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Gene Therapy for Glaucoma:



A case of giant lipoma involving thigh and retroperitoneum



Screening for ADHD in ID population



NICE recomended new Skin Cancer Treatment

Promoting Research & Innovation

# TRIBUTE TO Her Majesty The Queen Elizabeth II



An end of Elizabethan Era Queen of the United Kingdom and the Commonwealth 6 February 1952 - 8 September 2022

## His Majesty The King Charles III

# *"LONG LIVE THE KING!"*

The King ascended to the throne on Thursday 8 September, and formally proclaimed King on Saturday 10 September

Credit: Shutterstick

### **Beginning of a new era: King Charles III** King of the United Kingdom and the Commonwealth CORONATION WILL TAKE PLACE ON SATURDAY 6 MAY 2023 AT WESTMINSTER ABBEY IN LONDON



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Contact:

editor.swasthya@gmail.com M: 07776291298

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he year 2022 has ended and 2023 is unfolding, ushering us with new opportunities and challenges. 2022 witnessed the end of a remarkable Royal era of the inspirational Queen Elizabeth II, with her unwavering sense of duty and beginning of the new era of King Charles III. We join in welcoming and rejoicing; 'long live the King' and look forward to the coronation of King Charles III on May 6, 2023.

Among the 'white peaks', the selection of The Rt Hon Rishi Sunak MP, with an ethnic background, also created a historical milestone in British politics. Unfortunately, it also accompanied a fast changeover of health secretaries, leaving the policies in a more



confused state! The National Health Service is facing significant challenges coping with the aftermath of the Pandemic, winter pressures, workforce unrest and industrial actions..

As the general election is approaching, new promises will emerge with offers to tackle the current situation of our NHS desperately needing more GPs, Consultants and other health care professionals, a thorough look into the future of tech services. However, the pressures from post-COVID still linger on as the NHS front line faces intolerable pressure to clear the backlog of patient waiting lists.

On July 9, 2022, some members of the Swasthya editorial Team had the first face to face meeting to share thoughts on the development of the publication. This was an encouraging and productive event. Furthermore, I was invited to attend two events, one with British Indian Cardiologists Association and another with JAAUK, an opportunity to introduce Swasthya to many delegates.

I had a few challenges in compiling this winter issue -my health condition and professional colleagues with a challenging schedule for article editing and compilation. I want to thank Mr C R Chandrasekar, Dr Santosh Mudholkar and Dr Sharad Agrawal for their encouragement and support during this troubled period.

The editorial team is delighted to have Dr Vinoda Sharma, Consultant Interventional Cardiologist, Dr Anis Ahmed, Consultant Forensic Psychiatrist and Prof Santosh Chaturvedi, Consultant Psychiatrist joining the team and extending their support for Swasthya. We also welcome Mr Sanjiv Majure, Orthopaedic surgeon, and Dr Awais Bokhari, Consultant Cardiologist, to the Editorial advisory board. There is no doubt that Swasthya is receiving favourable acknowledgements from many colleagues in the medical fraternity, and therefore, our endeavours are aimed at progressing further on this platform of success.

### *Buddhdev Pandya MBE* Publisher and Managing Editor-Swasthya



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# **SURGERY**

Swasthya Health Journal for Professionals Volume: 2 Issue: 3 WINTER 2022





### Swasthya Surgery



**Chief Editor** *Mr C R Chandrasekar* Consultant Orthopaedic Surgeon



Associate Editor Mr Amit Sinha Consultant Orthopaedic Surgeon

The current issue of Swasthya highlights exciting developments, as well as sober assessment of failure of governance, resulting in harm.

Obstetrics is a challenging as well as exciting subspeciality, caring from conception to safe delivery and beyond. Teamwork is essential for continuity of care and a safe outcome. However, conflicts, lack of manpower, lack of resources, poor communication, failure of leadership and external scrutiny can result in failure of safe care. Ockenden report <sup>(1)</sup> and Kirkup report <sup>(2)</sup> highlight the failures of safe obstetrics in Shrewsbury and Kent. Dr Santhi Chidambaram provides a brief insight into Ockenden review. The conflict and power imbalance between midwives, obstetricians, neonatologists and managers will remain a challenge, as staffing challenges remain, due to poor recruitment, morale and retention. Good teamwork, collaborative leadership and robust quality assurance is essential for safe obstetric care.

