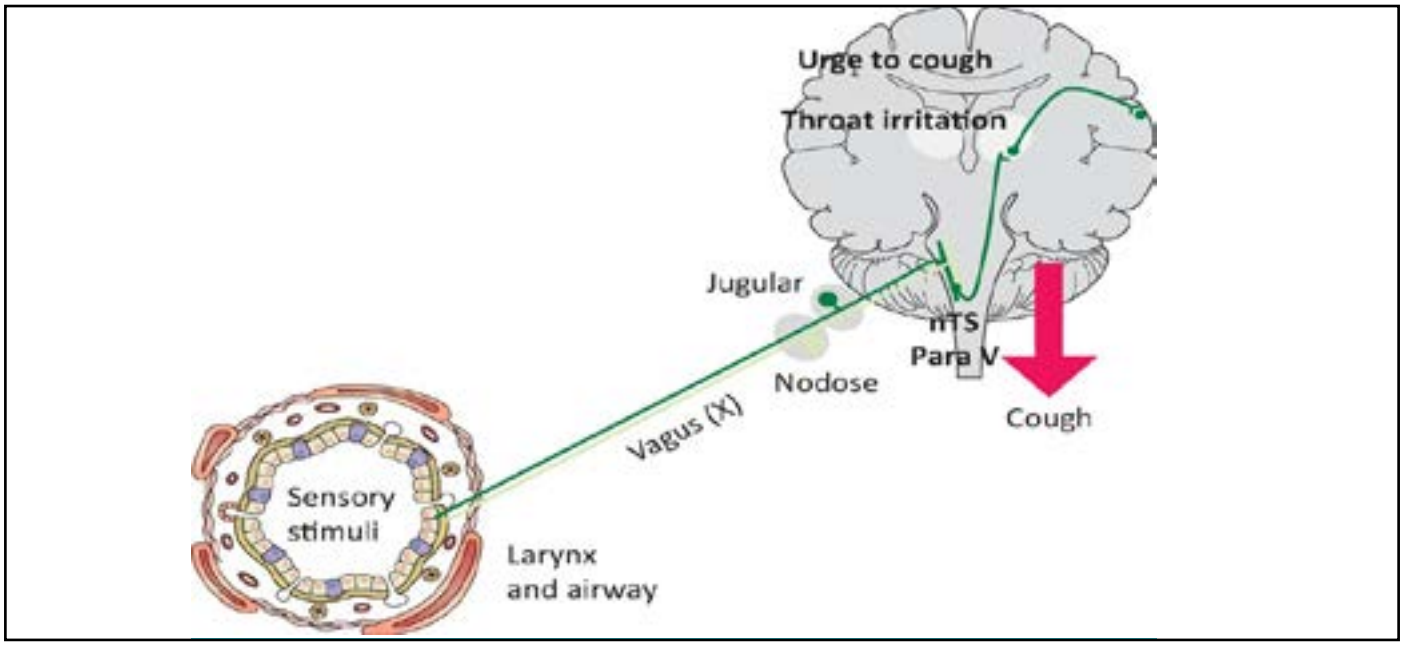


Fig 2: Schematic diagram representing the cough reflex. Vagal afferents transmit stimuli from the airways to the nucleus tractus solitarius (nTS) and paratrigeminal nucleus (Para V) in the brainstem. Neuronal signals are then transmitted to the somatosensory cortex via the thalamus causing throat irritation and urge to cough. These sensations, if great enough, lead to cough via activation of spinal motor neurons.

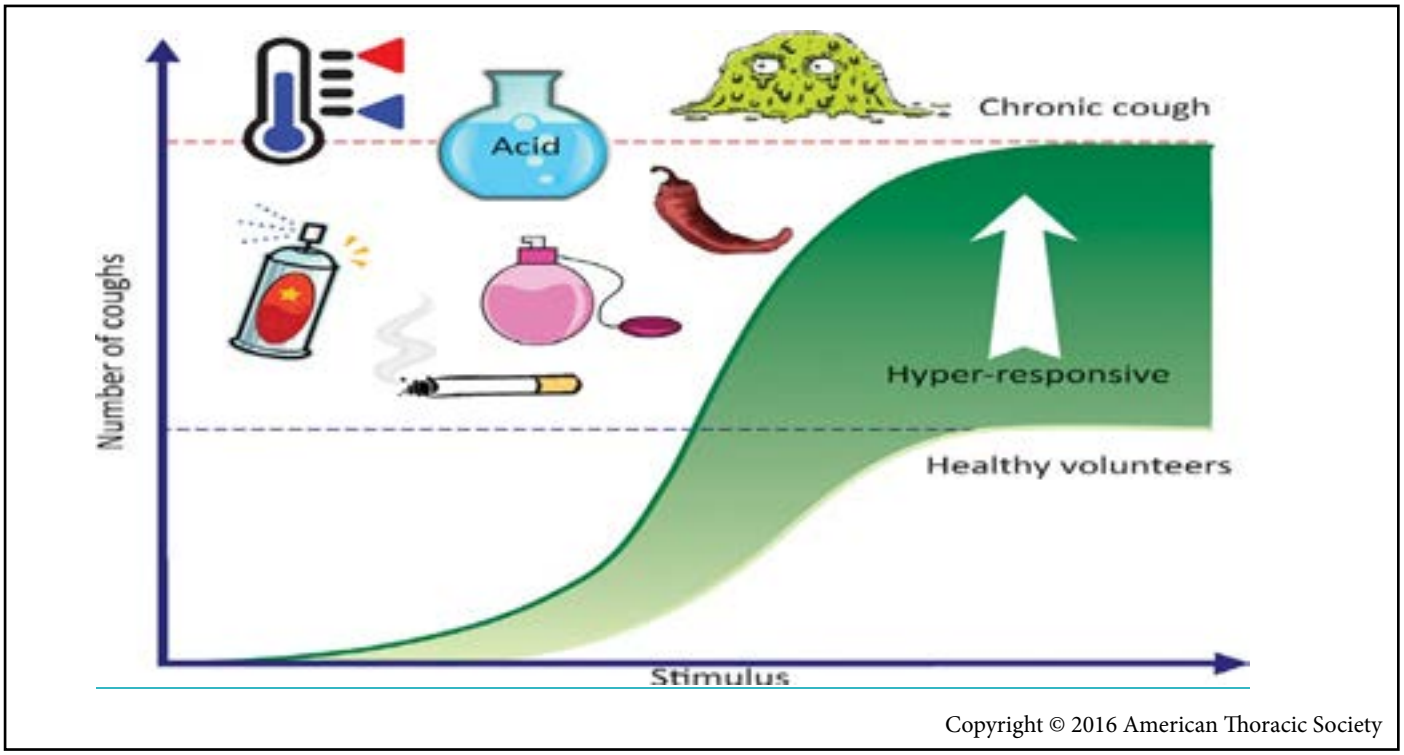
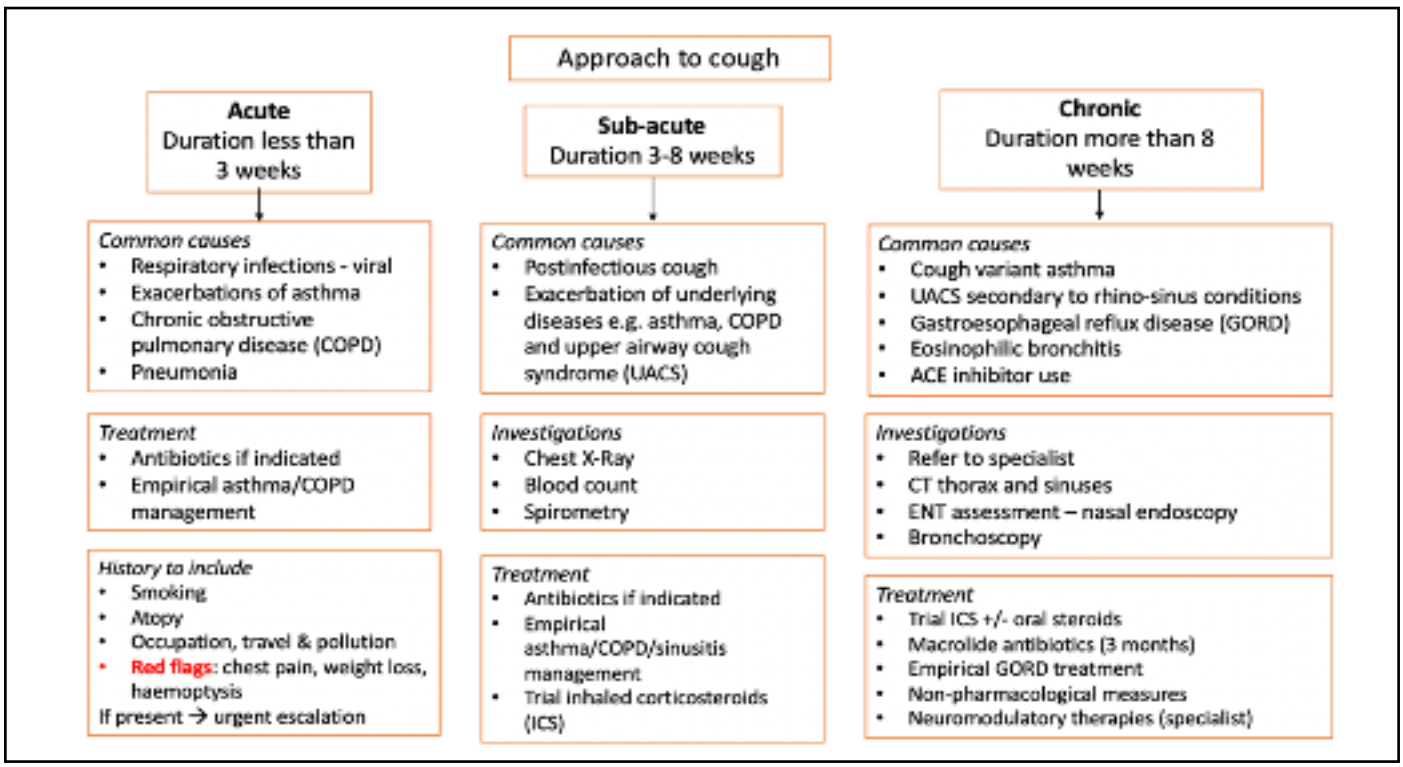