Prof Ramamurthy shares an interesting problem of a large lipomatous tumour, successfully treated with surgery. Many soft tissue tumours are presumed to be benign resulting in late presentations. Awareness and early diagnosis are essential for improving outcomes of soft tissue tumours.

Dr Corey Chan, discusses a trial involving 'novel' technique of improving surgical margins, which has the potential to reduce local recurrence, possibly improving survival. The ability of residual tumour cells being identified during surgery may improve local tumour clearance and a prospective trial may provide some guidance regarding the benefit of 'Sarcosight'

Gene therapy is increasingly becoming more relevant, due to advances in genomics. Whole genome sequencing and Nexgen sequencing are more readily available. Ophthalmology is a cutting-edge speciality, that has embraced modern technological advances than many other branches of medicine and surgery. Dr Ashwin Venkatesh, discusses the role of gene therapy in selected types of Glauoma.

The advances in technology and therapeutics are relentless and Surgery has to keep absorbing the safe and relevant advances. The importance of safety and 'Primum non nocre' should be at the core of medicine.

I hope the current issue of Swasthya can provide, through the insights it offers into the current possibilities and challenges.

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### Mr C R Chandrasekar

Orthopaedic Surgeon Chief Editor - Surgery Section



SURGERY



# A case of giant lipoma involving thigh and retroperitoneum

*Prof Dr Ramamurthy* Laparoscopic Surgeon & Surgical Consultant

INTRODUCTION

Lipomatous lesions are the commonest soft tissue tumours in adult. It is found commonly in the retroperitoneum, extremities, groins and abdominal wall. Lipomas are benign lesions while liposarcomas are malignant neoplasms derived from mesenchymal cells. Both tumours may share similar clinical presentations but differ histologically. Histology and tumour location are independent predictive outcome for long-term survival. Complete surgical resection is the main treatment followed by adjuvant therapy for malignant disease. We present a rare case of giant lipomatous lesion of the thigh swelling with extension into retroperitoneum.

#### CASE REPORT

A 54 year old man presented to us with swelling in the right thigh for the duration of approximately one year. The swelling is painless and slowly growing in size. Clinical examination revealed an anterior right thigh swelling. It was in the upper portion of thigh. Appetite, bowel movements and micturition were normal. He is not a known Diabetic or Hypertensive. He gives history of admission in

a nursing home about 2 months ago and operated. Because of the deeper involvement of the swelling between the thigh muscles, only biopsy was done and then referred to our centre. admission, we did MRI and CT Angiogram. The images

showed a well encapsulated, dumb-bell shaped mass occuping upper thigh and extending into lower portion of retro peritoneal space. The femoral vessels were anteriorly displaced. The tumour was excised using two different incisions, one in the thigh and the other in the right lower abdomen. The tumour was excised in two blocks because of its dumb-bell shape. Post operatively, the patient recovered well without any neurological deficit. The HPE report was benign lipomatous lesion with no evidence of malignancy. Patient remained symptom-free on 6 months follow up.

#### DISCUSSION

Liposarcoma and lipoma are two distinct histological tumours. Both commonly present in the 4th to 6th decades of life. They are slow growing usually originating from the extremities into the retroperitoneal space. They are usually painless, but its growth can compress surrounding



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Two incisions...One in lower abdomen and other in the thigh portion



structures such as ureter, blood vessels and nerves causing hydronephrosis, deep vein thrombosis and pain.

Lipoma is a mature adipose tissue with no lipoblast, floretlike giant cell or zones of atypia pleomorphic features. Microscopically lipoma showed spindle-shaped cells intermingled with multiloculated clear cells. There is no necrosis or mitosis present within the lipoma cells. It has no metastatic capability.

Although the resection of lipoma was easier, it was compressing on major vessel and nerve thus posed a challenge to our resection.

### CONCLUSION

Both liposarcoma and lipoma can present in a similar clinical fashion. Surgical resection is the main treatment option, with limited usage of adjuvant radiotherapy for liposarcoma.

Care must be taken to minimize collateral damage during surgical resection. Patients should be followed up long term to watch for recurrence.

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SURGERY

# Gene Therapy for Glaucoma: *a new frontier*

### Dr Ashwin Venkatesh

FY2 academic foundation doctor in clinical neurosciences

### Introduction

Glaucoma describes a group of progressive optic neuropathies characterised by retinal ganglion cell (RGC) degeneration, typically in association with raised intraocular pressure (IOP). It is often characterised into open or closed angle based on pathogenesis, and can be further classified as "secondary" glaucoma when a cause is identified (e.g. pseudoexfoliation) <sup>1</sup>. Glaucoma is the leading cause of irreversible blindness worldwide, affecting over 70 million in 2020 with an estimated 112 million expected to suffer from the disease by 2040 as the demographic shifts to an ageing population <sup>2</sup>. Despite the significant impact of the disease, models of treatment have traditionally centred around lowering IOP either through daily eye drops or surgery, and are limited in the extent or duration of therapeutic effect. Indeed, RGC loss and thereby visual deterioration can proceed despite successfully reducing IOP, highlighting that other pathogenic factors also underlie disease progression refractory to conventional treatments<sup>3</sup>.





		SURGERY				<u>Swāsthya</u>	
Open-angle Primary open-angle glaucoma (POAG)		le glaucoma Secondary Open angle glaucoma		Angle closure gl Primary angle closure glaucoma (PACG)		aucoma Secondary Closure glaucoma	
	Norma Glauco	l tension ma (NTG)		Acute	Chronic		
Risk factor	<ul> <li>Raised I</li> <li>Family h</li> <li>Older ag</li> <li>Afro-Can</li> <li>Steroid of Myopia</li> <li>T2DM</li> </ul>	OP listory ge ribbean ethnicity use					
Symptoms	<ul><li>Open an</li><li>Angle-cl</li></ul>	<ul> <li>Open angle: usually asymptomatic, insidious onset of peripheral vision loss</li> <li>Angle-closure: usually acute onset of blurry vision, painful, halos around lights</li> </ul>					
Evaluation	<ul> <li>Tonome</li> <li>Assessm</li> <li>Visual fi</li> <li>Pachymotonomet</li> <li>Goniosco</li> </ul>	<ul> <li>Tonometry to measure IOP (normal: 8-21 mmHg)</li> <li>Assessment of optic disc shows enlarged cup-to-disc ratio (&gt; 0.4)</li> <li>Visual field testing</li> <li>Pachymetry: measures corneal thickness (if corneas are thick, it may falsely elevate IOP on tonometry)</li> <li>Gonioscopy: gold standard for angle-closure glaucoma</li> </ul>					
Treatment	Ope     o p     o	<ul> <li>n-angle</li> <li>harmacologic</li> <li>increases aqueous ou prostaglandins (first- α-agonists</li> <li>cholinomimetics</li> <li>ecreases aqueous produ</li> <li>carbonic anhydrase i</li> <li>α-agonists</li> <li>β-blockers</li> <li>ser therapy</li> <li>trabeculoplasty</li> <li>irgical</li> <li>filtration bleb</li> </ul>	utflow -line) uction inhibitors				
	Ang     o in     o to     o     o	le-closure idotomy definitive treatment opical β-blockers and α2 ral carbonic anhydrase i IV if patient has naus	2-agonists inhibitors (a sea/vomitin	acetazolamide g	2)		
	<ul> <li>'fast progressors' with a progression rate between -1 and -4 dB/y</li> <li>most recent visual field (VF) mean deviation (MD) range of -4 dB ≥ MD ≥ -12 dB or ≤ -20 dB</li> <li>diagnosis of primary open-angle glaucoma (POAG) undergoing conventional glaucoma treatment</li> <li>age &gt; 50 years</li> </ul>						

The advent of gene therapy may represent a promising new therapeutic modality for glaucoma. Gene therapy involves introducing/augmenting, removing/suppressing or replacing/editing genetic material within cells to repair or compensate for the loss of function in a gene, and is delivered via viral (e.g. adeno-associated viruses) or nonviral (e.g. liposomes) vectors <sup>5</sup>. Over 20 gene therapies are now approved for use across the spectra of human disease, with particular momentum gained in ophthalmology <sup>6</sup>. The appeal of this treatment strategy derives from its ability to target specific disease pathways



The advent of gene therapy may represent a promising new therapeutic modality for glaucoma. Gene therapy involves introducing/augmenting, removing/suppressing or replacing/editing genetic material within cells to repair or compensate for the loss of function in a gene, and is delivered via viral (e.g. adeno-associated viruses) or nonviral (e.g. liposomes) vectors <sup>5</sup>. Over 20 gene therapies are now approved for use across the spectra of human disease, with particular momentum gained in ophthalmology <sup>6</sup>. The appeal of this treatment strategy derives from its ability to target specific disease pathways and exert lasting and effective outcomes, potentially with a single dose. This article will overview the current landscape of gene therapies and treatment strategies for glaucoma in relevance to the pathogenesis, and highlight opportunities for future exploration.