Fig 3: Schematic diagram representing cough hyper-responsiveness to airway stimuli displayed by chronic cough patients. Compared with healthy volunteers, patients with chronic cough predominantly exhibit heightened cough responses to airway stimuli, such as inhaled capsaicin and citric acid, in cough challenge test and report coughing triggered by changes in temperature, perfumes, aerosols, smoke and to small volumes of mucus.



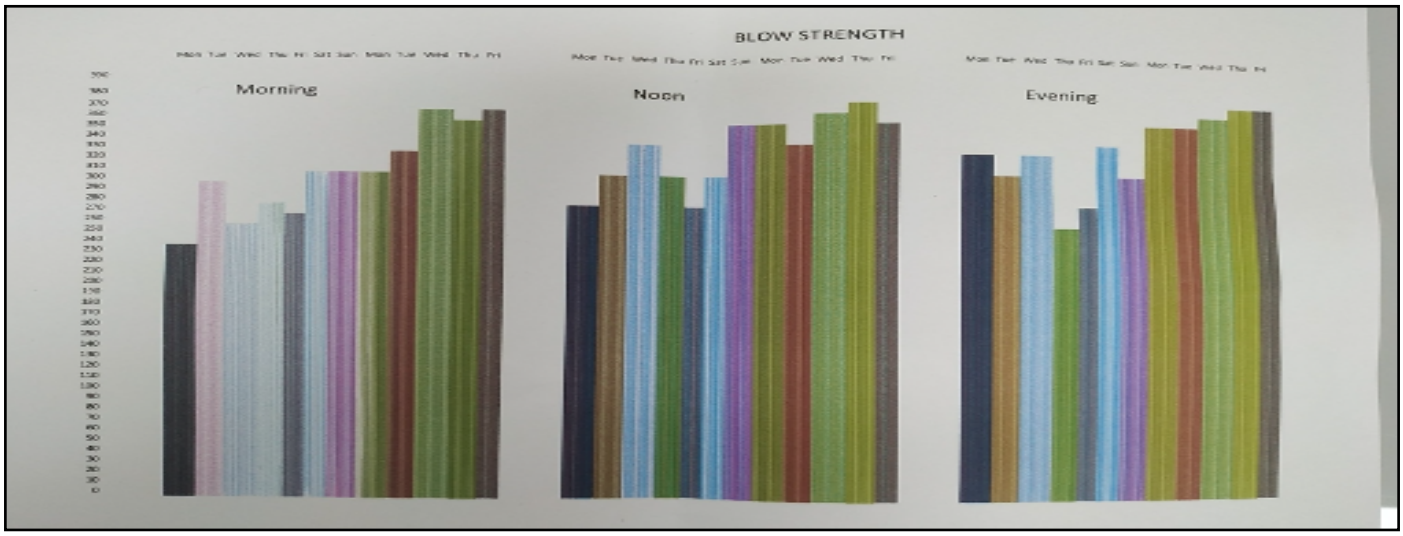


Figure 4: (above) Case files showing serial Peak expiratory flow rate in a patient on treatment with chronic cough

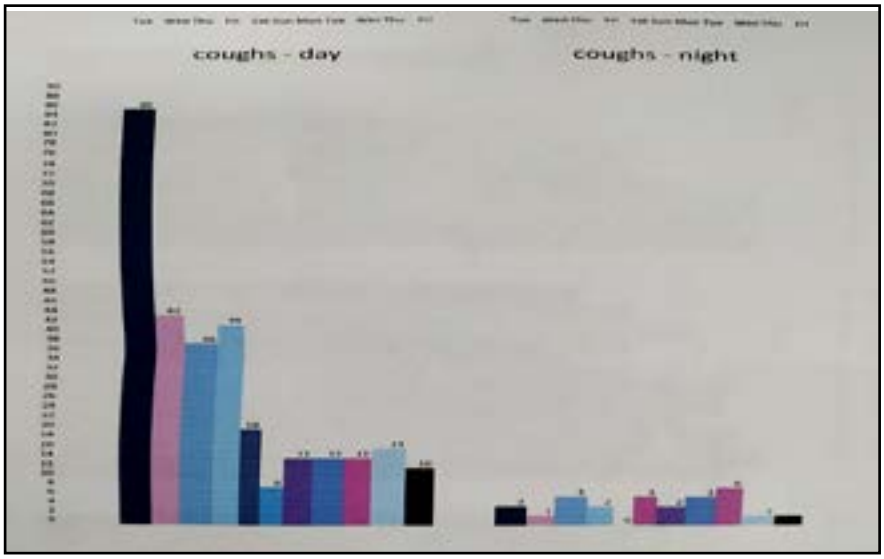


Figure 5: (Right) Case files showing the cough counter data for a patient during treatment

Supported Return To Training (The SuppoRTT Programme)

After almost a decade since Bawa-Garba: *Has the culture changed?*

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ABSTRACT
The Supported Return to Training programme (SuppoRTT) was established and funded in England by the Department of Health after recommendations from various professional bodies, trade union organisations and regulatory agencies. There may be a link between the awareness raised amongst the entire profession and the public by the tragic case of the loss of life of a young boy, and the SuppoRTT programme. Although organisations have signed up to the SuppoRTT programme, and resources have been made available, there are still challenges. Principal amongst them is the lack of information amongst trainees and trainers alike, as well as the culture of 'resilience or coping silently' with all eventualities that is inbred in the profession to its own detriment. The lack of a supportive culture amongst peers and a stressed workplace also contributes to burnout. This article explores the challenges and offers to increase awareness. Solutions and a change of hearts and minds will have to come from within the profession.

Keywords; Supported return to training; resilience; phased return; career break;

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Background
Training to be a doctor begins formally as a young adult entering university, continues for half-a decade and then as a postgraduate learner, remaining the primary focus for several more years. The learning never quite stops, as the race to keep abreast of a rapidly evolving field of medical science, social expectations and culture keeps medical professionals on their feet and engaged in a lifelong quest. Combined with this are other factors: personal motivation to seek the best for every patient, empathy for the fellow human being, coping with a challenging environment of diminishing resources, rising demand for better health, an ageing population with multiple comorbidities, a health service frequently at the mercy of domestic politics, international conflict or economic downturns; thus creating a recipe for lifelong stress and burnout. [(1)]

Sometimes, a basic fact of life often escapes the attention of healthcare strategists and workforce planners, that parallel to the need for progress and competency for healthcare professionals; exists the need for emotional, social and financial stability in order to establish oneself in a traditional conservative profession balancing sometimes the start of a life relationship, or sometimes the demands of a young family.[(2)] Based on socio-cultural and educational norms in many societies, such 'burden/ responsibility' often falls disproportionately on women, who therefore find it seemingly more difficult to keep up with the demands of their chosen vocation or the oft punishing lifestyles of their peers. Often inadvertently ignored is personal health and well-being, therefore, contributing adversely to their own physical or mental health status.

When one takes a break from career or training, there is an artificial hiatus from the pace of learning and the adrenaline that keeps professionals constantly focused on progress and development. The common reasons for such career breaks can be parental leave, personal health related issues, family demands or more rarely as a consequence of medical errors or litigation. [(2)] Healthcare professionals who take parental leave identify a lack of an universal leave policy, strain of maintaining relentless training goals, loss of education time, lack of flexibility of programs and workplaces, and lack of support from faculty/peers as the major obstacles to taking leave during specialty training. [(3)]

More recently, the millennial generation have chosen to manage their own careers at their own pace or at a place of their choosing. This phenomenon became apparent after the regimentation of training programs was established and the rigidity of training pathways offered limited manoeuvring for individual tailoring or capacity to create temporal space for life events. [(4)] More than half of foundation doctors are taking a break after completion instead of directly entering specialty training programmes, choosing instead to do an "FY3", to explore a variety of specialties, go travelling or experience healthcare in distant lands.[(5)] Doctors within core and higher training are continuing the tradition of taking out of programme breaks for research, education or leadership roles. These phenomena throw up an increasing cohort of

doctors who are now returning to practice after time away for various reasons.