### **Gene Therapy Strategies**

### Genetic Risk Factors

Glaucoma is a complex polygenetic disorder, with several genes influencing the onset and rate of disease progression. Genome-wide associated studies have implicated 127 genetic loci associated with primary open angle glaucoma (POAG), of which four genes (MYOC, NTF4, OPTN, and WDR36) have been definitively linked <sup>7</sup>. Similarly, 13 loci have been strongly associated with primary angle closure glaucoma (PACG) <sup>8</sup>. The effect sizes of any individual genes appear to be variable, and these interplay with environmental factors in causing the disease, therefore genotyping patients may be valuable in offering a potential risk score.

Trabecular Meshwork

Raised IOP in glaucoma is caused by a mismatch of aqueous humour production and outflow. AQP1 is an important gene for aqueous humour production by the ciliary body epithelium, and pre-clinical mouse models have shown that CRISPR-Cas<sup>9</sup> targeting of this gene can reduce IOP and RGC loss 9. The trabecular meshwork (TM) is the primary outflow pathway, and consists of a series of fenestrated beams and sheets of extracellular matrix (ECM) covered with endothelial-like trabeculocytes, and perturbations in this structure may lead to glaucoma. For instance, disturbances in ECM homeostasis explain associations of glaucoma with the TGFβ2 and caveolin-1 and -2 genes that lead to increased ECM deposition and altered aqueous humour drainage when mutated. Additionally, endothelial dysfunction is purported to occur from cytotoxicity/mitochondrial impairment due to mutations in MYOC. Pre-clinical studies using CRISPR/Cas9 to disrupt the mutant MYOC gene via an intravitreal injection have improved aqueous humour outflow and improved RGC function in mice 10

### **Retinal Ganglion Cell**

RGC degeneration is central to glaucoma. Whilst raised IOP is the mechanism most often touted, other pathogenic mechanisms may include low ocular perfusion pressure, apoptosis, altered immunity, inflammation, excitotoxicity, and oxidative stress, excessive intracellular calcium and changes in glial cells, and indeed aberrations in RGC-specific genes and neurotrophic factors essential for survival (e.g. OPTN, BDNF, CNTF). Other factors such as the intrinsic inability of RGC axons to regenerate (e.g. PTEN-mediated) and extrinsic factors such as reactive glial scarring and defects in myelin may hamper axonal regeneration.

Trals	Ophthalmic Diagnosis	Location	Trial Summary	Phase	Endpoints
Dual Intravitreal Implantation of NT-501 Encapsu- lated Cell Therapy for Glaucoma	Glaucoma	Stanford University	To determine the safety and effica- cy of dual NT-501 CNTF encapsu- lated cell therapy (ECT) on visual impairment related to glaucoma	II	Visual fields, structural measurement of GC-IPL and RNFL
Study of NT-501 Encapsulated Cell Therapy for Glaucoma Neuroprotection and Vision Restoration	Glocoma	Stansford University	To determine efficacy of NT-501 CNTF encapsulated cell therapy (ECT) on visual impairment related to glaucoma	II	Visual fields, structural measurement of GC-IPL and RNFL
RESCUE and RE- VERSE Long-term Follow-up	Leber's He- reditary Optic Neuropathy	GenSight Biologics	To assess the long-term safety and efficacy of GS010 and quality of life in subjects with LHON due to the G11778A mitochondrial mutation in patients five years post treat- ment	III	Adverse events, BCVA, and HVF
Safety Study of an Adeno-associated Virus Vector for Gene Therapy of Leber's Hereditary Optic Neuropathy	Leber's He- reditary Optic Neuropathy	National Eye Insti- tute	To study the potentially toxic effects of scAAV2-P1ND4v2 in patients with LHON due to the G11778A mitochondrial mutation	I	Assessment of toxicity



### Conclusion

Gene therapy as a novel strategy targeting the various pathogenic mechanisms underlying glaucoma and associated optic neuropathies is under intense investigation in both pre-clinical and clinical studies. Once safety and efficacy can be determined in the long term, the next major challenge will be to scale this solution sustainably so that eligible patients can equitably access a lasting efficacious treatment for this leading global cause of "irreversible" blindness.