The Curious Case of Bawa-Garba

For what is now probably the most influential case in the history of medical training in the UK, the tragic circumstances leading to the death of a young boy presenting with sepsis in 2011 and the sequelae for the involved healthcare professionals, shook the profession to its core. [6] Most attention has focused around the working environment, culture, support infrastructure, attrition of clinical skills during a period of break, senior supervision, gaps in the rota, unfamiliarity of the clinical environment among other factors which may have contributed to the tragedy. Dr Bawa Garba was sentenced for manslaughter, her licence erased from the register of medical practitioners and eventually partially restored. The focus of this article is not to debate the pros and cons of the case, nor how the regulator may have handled the investigation and the conflicts around the erasure, but to focus on the circumstances that may have left a young doctor vulnerable on her return to work after a period of parental leave. We know now that the support provided to this individual was non-existent. Hers was not an isolated incident, the story resonated with the entire frontline healthcare workforce.

Hundreds of doctors, nurses and other healthcare professionals are returning to clinical practice with little or no acknowledgement that they may have lost the sharpness of their clinical or procedural skills, that they may need a period of time to orient themselves with the much changed clinical environment and teams to regain their confidence. It is not anyone's fault, as most clinicians would not hesitate to agree that when away from frontline clinical work for prolonged periods, one loses one's speed and accuracy of decision-making. This attrition of skills is most easily quantifiable in surgeons and those that depend on procedural skills or physical dexterity. [7–9]

Attrition of Skills

The science of this recognised decay of clinical acumen, decision-making, accuracy of prescribing or dexterity in procedures is not well-documented barring few exceptions. Studies involving resuscitation where adherence to strict protocols may affect outcome or in specific surgical procedures (e.g. total hip replacement) show that periods of absence may adversely affect performance accuracy and recall. In non-surgical disciplines, this attrition of skills is more challenging to measure and quantify. Although the evidence base is weak, most trainees and trainers agree that there is attrition and that a period of refresher/ retraining is necessary. [10]

Rationale for SuppoRTT

Although there is consensus in the profession that accuracy and comprehensiveness of professional education and training status (i.e. competency) does deteriorate during a period of absence, there is little evidence to suggest a minimum threshold for this loss. The rough consensus is around a period between 3-4 weeks (for certain highly skilled procedure dependent specialties) to 3 months before there is a noticeable change in performance. The attrition is also dependent heavily on the state of proficiency of the previously acquired skill before cessation [8] of practice and on the duration of the absence. It is expected that a doctor who has barely achieved minimum proficiency in a procedure or clinical decision-making will lose this skill quicker than one who has been practicing at an expert level for a longer period of time. [7] Hence on return, the more inexperienced learner will need more time and support than a more previously experienced professional. The bottom line is that the time and resources required for returning to expected proficiency is determined at an individual level, recognising the specialty and the clinical environment.

Uptake and Awareness

The SuppoRTT has been running for the last 2 years and funded by United Kingdom Department of Health (DoH) to the tune of GB£10 million.[11] Health Education England (HEE) has funded the appointment of champions within all NHS Trusts across England, set aside additional funding for a safe and supported return by means of refresher courses, funding for a period of enhanced supervision, coaching and mentorship. Each HEE Specialty School has appointed leads for developing the framework for delivery of minimum standards for safe return to clinical practice and education supervisor upskilling to better supervise the needs of this group is being delivered across England. [11] Yet, in the first 2 years of available data suggests that the uptake of the additional resources and funding in different regions, ranges from none, to a quarter of returning trainees. There are several factors that may be contributing to this; namely, a lack of awareness both amongst trainees and their supervisors, poor information or database infrastructure within human resource (HR) departments, inability for HR databases to exchange information about the absence of trainees adequately with the training programmes and vice versa.

In the health sector there exists a perception that one would be judged unfairly, that one may appear weak and incompetent if asking for additional help. This is particularly true for those returning from non-parental leave and in traditionally demanding specialties e.g. surgery, cardiology etc. For international healthcare staff, they may be subject to prejudices, have their own cultural deference to authority, come from systems with less support which may pose additional challenges, i.e reluctance in asking supervisors for the action planning meetings, for additional resources, and the implications that may have on their career progression in an environment that may already contain a bias. There is a culture of being stoic and "just getting on with it", but in the event of an inadvertent clinical error, one is often faced with a punitive face of that culture which has often ended up holding a trainee negligent for systemic failings.[12]

Challenges

There are several hurdles that will need to be understood and addressed if this system were to be successful in achieving a safe and supported return to practice for all healthcare professionals. Educational programs also face challenges: cost of development and maintenance; allocation of staff and faculty time to re-educate returning physicians alongside other learners; provision of emotional support, counselling and career guidance; interpretation of varied licensing guidelines; and the need to tailor one's program to individual

trainees. In some specialties there may be a number of sub-specialties with varying needs, and others the various grades of the returning trainees can pose a problem for pitching the course at the right level. Years out of practice and increasing physician age are predictors of poor performance.

The major themes that often emerge from the analysis of interviews from healthcare professionals returning are: compromise and feeling valued. The experience of returning to work is a process of compromise in which staff find strategies to cope with their changing roles vs demands, to find a balance between home vs work life. Staff want to feel valued by their managers and co-workers, as this enables them to feel comfortable, confident with some of the compromises they made.[13] Another challenge is in relation to physical and mental health related absences, where the assessment and intervention of an occupational health (OH) team is critical to success. The OH teams may have to prescribe phased return and limitations on activities as well as duration. Integrating such specific requirements to a demanding schedule may be particularly challenging as it would be to provide additional on-site supervision. [14]

The elephant in the room is the large proportion of doctors who are not in training posts (often overseas qualified doctors), moving between training programmes or specialty schools or even between UK NHS regions (SuppoRTT is only available in England). There is no system or framework to recognise this large 'fluid population' of doctors and provide any oversight, supervision or support. At various workshops the discussion has often revolved around 'who should be responsible?'. The answer is often that it has to be the doctor who requires this support. No one would deny that and often the awareness of the deterioration in skills, competence and confidence is most acute in the doctor who is faced with this prospect. But these are the doctors who are most likely to be vulnerable, in fear of being considered incompetent or unsafe, or of losing their hard earned reputation as a reliable professional. The stakes are usually high and the odds often steeped against them. [15-17]

While there are now emerging frameworks for doctors who are returning after breaks, there are little structured resources to support nurses, midwives, paramedics and other frontline healthcare staff. The General Medical Council and Nursing & Midwifery council are starting to set up requirements for registrants returning after career breaks. Other registration bodies such as the General Pharmaceutical Council or the Healthcare Professions should follow soon.

There may be registration requirements, funding sources for trainee doctors and for all staff in statutory parental leave with Keep in Touch (KiT) days, but who will provide the funding needed for non-trainee doctors, consultants, nurses, midwives and allied health professionals who may be in rotational appointments or shorter contracts. None of the NHS Trust finances are in a healthy position to support the additional funding needed for supernumerary or phased return. Yet we must consider that at the receiving end of any delay or inaction in this area will be the unsuspecting patient who may suffer consequences of a healthcare professional whose clinical acumen and skill has decayed through a planned or unplanned break. However, one must not forget the consequences on the 'second victim' - the professional themselves.[12]

There also remains the challenge of the low uptake and awareness. If there is an underspend in the funding due to poor awareness and implementation by trusts, supervisors and trainees, as with most budgets in healthcare, there is a risk of it being taken away for causes deemed more noteworthy.

Conclusion

The only proper way to view this challenge of facilitating doctors (and all healthcare professionals) to take career pauses or breaks and to return them safely back to practice would be from the lens of the patient receiving treatment by the ethical principles of 'do no harm' as most critical decisions in healthcare are based on. Once the culture of safety, blame free learning and planned risk avoidance becomes mainstay, the funding and resources will follow. SuppoRTT champions have a key role to play in the near future to develop frameworks, set minimum standards and monitor progress towards a safe and supportive NHS for all.

CASE STUDIES

"Deena is an oncology registrar, who has taken time off to be a carer for her elderly father who has had a long battle with cancer and has tragically passed away. She has done an odd shift in A&E as a locum during this time. She is due to return to training in 2 months in the same hospital where her father was treated. She cannot begin to contemplate how this will feel to walk into those rooms without him and see the same healthcare professionals who treated him and how she will adjust to becoming the clinician treating patients from being on the other side. She is uncertain how to raise this with her educational supervisor in case it impacts on her career progression, she already feels behind due to her time out.

"Jyoti is an ST4 in ENT, who had to take time out of training to have emergency cardiothoracic surgery. She has recently tried to get in touch with her last clinical supervisor and training programme director to indicate her clinician is happy for her to return to training. She has had [11] months of sickness absence and is concerned about her level of deskilling and how she will cope with returning to a completely new workplace and how supportive her supervisors will be"

Questions to consider

- In your educational supervisor role, how would you assess these trainee's needs and prepare an action plan for their return? Who else would need to be involved?
- As a clinical supervisor how could you facilitate informing your department managers and rota coordinators in time so they can access the supernumerary funding and make suitable adjustments to accommodate the trainees safe return to training?
- As the training programme director how would you in your role support the trainee's transition in terms of navigating the effect on training time, highlighting the SuppoRTT process and funding and other resources

the trainee could make use of?