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### Dr Ashwin Venkatesh

FY2 academic foundation doctor in clinical neurosciences Barts Health (London), Honorary Clinical Lecturer at the centre for Neuroscience, Surgery and Trauma at the Blizard Institute (Bart's/ QMUL) and Clinical Research Fellow at Moorfields Eye Hospital. He graduated with distinction from the University of Cambridge with First Class in Pre-Clinical Medicine and Neuroscience (BA Hons.), 13 undergraduate pre-clinical prizes and the William Harvey Studentship.





SURGERY

# Improving surgical margins with fluorescence guidance in sarcoma

**Dr Corey D. Chan MBBS MRes** NIHR Academic Clinical Fellow in Trauma and Orthopaedic Surgery



### **Key points**

- For sarcomas, surgery is the mainstay of treatment with the aim of resecting the tumour with clear margins.
- Positive surgical margins correlate with increased local recurrence, development of distant metastases and increased mortality.
- Indocyanine green (ICG) is a fluorescent dye which has been shown to be preferentially taken up and retained by sarcoma tumours.
- By injecting patients with ICG and then using a near-infrared handheld camera, surgeons can visually identify tumour from normal tissue intraoperatively.
- A large UK randomised control trial (SarcoSIGHT) will formally investigate whether this technique reduces the unexpected positive margin rate compared to conventional surgery.

### Background

Sarcomas are rare malignant cancers with significant heterogeneity, arising from tissues of mesenchymal origin<sup>1</sup>. Sarcomas can arise from any anatomical site, with approximately 80 percent occurring in the soft tissues of the extremities<sup>2</sup>. Despite advancements in anti-cancer therapy, surgery remains the mainstay of treatment with the aim of resecting the tumour with clear margins, whilst leaving as much normal tissue as possible to maximise the functional outcomes for patients. Wide surgical excision can be challenging for orthopaedic tumour surgeons, as large sarcomas often invade nearby structures, and due to their large size and heterogeneity, often result in abnormal anatomy. Apart from computer navigation for bone sarcomas, there are currently no established intra-operative techniques available to help guide surgeons, particularly for the identification of the soft tissue component. Over the past decade, innovative widefield near infrared (NIR) cameras have become available, with ergonomics focussed on intraoperative use. In conjunction with the fluorescent dye indocyanine green (ICG), these camera systems can be used for fluorescence guided surgery (FGS) to visually identify tumour from normal tissue. Surgical margin status correlates with local recurrence, the development of distant metastases, and increased mortality rates3. Therefore, obtaining clear margins at the primary surgery is critical for oncological outcomes.

### Indocyanine Green (ICG)

ICG is a near infrared fluorescent tricarbocyanine dye which

has been used for several decades across various medical fields, including retinal vein imaging, monitoring of cardiac output, and assessment of hepatic function<sup>3</sup>. It has a wellestablished safety profile<sup>4</sup> and is approved for clinical use by the Food and Drug Administration and the European Medicines Agency. More recently, ICG has been utilised for fluorescence guided surgery to assess real-time blood flow to tissues, identify key structures, and to identify solid tumours<sup>5</sup>. ICG is a non-targeted imaging agent and relies on alternative mechanisms for preferential tumour uptake<sup>6</sup>. It has a predictable and extensively studied pharmacokinetic profile, and its NIR spectral properties allow for the detection of ICG even within deeper tissue<sup>5</sup>. This makes ICG well suited for use in sarcoma surgery, where tumour is covered by a pseudocapsule.

### Fluorescence Guided Sarcoma Surgery with ICG

The concept of FGS with ICG for sarcoma involves injecting the dye (1 mg/kg intravenously) 12 - 24 h before surgery (*figure 1*). Sarcoma tumours preferentially take up and retain the dye to a much greater extent than normal tissue<sup>7</sup>. Although the exact mechanisms of preferential tumour uptake of ICG are not fully understood, previous work has suggested a combination of the enhanced permeability and retention (EPR) effect and increased active tumour cell uptake by sarcoma cells<sup>6,8</sup>. Suboptimal fluorescence is observed in low grade tumours, and therefore this technique is most suited for intermediate to high grade sarcomas<sup>7, 9</sup>.

FGS with ICG allows surgeons to visually distinguish between areas of tumour and normal tissue (*figure 3*), with the aim of reducing the risk of a positive margin. The surgeon uses a





handheld NIR camera (Stryker SPY-PHI) intraoperatively to visualise ICG fluorescence in real-time (figure 2). The camera system has a "normal" brightfield mode, along with a number of different NIR modes which the user can switch between. A recent extended case series at The North of England Bone and Soft Tissue Tumour Service, where 39 patients received FGS with ICG, has shown that this technique may reduce the positive margin rate compared to conventional surgery<sup>9</sup>. Out of the patients given ICG, 37/39 tumours fluoresced, and surgeons felt the procedure was guided by the intra-operative images in 11 cases. To formally validate this technique, the SarcoSIGHT trial, led by Mr Kenneth Rankin (Consultant Orthopaedic Surgeon and Honorary Senior Lecturer at Newcastle University), will be the first randomised control trial with a surgical intervention for sarcoma. This £1.45 million multi-centre prospective randomised control trial will look at whether FGS with ICG reduces the unexpected

positive margin rate compared to conventional surgery, and is due to start recruitment in 2023.

### **Future Direction**

FGS for sarcoma is a rapidly evolving field. Current and future work by our research group is looking at the development of targeted agents, involving a fluorescent dye conjugated to a sarcoma-specific antibody. This will allow tumour specific FGS, which could be used instead of, or in combination with ICG. Other advancements will involve novel camera technology, with the aim of improving the sensitivity and specificity of ICG detection both intraoperatively and at the microscopic level. Together, these developments will help to improve the translational applicability of this technology, with the aim of reducing the positive margin rate for sarcoma patients.



Figure 1. Schematic showing the workflow of FGS with ICG. ICG (green) is injected intravenously 12 - 24 h prior to surgery. The sarcoma tumour uptakes and retains the dye to a greater extent than normal tissue. During surgery, the Stryker SPY-PHI NIR camera is used to visualise the florescence signal in real-time on a 4K display.



Figure 2. Taken from Nicoli et al. (2021). Intraoperative images of 78-year-old male with a pleomorphic soft tissue sarcoma in the groin (A–C), taken using the Stryker SPY-PHI handheld NIR camera. Image (A) taken in brightfield mode without NIR, images (B-D) taken using various NIR modes which causes the ICG to fluoresce. Image (D) shows a large lymph node with high signal which was resected and subsequently confirmed as containing tumour.

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Figure 3. NIR images of 3 tissue samples following surgical resection of a grade 3 leiomyosarcoma using ICG (green). Images were taken using the Stryker SPY-PHI camera and demonstrate the differences in fluorescence between nontumour tissue (muscle and fat), and tumour tissue.

### **Author Biography:**

### Dr Corey D. Chan MBBS, MRes

NIHR Academic Clinical Fellow in Trauma and Orthopaedic Surgery

Newcastle University Centre for Cancer, UK

Dr Chan is a Clinical Research Fellow in orthopaedic oncology and part of the Newcastle University Sarcoma Research Group, led by Mr Kenneth Rankin. His research focuses on basic science and translational research for fluorescence guided sarcoma surgery. His recent work has involved investigating the cellular mechanisms of ICG uptake, as well as developing novel targeted imaging agents in the form of antibody conjugates. Dr Chan has received several awards for this work and has undertaken research fellowships at Harvard Medical School and Massachusetts General Hospital, and at The Nuffield Orthopaedic Centre, Oxford.

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SURGERY



# Report of Ockenden review and its wider implications

### Dr Santhi Chidambaram

Consultant Obstetrician & Gynaecologist Chesterfield Royal Hospital NHS Foundation trust, UK

This was an independent review commissioned in 2017 by the secretary of state for health and social welfare, United Kingdom, after the efforts of the families seeking answers following their experience of maternity care in Shrewsbury and Telford NHS Hospitals.

Intense scrutiny and cross sectional national reviews are not new to maternity services in the UK and independent reviews into individual services have also been triggered, fortunately rarely, by concerns about clustered adverse outcomes. Reviews of maternity services in Northwick Park Hospital in 2008 and Morecombe NHS Trust in 2015 (Kirkup report) produced significant recommendations. However the timing and impact of this review have been unique due to the magnitude of the problem and the wider reach of the findings across the boundaries of the NHS and to the public. Ockenden review included 1,592 clinical incidents in the maternity care of 1,486 families over a period from 2000 to 2019. The multiprofessional team examined the trust's internal investigation procedures and reports as well as reports from external reviews in relation to the accounts of the individual families. They also invited staff members to voice their experiences and opinions.

The review concluded that different courses of action could have resulted in a better outcome in 1 in 4 cases of stillbirths; substandard care was identified in 3 out of 4 cases of maternal deaths.