- As a trainee stepping out of training, who would you contact to get more information and support and how can you enable yourself to have the right conversations with the key individuals who can make a positive difference to your return to training?

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Simulated procedures
Image Technology

CPD – Radiology Quiz Answers

Kassiani Iliadou

The main Chest XR findings are:

1. Left pneumothorax
2. Left collapse - consolidation
3. Chilaiditi sign

The symptoms were attributed to the pneumothorax and he underwent therapeutic thoracentesis (pleural aspiration).

Pneumothorax (1)

A pneumothorax is the abnormal presence of gas (air) in the pleural space.

Collapse - Consolidation (2)

A collapse or atelectasis refers to the loss of normal aeration and associated loss of volume. The term **consolidation** refers to the displacement of the air in the alveoli, smaller bronchi, or bronchioles, by exudate or oedematous fluid.

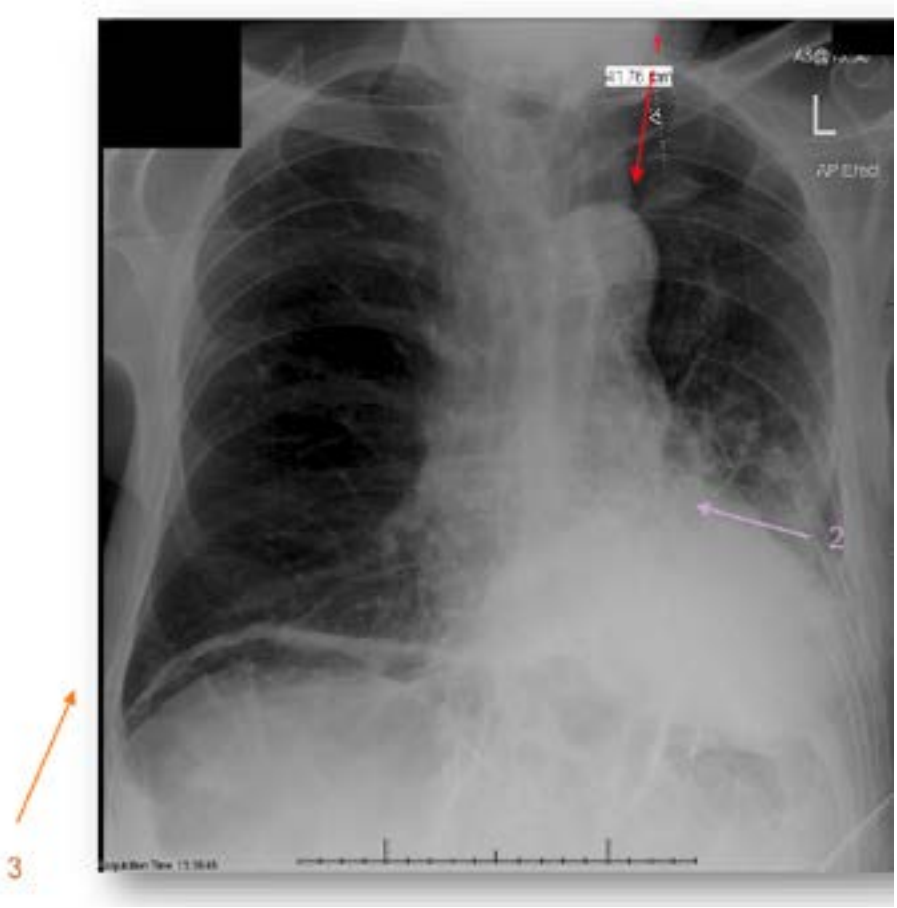
Chilaiditi sign (3)

(interpositio hepatodiaphragmatica, subphrenic displacement of the colon, subphrenic interposition syndrome)

Chilaiditi sign is a cause of pseudopneumoperitoneum, a term used to describe any gas within the abdominal cavity that masquerades as free intraperitoneal gas. This sign refers to the interposition of the bowel, between the inferior surface of the right hemidiaphragm and the superior surface of the liver. Usually, the part of the bowel seen is the transverse colon. Normally, the person is asymptomatic, and the sign is an incidental finding. Its presence can be permanent or sporadic.

Chilaiditi syndrome

Chilaiditi syndrome refers to the medical condition in which a Chilaiditi sign is accompanied by clinical symptoms. The most common symptoms are gastrointestinal (eg, abdominal pain, vomiting, constipation), followed by respiratory distress and rarely angina-like chest pain. Rare complications are volvulus, coecal perforation or perforated subdiaphragmatic appendicitis. 1, 2, 3



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Causes

The exact cause is unclear. It can be seen in patients with dolichocolon, chronic lung or liver disease, diaphragmatic paralysis, causes of increased intra-abdominal pressure, chronic constipation, aerophagia. There is a relation to anatomical variations of the ligament suspending the transverse colon or the falciform ligament, congenital

malpositions.

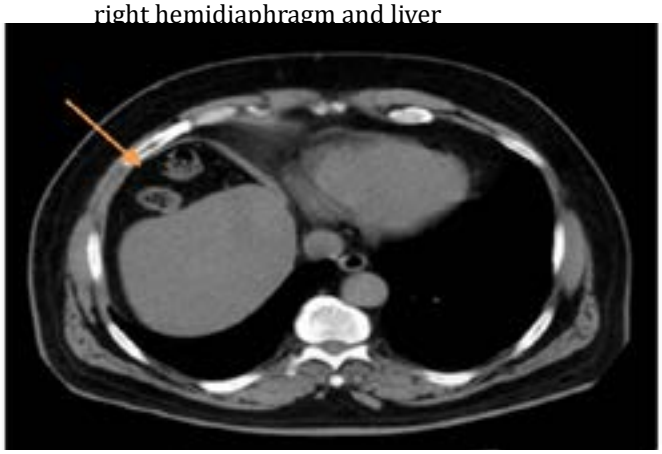
Radiographic features of Chilaiditi sign

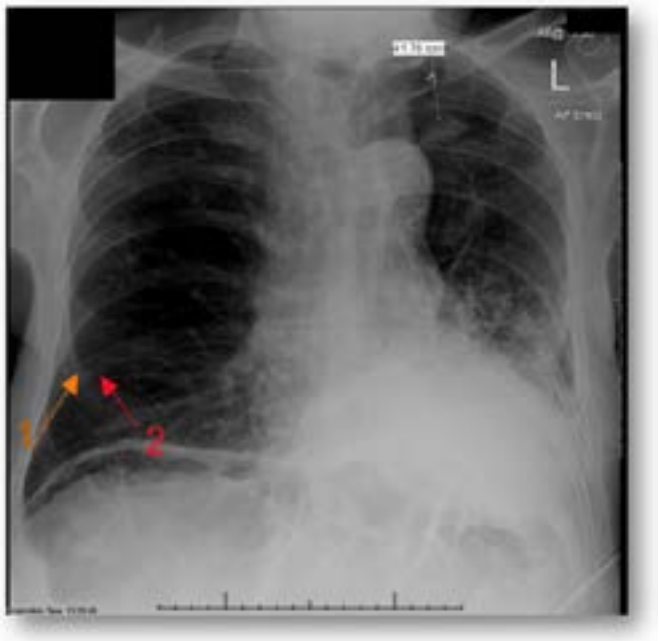
Plain radiograph

1. Gas between liver and diaphragm.
2. Haustra within the gas suggesting that it is within the bowel and not free
3. Changing the position of the patient will not change the position of the radiolucency

Computed Tomography

1. Interposed colonic loops between the right hemidiaphragm and liver





1. Gas between liver and diaphragm 2. Haustra within the gas

Differential diagnosis

True pneumoperitoneum (indicative of perforation), bowel ischaemia, subphrenic abscess are diagnoses to be excluded. The correct identification is crucial, since the misinterpretation may lead to unnecessary further investigations and surgical interventions. 4

Complications

Complications are rare but can be seen in Chilaiditi syndrome. These are volvulus, cecal perforation or perforated subdiaphragmatic appendicitis, intestinal obstruction of either the large or small bowel, colonic pseudo-obstruction (Ogilvie syndrome).5

Management

Asymptomatic patients do not require further imaging or intervention. It is important to be identified, if a percutaneous transhepatic procedure or liver biopsy is to be performed to avoid perforation. Colonoscopy should be performed cautiously, given the risk of perforation because of air entrapment in an acutely angulated bowel. In Chilaiditi syndrome, bowel decompression with enemas and laxatives is indicated. In the extremely rare case that there is no response to conservative management, then surgical intervention may be necessary. 6

Other causes of pseudopneumoperitoneum

- basal linear atelectasis
- pneumomediastinum
- pseudo-Rigler sign
- diaphragmatic undulation
- gas within skin folds
- fat within the subdiaphragmatic space
- properitoneal fat stripe
- biliary, portal vein or bowel wall gas
- benign post-traumatic pseudopneumoperitoneum

History

It is named after Demetrius Chilaiditi (1883-1975), Greek radiologist who described the radiographic findings in 1910 whilst working in Vienna, Austria.

Etymology of pseudopneumoperitoneum
pseudo- (from Greek ψευδής, "lying, false")
pneumo- (from Greek πνευμ-, ''related to breath or spirit'')
peri- (from Greek περι-, ''around, about'')
ton- (from Greek τόνος, ''stretched, tension'')
eum (Latin suffix)

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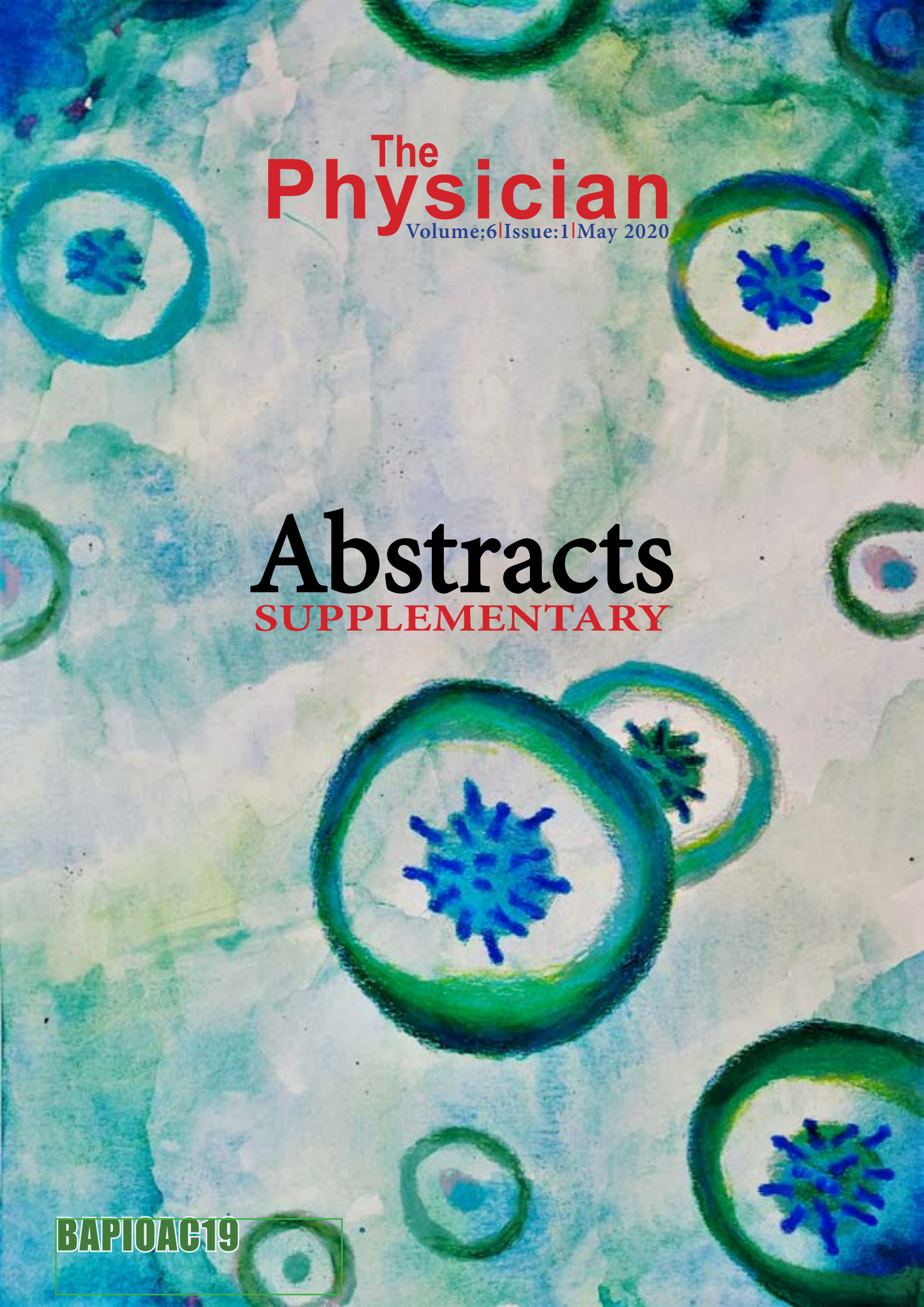
Abstracts
SUPPLEMENTARY



BAPIOAC19

Abstracts

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Abstracts Supplementary https://doi.org/10.38192/1.6.1

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BAPIOAC19-01

Gene expression analysis of oncogene transcript in aberrant crypt foci, in comparison to the normal colonic mucosa and colorectal carcinoma, from formalin fixed paraffin embedded tissue samples

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cite as: Sulaiman, M., Jayati, S., Ghosh, S., Gupta, B., Ahuja, E.V., Pal, S., Shahni, P., DattaGupta, S, & Panda, S.K. (2020) Gene expression analysis of oncogene transcript in aberrant crypt foci, in comparison to the normal colonic mucosa and colorectal carcinoma, from formalin fixed paraffin embedded tissue samples. The Physician 6(1):c1 DOI: 10.38192/1.6.1.c1

Background and aims
Aberrant Crypt Foci (ACF) are early microscopic mucosal lesions in the colon which can be detected by magnified chromoendoscopy. The main purpose of this study was to develop an ex-vivo model of identifying the ACF-like lesions on grossly normal looking colonic mucosa so that the model resembles the chromoendoscopic procedure. We investigated the comprehensive gene expression analysis in ACF to understand them better. Further, correlation between genetic alterations amongst various topographic ACF-groups were also analysed.

Methods
A total of 35 positive cases with numerous ACF (more than 4 per 2 sq mm mucosal fragment) and corresponding tumour cases were selected out of 302 colectomy specimens received in the department. Another 20 cases were selected retrospectively as controls from colectomies performed for causes with no malignant potential. Gene expression analysis by Real Time polymerase chain reaction (RT-PCR) was performed on ACF in relation to control and tumour, and immunohistochemical test was performed to correlate the gene expression and protein expression for some of the transcripts. Gene expression data was correlated with the clinical parameters, as site and size of the tumours, tumour stage and lymph node metastasis, histological and topographical types of ACF etc.

Results
In comparison to the controls, ACF positive samples showed significant alterations in KRAS, CDKN1A, CDKN2A, MLH1, VEGFA, and CCL5 genes. Similarly, alteration in CDKN2A, PTEN, and SMAD4 genes were noted in ACF positive samples compared to tumour. No correlation between gene expression and ACF characteristics were noted.

Conclusion
Irrespective of morphological characteristics any ACF-like lesions needs to be addressed seriously with regular screening and follow up. Pathogenesis of such early neoplastic lesions in human colon is multifactorial and complex. Further studies may throw light on identifying prospective pathways which can be targeted to prevent the progression of these lesions. ❑

BAPIOAC19-02

Importance of Communication in Reducing Sepsis; Risk in Children via Administration of Antibiotics in the Golden Hour

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Cite as: Ignatius, V.P., Divya, R. & Gupta, R. (2020) Importance of communication in reducing sepsis risk in children via administration of antibiotics in the golden hour. The Physician 6(1):c2 DOI: 10.38192/1.6.1.c2

Background:
Sepsis is a preventable cause of death. According to NICE guidelines, the first hour of diagnosing sepsis is considered the golden hour as the outcomes are better if the treatment is started at this hour. This observational study was conducted at a district general hospital to assess the compliance of the antibiotic administration within the first hour of diagnosis of sepsis.

Methods:
This study was conducted at Paediatric Department of Barnsley District general hospital and the data was collected from all the admissions to children's ward between October 2018 and June 2019 with a diagnosis of SEPSIS. Data was collected regularly and analysed every month by a team comprising of Paediatric doctors, antimicrobial pharmacist, patients safety team members and microbiologist. Periodic communication and feedback was sent to all the members of the team to reinforce the importance of the golden hour in

sepsis management. Also, it was discussed in the handover and emphasised in induction.

Results:
Analysis of the data revealed that 77 children out of the 90 children (86%) received the first dose of antibiotics within 1 hour as per the NICE guidelines. Most common reason for missing the 1 hour deadline was difficult intravenous cannulation. It was observed that the children who were admitted to children's ward from A+E were more likely to get the 1 st dose of antibiotic within the first hour of sepsis diagnosis than the children who were admitted through the Children's Assessment unit.

Conclusions:
The percentage of children receiving the first dose of antibiotic within 1 hour of diagnosing sepsis increased when everyone in the team were reinforced about the importance of the golden hour in sepsis. According to a previous study conducted in our hospital in the year 2018, the percentage of children receiving antibiotics within 1 hour of diagnosis was just under 60 %. Hence, it can be concluded that by periodic communication via emails and feedback during the handover / teaching improved the compliance of antibiotic in the golden hour thereby improving patient safety. ❑

BAPIOAC19-03

To Develop a Non-invasive Technique as a Preliminary Tool to Determine Type 2 Diabetes

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Cite as: Joshi KR, Haris P, Pena-Fernandez, A. (2020) To develop a non-invasive technique as a preliminary tool to determine type 2 diabetes. The Physician 6(1):c3 DOI: 10.38192/1.6.1.c3

Abstracts

Background and aims:
A study was designed to understand a three-dimensional cause and effect relationship among ethnicity-based diet, relevant macro, and micro-nutrients obtained from diet, and prevalence of type 2 diabetes. If such relationship exists, then this link can be used to develop a preliminary non-invasive screening technique to determine if the patient needs any further invasive techniques.