### Common themes identified by the review:

- Inadequate risk assessment
- Inappropriate management plans made often as a result

of the above

JENDEN REPORT - FINAL

• Failure to listen to the concerns of women and their families

*Pcture credit source: The Ockenden report (Jacob King-PA Wire)* 

- Failure to recognise clinical deterioration or acknowledge/act on it
- Care providers either not updating their skills or acting beyond their competence
- Inadequate local clinical governance processes
- Lack of compassion when communicating with the families involved
- Lack of oversight at the Trust board level of the governance processes

The detailed accounts of women, their families and some staff members have indicated that the prevailing culture in the service was not supportive to effective escalation between the members of the multidisciplinary team. In addition to this, the review has revealed lack of compassion and openness when providing care or addressing concerns when raised.

There was also evidence of unsafe practice being unchallenged and continued due to inadequate staffing in many areas including midwifery, obstetric and anaesthetic groups. There was lack of continuity in the leadership due to frequent change of senior members of the Trust board and the clinical governance output from maternity service was not scrutinised.

Many of these findings have been identified in other reviews especially in the confidential enquiries into maternal and perinatal deaths; however, they were isolated incidents of substandard care resulting from a cumulative effect of multiple factors. The MBRRACE UK (confidential enquiry



into maternal and perinatal deaths) reports show that for the years 2013-2016 stabilised and adjusted extended perinatal mortality rates at The Shrewsbury and Telford Hospital NHS Trust were up to or more than 10% higher than comparable UK NHS Trusts. The stabilised and adjusted extended perinatal mortality rates were also up to 5% higher.

It is apparent that lack of learning from incidents, implementing actions recommended from internal and external reviews, and failure to listen to the user's voices would lead to any service spiralling down this path.

Therefore both the interim report published in December 2020, and the final report in March 2022, have outlined Local actions for learning and Immediate and essential actions(IEAs) for the Trust being reviewed as well as for the maternity services across the country.

### Immediate & essential Actions (IEAs) recommended in:

- 1. Workforce planning and sustainability
- 2. Safe staffing
- 3. Escalation & Accountability
- 4. Clinical Governance Leadership
- 5. Clinical Governance Incidents & complaints
- 6. Learning from maternal deaths
- 7. Multidisciplinary training
- 8. Complex antenatal care
- 9. Preterm birth
- 10. Labour & Birth
- 11. Obstetric anaesthesia
- 12. Postnatal care
- 13. Bereavement care
- 14. Neonatal care
- 15. Supporting families

The review team acknowledge the challenges facing the frontline workforce in maternity, in terms of resources as well as the time critical nature of decisions to be taken in an area of high intensity workload. Therefore there is recognition of the need for meaningful investment into maternity as well as the professional bodies such as Royal colleges who set the standards to lead on implementation of these IEAs.

There is emphasis on setting the timeframe for implementation of actions generated due to learning from incidents to a maximum of 6 months. Formalisation of a maternity voices advocate role is also proposed.

Though the findings of this review are disheartening for all providers of maternity care, we owe it to the women and their families to acknowledge their suffering and take actions to prevent this happening anywhere by providing best possible and compassionate care. It is notable that around the time when this review was commissioned, the Each Baby Counts project (EBC reports 2015 to 2019) led by the Royal College of Obstetricians and Gynaecologists (RCOG) was ongoing and standardised review of perinatal deaths with input from external experts was recommended to produce effective actions for the unit to prevent such adverse outcomes.

The joint venture by RCOG and Royal college of Midwives (RCM) called EBC Learning & support project (2019 to 2021) which followed, specifically addressed the need to develop a culture to promote psychological safety in the service and enable staff to escalate concerns effectively within and outside their teams.

Elements of the Saving Babies Lives Care Bundle which is being actively implements across the NHS maternity services to realise the vision of halving the stillbirth rate in the UK by 2030, also focus on some crucial elements raised in the Ockenden report such as responding to concerns regarding fetal movements, training the staff in robust risk assessment and fetal monitoring.

It is recognised that UK remains a safe place to give birth and there has been ongoing reductions in perinatal mortality and in maternal mortality. There are socio-demographic factors which contribute to higher than national rates of mortality which may be beyond the control of healthcare professionals. However by recognising these factors when planning care and by listening to women and their families' concerns it would be possible for us to optimise outcomes even in those groups and facilitate a positive experience in childbirth.

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Dr Santhi Chidambaram

MBBS, DGO, FRCOG, MD (Nottingham, UK) Consultant in Obstetrics & Description (Second Second S

• Maternal and fetal medicine, Benign gynaecology & amp; Colposcopy and Clinical Education - Tier 3 RCOG Faculty of educators

Consultant since 2006, LW lead for 9 years and now lead for antenatal screening and fetal medicine, RCOG College tutor until 2018

Facilitator: regional training courses ( LW ATSM course, US course, RCOG BPS )

Organiser: RCOG RoBuST course).