Methods:
A questionnaire and lab-based techniques were used to gather data and samples from 400 participants from community services and NHS GP practices within Leicester, UK.

Results:
Out of 400 participants, Indian (61%), Pakistani (19%), White British (9%) were the top three ethnicities in the research. From the total Cohort, 188 (47%) were diagnosed with type 2 diabetes (T2DM) of which 86% were managing their condition through oral medication, and maximum number of respondents (87%) were unaware of the fact as T2DM preventable and potentially reversible. Ethnically diverse non-diabetes subjects were consuming a high carbohydrate, protein-rich diet. Fat intake was high among non-diabetes Indian, Pakistani, Bangladeshi, and African except White British. Using FETA technique, average food intake of 14 food groups and dependent key elements were found. Magnesium and Zinc which are important for T2DM management were high in non-diabetes subjects whereas Selenium, which acts as an antioxidant in case of T2DM, was found in low concentration within both T2DM & non-diabetes population. Currently, this research is in a lab work analysis phase to determine how the scalp hair and toenail samples using elemental techniques provide the level of macro and micro-nutrients within cohort.

Conclusion:
By accessing dietary data, it is possible to determine the status of nutrients and its importance in prevalence of T2DM.

Picture source:healthline.com

BAPIOAC19-04

Lead The Way - Why Emotional Intelligence is Needed for Leaders in 21st Century Primary Care.

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Cite as; Hussain,P, Ikar AW, Okhira T, Sivapalan A, Thakor S, Chaudry A, Halari S & Meyer E. (2020) Lead The Way. Why Emotional Intelligence is Needed for Leaders in 21st Century Primary Care. The Physician 6(1)c4 DOI; 10.38192/1.6.1.c4

Background
The need for leadership within 21st Century healthcare is ubiquitous, with better leadership being shown to improve health outcomes. Whether that be leading a ward round, an MDT meeting, or even a cardiopulmonary resuscitation; leadership is a vital necessity in a healthcare setting. When it comes to Primary Care, there is currently a huge demand from patients, colleagues and the NHS, that GPs must meet. With over 50% of medical students in the UK progressing to specialise in Primary Care, developing leadership skills within this field is vital. Emotional intelligence (EQ) is a core skill found to combine over 12 competencies of leadership. However, soft skills such as EQ have been overlooked during medical training. Our research explores the impact and importance of EQ for leaders in Primary Care.

Methods
A systematic review highlighted the importance of EQ for healthcare leaders and assesses its impact on key performance indicators. Appropriate search terms were used to systematically search five databases for literature published after 2014. Inclusion and exclusion criteria were applied to screen abstracts and full texts. Final articles included a focus on EQ within healthcare leaders with impact on at least one performance indicator. Primary data collection with GPs was conducted in the form of semi-structured interviews (SSIs) in order to understand the impact of EQ on workplace behaviours and attitudes within Primary Care. Purposive sampling was used to select potential study participants with the aim of providing the most credible information to the study. GPs were recruited through the Royal College of General Practitioners (RCGP) and the Faculty of Medical Leadership and Management (FMLM) and inclusion and exclusion criteria were used to screen participants. Ethical approval was received from Imperial College Research Ethics Committee. Interviews were then transcribed, and thematic analysis was used to generate codes and overall themes. Thematic analysis was conducted by analysing each written transcript, generating initial codes, searching for themes and categorising them into overall sub-themes and higher themes.

Results
The search produced 3638 articles of which 44 were included for full text screening. We found that EQ in healthcare leaders had an impact upon key performance indicators: Job Satisfaction, Patient Satisfaction, Stress, Worker Burnout. A total of 15 SSIs were conducted with GPs across London. From the thematic analysis, 3 higher themes were generated (Patients, Primary Care as an Organisation, and General Practitioners) and 10 sub-themes which portrayed that EQ has a positive impact on job satisfaction, interpersonal relationships, teamwork and levels of burnout for GPs. In addition, EQ was described as being beneficial for patient consultations and thus improving patient satisfaction. With regard to leadership in Primary Care, EQ was found to play a positive role towards change in organisational culture.

Conclusions
EQ is a widely endorsed skill required for leaders within Primary Care, shown to play an important role for 21st century healthcare. Research determining the efficacy of EQ and its impact in Primary Care can simmer the dispute regarding the importance of EQ within healthcare and ultimately, provide an evidence base to support the creation of EQ training schemes within Primary Care. ❑

Source:medics.academy

BAPIOAC19-05

Innovation in ADHD Care Pathway in a DGH Setting

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Cite as: Shekhar S & Mani P. Innovation in ADHD care pathway in a DGH setting. The Physician 6(1):c5 DOI: 10.38192/1.6.1.c5

Background:
In UK, the prevalence of ADHD in children (age 5 to 16 years) is 3-5%. Symptoms of ADHD should meet the diagnostic criteria in DSM-5 or ICD-10. Children with ADHD would benefit from improved organisation of care and better integration of child health services, CAMHS and adult mental health services (NICE guidelines 2008). We describe changes made in the ADHD pathway at a DGH hospital to improve the patient journey.

Methods:
1. GP referrals did not contain relevant information, hence referrals from school/SENCO was introduced. To improve the quality of school report and support provided, ADHD study day was organised (attended by 120 SENCO/school teachers). 2. ADHD nurse specialists have been trained to help with improved communication and follow up of patients. 3. Qb test (a computerised test to look quantitatively at hyperactivity, impulsivity and inattention) is done to ensure comprehensive assessment. 4. A clinic proforma was developed to ensure compliance with NICE guidelines. 5. A study day was organised for GPs to improve adherence to shared care guidelines. 6. We liaised with Adult ADHD services to improve transition clinics, and CAMHS team to manage co-morbidities.

Results:
Improved efficiency- Reduction in clinic time needed for a diagnosis (25 new ADHD assessments in 2018 needed 30 clinic appointments, 60 clinic appointments needed in 2015). Reduction in ADHD assessment waiting times to 8 weeks (16-18 weeks in 2015). Patient satisfaction - DNA rates have decreased from 22% in 2015 to 4-5% in 2018. Feedback forms have shown significant improvements. Audit looking at compliance to NICE guidelines (NG87) for assessment, counselling, drug treatment, monitoring and transition has shown an improvement across all parameters. All GP surgeries do prescriptions according to shared care guidelines.

Conclusions:
The new innovative ADHD care pathway has led to safe, effective, efficient and sustainable delivery of ADHD services.

BAPIOAC19-06

Patient Information Leaflets: Our Clinic Experience in Using QR codes and bit.ly for STI and Contraception Leaflets

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cite as: Sivaraj V, Artykov R, Drysdale J, Cox S, Sethi C, Kulasegaram R, Menon-Johansson A. (2020) Patient information leaflets: Our clinic experience in using QR codes and bit.ly for STI and contraception leaflets. The Physician 6(1):c6 DOI: 10.38192/1.6.1.c6

Introduction:
An innovative approach to deliver patient information leaflets for STI and contraception through QR code to smart phones was initiated as a quality improvement project in our sexual health clinics.

Methods:
A survey was conducted among sexual health clinic staffs on tools used for distribution of patient information leaflets and acceptability of QR code and short url for usage. QR codes linking to official BASHH and FPA online patient information leaflets were created from trust Microsoft word software and displayed as small stickers at clinic rooms for usage.

Results:
On initial baseline survey of our clinic staffs (n=22, 9 Doctors, 7 Nurses, 2 Health Advisers, 4 Receptionist) on their practice of distributing information leaflets, 28% were showing websites on computer monitor, 24% mentioned name of the website verbally, 9% gave handwritten website information, 19% were using other methods. Survey also showed 81% agreed for bit.ly and 76% agreed for QR codes as tools to distribute patient information leaflets. Feedback from staff on QR code usage (n=10) revealed QR code an acceptable tool which is easy to use, faster, secure, reliable during consultation for distribution of patient information leaflets. It worked only in clinic area with good mobile network and if patient using a smart phone. On second stage of the project, bit.ly codes were created for different clinic sites (bit.ly/srhbs, bit.ly/srhwr, bit.ly/srhsh) and were incorporated to second version of QR codes. Virtual monitoring of leaflet distribution was created through bit.ly portal. The total budget for this project was zero.

Discussion:
Newer generation smart phones have camera with built in QR code scanner. Bit.ly codes are widely used by NHS trusts. Both these tools can be safely and effectively used for distribution of patient information leaflets in sexual health clinics with no additional cost to the service. ❑

BAPIOAC19-07

Combination Correctors and Potentiators for Cystic Fibrosis: A Systematic Review and Meta-analysis

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Cite as: Basta, K & John C. (2020) Combination correctors and potentiators for cystic fibrosis: a systematic review and meta-analysis. The Physician 6(1):c7 DOI: 10.38192/1.6.1.c7

Background:
The most common cause of cystic fibrosis (CF) is the Phe508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) protein, resulting in CFTR's reduced trafficking, targeted by correctors, and reduced functioning, targeted by potentiators. For the majority of CF patients, the combination correctors and potentiators (CCPs) lumacaftor/ivacaftor and tezacaftor/ivacaftor, are the only treatments licensed to target the disease origin.

Objectives:
To assess the effects of CCPs on clinical efficacy outcomes, adverse events (AEs) and quality of life in CF patients. Methods: Electronic databases and clinical trial registries were searched before March 31st for randomised controlled trials comparing CCPs to placebo in CF patients. Bias assessments were conducted and data extracted for primary outcomes; change in percentage predicted forced expiratory volume in 1 second (ppFEV1), pulmonary exacerbations (PEx) and change in the respiratory domain of the cystic fibrosis revised questionnaire (CFQ-R-RD). AEs and discontinuations were analysed as secondary outcomes. Meta-analyses were conducted with subgroup stratification by CF mutation type and CCP drug.

Results:
9 studies were included (n=2543) lasting 4-24weeks. Overall CCPs compared to placebo decreased PEx, relative risk (RR)=0.69 [95%CI=0.60,0.80], increased ppFEV1, mean difference (MD)=3.03 [95%CI=1.61,4.45] and increased CFQ-R-RD scores, MD=5.07 [95%CI=2.30,7.83]. All efficacy outcomes were significant in Phe508del homozygotes, whilst only CFQ-R-RD increases were significant in Phe508del heterozygotes. In Phe508del heterozygotes with a residual function mutation increases in CFQ-R-RD scores and ppFEV1 were significant. Overall participant completion was >95% but discontinuations due to AEs were higher with CCPs, RR=1.87[95%CI=1.10, 3.19]. This was significant with lumacaftor/ivacaftor but not with tezacaftor/ivacaftor.

Conclusion:
Overall CCPs are safe and well tolerated. High quality evidence shows CCPs lead to modest improvements in ppFEV1 and reduce PEx in the short term for Phe508del homozygous patients. The clinical significance of these effects on long term outcomes for CF needs further research.❑

BAPIOAC19-08

A cost-utility analysis of small versus large bite sutures in the closure of midline laparotomies in the UK NHS

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cite as: Gokani S, Elmqvist K, El-Koubani O, Ash J, Biswas S & Rigaudy M. (2020) A cost-utility analysis of small versus large bite sutures in the closure of midline laparotomies in the UK NHS. The Physician 6(1)c8 DOI: 10.38192/1.6.1.c8

Background:
This study aimed to perform an economic evaluation of small bite sutures versus large bite sutures in the closure of midline laparotomies in the United Kingdom National Health Service (NHS).

Methods:
A cost-utility analysis was conducted using data from a systematic literature review. Large bite sutures placed 10 mm from the wound edge were compared to small bite sutures 3-6 mm from the wound edge. The analysis used a 3-year

time horizon in order to take into account complications including incisional hernias and surgical site infections (SSIs). Cost and benefit data were considered from the perspective of the NHS. A two-way sensitivity analysis was conducted to assess the impact of a variation in the clinical effectiveness of small bite sutures.

Results:
The incremental cost-effectiveness ratio was calculated to be -£482.61 per quality-adjusted life year (QALY) using the proposed small bite suture technique, indicating a cost saving to the NHS. Sensitivity analysis demonstrated that small bites are a cost-neutral technique provided that the cost of using small bites is less than £98 per patient. Small bites cost less than £20,000/QALY when they reduce either the rate of SSIs by more than 15% or the rate of hernias by more than 3.4%.

Conclusion
This study proposes that small bite sutures should become the mainstay suturing technique in the closure of midline laparotomies, replacing large bite sutures, which dominate current practice. The financial savings accompanied by the decrease in SSI rates and herniation warrant the use of this new technique. The sensitivity analysis demonstrates that findings hold true for a wide range of levels of clinical effectiveness for small bites.

BAPIOAC19-09

THIRD PRIZE - ORAL PRESENTATION

Investigating the Link Between Trisomy 21 and Acquired Mutations in the GATA1 Gene

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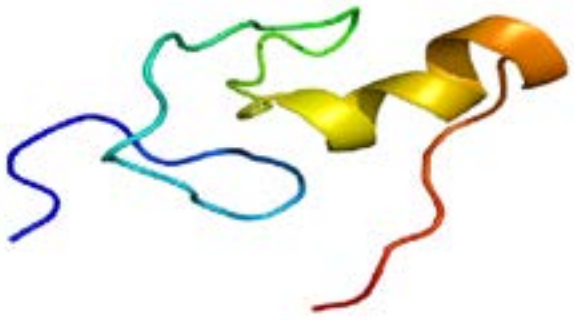
cite as: Chakravorty T & Roberts I. (2020) Investigating the link between trisomy 21 and acquired mutations in the GATA1 gene. The Physician 6(1)c9 DOI: 10.38192/1.6.1.c9

Background:
Children with Down syndrome (DS) due to trisomy 21 (T21) are at an increased risk of developing the neonatal preleukaemic disorder transient abnormal myelopoiesis (TAM), which may transform into childhood acute myeloid leukaemia (ML-DS). Leukaemic cells in TAM and ML-DS have acquired mutations in the GATA1 gene. Although it is clear that acquired mutations in GATA1 are necessary for the development of TAM and ML-DS, questions remain concerning the mechanisms of disease. TAM mostly resolves spontaneously within three months; only ~1 in 10 cases progress to ML-DS, and this transformation always occurs before age four years. This suggests that the foetal cellular environment created by T21 may be important for the acquisition of GATA1 mutations.

Methods:
To investigate the importance of the foetal cell context in TAM and ML-DS, GATA1 mutational analysis was carried out using next generation deep sequencing on blood samples collected from DS children enrolled into the Oxford-Imperial Down Syndrome Cohort Study.

Results:
Here it is shown that children with GATA1 mutations present at birth do not acquire additional new mutations in GATA1 in the first four years, and children without GATA1 mutations at birth do not subsequently acquire mutations in GATA1.

Conclusions:
The results suggest that the foetal cellular environment in T21 is critical for the acquisition of GATA1 mutations. It is likely that GATA1 mutant clones require factor(s) present specifically in the foetal liver microenvironment to sustain their proliferation and survival. Furthermore, screening for GATA1 mutations at birth in DS children is likely to be a reliable way of identifying those at reduced risk of developing ML-DS. ❑



Source: GATA1 - Interbnet

BAPIOAC19-10

A Comparison Of The Efficacy And Safety Of Oral Anti-Diabetic Drugs In Caucasians And South Asians: A Systematic Review And Meta-Analysis

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Cite as: McMullen A, Skarnes C & Richardson M. (2020) A comparison of the efficacy and safety of oral anti-diabetic drugs in Caucasians and South Asians: A systematic review and meta-analysis. The Physician 6(1)c10 DOI: 10.38192/1.6.1.c10

Background:
Type 2 diabetes mellitus is more prevalent, and presents differently, in South Asians than Caucasians. This suggests a possible difference in the genetic disposition of South Asians for this condition. Such genetic difference could also confer a difference in the response of patients of different ethnicities to oral antidiabetic drugs (OADs).

Methods:
This systematic review, with meta-analysis, compares the efficacy and safety of OADs in Caucasian and South Asian type 2 diabetics, using randomised trials published until February 2019. A systematic search of PubMed, Web of Science, Ovid and Scopus databases was performed. 27 studies met the inclusion criteria, with nine eligible for meta-analysis. Data on the change in % glycosylated haemoglobin (HbA1c) and adverse events (AEs) was studied.

Results:
This review is limited by small number of included studies, which were often of poor quality. A significant difference in efficacy was found in only one drug. However, trends were noted with other drug classes, but the volume of data was insufficient to draw statistically test. Similarly, there was little data relating to AEs, although some trends were again noted.

Conclusions:
Although the results were disappointing, this study has revealed that research is often presented in a way which prevents race-specific outcomes from being measured. This paper concludes by making recommendations which would enable larger studies to be conducted, potentially finding correlations between ethnicity and drug-related outcomes. This could in turn inform prescribing, allowing patients to be given medications which are more likely to be effective, and less likely to cause them harm. ❑

BAPIOAC19-11

Are Circulating miRNAs Predictive of Response to Therapy?

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Cite as: Kannappa LK, Khalid MS, Singh B & Guttery D.. Are circulating miRNAs predictive of response to therapy? The Physician 6(1)c11 DOI: 10.38192/1.6.1.c11

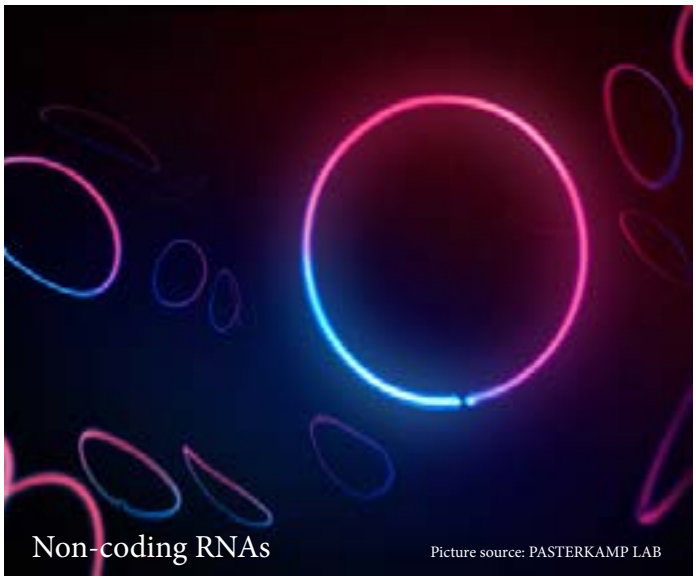
Introduction:
Colorectal cancer (CRC) is the third commonest cancer with nearly 1.4 million new cases identified throughout the world in 2012. There is a pressing need for new non-invasive blood based test to improve early detection and monitoring of CRC. MiRNAs are small non-coding RNAs involved in fundamental cell processes such as proliferation, survival and death. Studies have identified miRNAs in plasma of cancer patients in a stable form. This study aimed to evaluate whether circulating microRNAs are predictive of response to therapy.

Methods:
44 patients with CRC were selected from our institution's CRC surveillance programme. All selected patients at follow-up had no evidence of tumour recurrence on clinical, radiological and endoscopic assessment. Blood samples were obtained pre-treatment and at a median follow-up of 36 months. A total of 32 pairs of blood samples were matched pre- and post-treatment. Plasma RNA was extracted and target miRNAs were identified on pooled case TaqMan Low Density miRNA array (TDLA) cards and quantitative RT-PCR.

Results:
Of the nine microRNAs tested, only miR-134 (P = 0.03), miR-135b (P = 0.03) and miR-431 (P = 0.031) were statistically different in post-treatment samples using a Wilcoxon signed rank test. Comparison of each miRNA with clinicopathological features using multiple linear regression tests showed miR-

135b pre-treatment and miR-431 post-treatment levels to be significantly associated with both node status (positive/negative) and number of nodes involved. Pre-treatment miR-132, miR-134, miR-21, miR-27b and miR-184 were also significantly associated with node status. Further, miR-134 post-treatment was significantly associated with gender and miR-203 pre-treatment was significantly associated with all Duke's stages. However, multiple-linear regression of all miRNAs and clinicopathological features revealed only miR-135b levels pre-treatment to be significant in the overall model (P = 0.043).

Conclusion:
MicroRNA levels of miR-134, miR-135b and miR-431 showed a potential response to therapy with higher levels pre-treatment and lower after treatment. miR-135b pre-treatment levels correlated significantly to lymph node status and number. However, larger cohorts of patients are needed to validate these findings.❑



BAPIOAC19-12

SECOND PRIZE - ORAL PRESENTATION

Effects of various treatment regimens on the survival of HER2-positive breast cancer patients with brain metastasis

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Cite as: Edirappuli S & Beddowes E. (2020) Effects of various treatment regimens on the survival of HER2-positive breast cancer patients with brain metastasis. The Physician 6(1)c12 DOI: 10.38192/1.6.1.c12

Background:
Overexpression of HER2 (human epidermal growth factor receptor 2) occurs in around 20% of breast cancers. This particular subtype is known to be very aggressive and had the worst prognosis prior to the introduction of targeted therapy. The development of anti-HER2 therapies such as trastuzumab and pertuzumab have shown to dramatically improve the prognosis of patients with HER2-positive breast cancer. Despite these improved prognoses with newer drug therapies, the development of brain metastases and subsequent intracranial progression is often fatal in patients. The traditional options for treatment of brain metastases include neurosurgical resection, whole brain radiotherapy and stereotactic radiosurgery. This study aims to provide an analysis of the various treatment regimens that are employed and their effects on overall survival in patients.

Methods:
27 relevant patients (those with HER2-positive breast cancer and brain metastasis) were extracted from the ongoing DETECT study based in Cambridge. The effect of various parameters, including treatment regimens, was analysed using Kaplan-Meier curves.

Results:
The results showed that patients who received neurosurgical intervention had a statistically significant greater overall survival time compared to patients who had not received any neurosurgical intervention (median survival = 40.80 vs 12.35 months, p=0.011). The data further showed that neither radiotherapy nor drug therapies (chemotherapy, hormonal therapy or anti-HER2 therapy) significantly affected the overall survival.

Conclusions:
Of the current therapies employed by clinicians, neurosurgical intervention alone correlates with a significantly increased overall survival in patients. The explanations for this are varied but not limited to the specificity of this treatment in targeting intracranial tumours. Additionally, the clinical decision-making process for which patients may be considered eligible for surgery selects for those with a better prognosis. Future options for therapy include prophylactic cranial irradiation which may prove effective in targeting the, often-fatal, intracranial progression of this cancer. ❑

BAPIOAC19-13

Risk Factors of Poor Pregnancy Outcome in Living Kidney Donors in UK

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cite as: Basker S & Daga S. (2020) Risk factors of poor pregnancy outcome in living kidney donors in UK. The Physician 6(1)c13 DOI: 10.38192/1.6.1.c13

Background:
Despite thousands of kidney donations every year across the world, there is decline in donations particularly within the BAME (Black Asian Minority and Ethnic community). Young female faces a dilemma of future pregnancy when considering decision to donate a kidney. The study aims to describe the risk in pregnancy based on ethnicity, gender and regional variations.

Method:
This project uses Hospital Episode Statistics (HES) Admitted Patient Care (APC) data from 1997/8 to 2017/18 (20 years) with pseudo-anonymous data filtered by kidney donation codes.The dataset was extremely imbalanced with total of 420 records of which 279 negative class (no risk) and 141 (risk) positive class From available 128 columns Mothers Age, Ethnicity (Black, White, South Asian and Other), Deprivation Index (Low, Medium and High Deprivation Index), Provider Centre (Low, Medium and High provider), hypertension before or at donation, Smoking, Obesity, Risk After Donation Days were taken as features to analyse the data.

Results:
Mother's Age at delivery, smoking and obesity have been outlined with p-value less than 0.05 and proved to be most significant feature. The Odds Ratio showed, 1 unit increase is 1.067 times more likely to cause risk, whereas 10 unit increase is 9 times more likely to have risk in pregnancy after donation. With smoking, it was 2 times more likely to cause risk in pregnancy. The analysis showed Obesity would cause 8 times more risk in pregnancy after donation.
Conclusions:
Mother's age at pregnancy, smoking and obesity were the significant features that would cause risk in pregnancy. Ethnicity has no relevance or influence at all. ❑

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Cross-Sectional Survey of Viral Testing on Nasopharyngeal Aspirates by Laboratories in the UK – is Targeted Testing the Way Forward?

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Background
Acute viral bronchiolitis is the most common cause of hospital admissions amongst infants in the UK. The diagnosis is primarily clinical with most infants requiring supportive management. RSV is the main cause and routine confirmation has, until recently, been undertaken via nasopharyngeal swabs or aspirates (NPA). This is no longer recommended by the American Academy of Paediatrics (AAP) with the exception of at risk groups. NICE guidelines confirmed the diagnosis was primarily clinical but didn't explicitly recommend against routine testing.

Methods
This study aimed to review the current practice for testing of children admitted with suspected bronchiolitis in hospitals across the UK using a structured questionnaire.

Results
In total, 199/209 (95%) laboratories responded. Of these, 140 (70%) performed NPA testing on site with the remainder undertaken elsewhere. Approximately seventy percent [N =99] of trusts performed routine testing on infants with suspected bronchiolitis. Extended viral PCR testing was offered by some trusts (30%) based on either initial negative screening tests, clinical decision making (36.4% [N=51]), or as part of a mandatory protocol (26.6% [37]). Extended viral PCR testing was not offered by 13 trusts (9.3%). Point of care (POC) testing for RSV across the UK was available at 47 hospitals. Apart from POC, 46 laboratories did not perform tests out-of-hours although 8 would if requested by a Consultant Paediatrician.

Conclusion
We recommend more consensus based on patient outcomes and cost benefits. Locally, we follow targeted NPA testing only for high risk patients in keeping with the AAP guidance.

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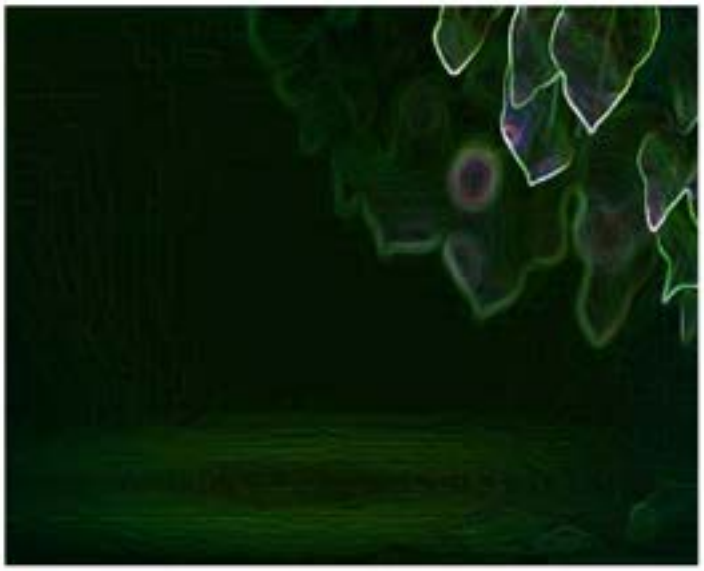

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