Educational and clinical supervisor & amp; Part 3 MRCOG examiner.

Research: MD for research on endometriosis.

Member – Local O&G research team









### Swasthya Cardiology



**Chief Editor Dr Sharad Agrawal** Consultant Cardiologist



Associate Editor Dr Vinoda Sharma Consultant Interventional Cardiologist

### CARDIOLOGY EDITORIAL

I am delighted to announce the expansion of our Editorial team of Cardiology with Dr Vinoda Sharma, Consultant Interventional Cardiologist from Birmingham City Hospital, joining me as an Associate Editor. She is a highly skilled interventional cardiologist and takes special interest in teaching and training activities. She has been very active in organising regular educational meetings for the Cardiologists at the regional and national levels. Dr Sharma is also an active member of Education and Programme committee of the British Association of Cardiologists of Indian Origin (BACIO). In this issue she has written an article on 'Cardiovascular disease in persons of South Asian descent' with particular emphasis on prevention rather than cure.

The picture below shows a group of eminent consultant cardiologists working in different hospitals across the United Kingdom, gathering to attend annual scientific meeting of the British Association of cardiologists of Indian Origin (www.BACIO. org.uk), which is organised every year alongside the Annual congress of British Cardiovascular Society. A buzz of excitement and anticipation is visible among the attendees to learn about the latest innovations in the field of Cardiology.

Cardiology as a specialty, has seen remarkable advancements in recent years. The advent of new technologies has greatly improved the ability of medical professionals to diagnose and treat heart diseases. From minimally invasive procedures to cutting-edge imaging techniques, these innovations are helping to save lives and improve the quality of life for millions of people around the world.

One of the most notable developments in cardiology has been the rise of minimally invasive procedures, such as transcatheter aortic valve replacement (TAVR) and percutaneous coronary intervention (PCI). These procedures offer many benefits over traditional surgical options, including smaller incisions, less trauma to the body, and faster recovery times. This has made it possible for many patients who would have been considered too high-risk for surgery in the past to receive the treatment they need.

Precision medicine is another area where cardiology has seen major advancements in recent years. This personalized approach to medical treatment takes into account an individual's unique genetic makeup and lifestyle, allowing for more targeted and effective treatments.

In addition to the above, recent developments in medical imaging technology have greatly improved the ability of cardiologists to diagnose and treat heart disease. Advances in CT scans and MRI have led to higher-resolution images of the heart and blood vessels, allowing for more accurate diagnosis of conditions such as heart disease, blockages in the coronary arteries, and aneurysms.

Wearable technology has also become an important tool in the management of heart disease, with devices such as heart rate monitors and smartwatches providing real-time monitoring of heart health. This can help people stay on top of their health and alert medical professionals in the event of a cardiac emergency.

In conclusion, recent innovations in cardiology have led to significant improvements in the diagnosis and treatment of heart disease. From minimally invasive procedures to precision medicine and cutting-edge imaging techniques, these advances have helped to save lives and improve the quality of life for millions of people. We can only imagine what the future holds for this exciting field, and we look forward to the continued progress and advancements in cardiology that will benefit patients everywhere.

**Dr. Sharad Agrawal** (MBBS; MD (Med); DM (Cardio); FICC; FRCP (Lond); FESC (EU); FACC (USA).

Consultant Cardiologist & Honorary Senior Lecturer Sunderland Royal Hospital, STSFT NHS Trust, United Kingdom Chief Editor, Cardiology Section



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CARDIOLOGY



# Cardiovascular disease in persons of South Asian descent

# *- prevention is better than cure*

**Dr Vinoda Sharma MBBS FRCP** Consultant Interventional Cardiologist Birmingham City Hospital, United Kingdom



### Abstract:

Cardiovascular disease (CVD) is the leading cause of healthcare cost, morbidity and mortality. The incidence of CVD is much higher in those of South Asian (SA) descent than non-South Asians. A multitude of factors are responsible including genetics, diet and lifestyle factors. Simplistically speaking- a spiralling vortex of poor physical activity, poor diet, increased body-mass index, the development of Diabetes Mellitus (DM) or metabolic syndrome consequently leads to increased risk for CVD. Much needs to be done for primary prevention of CVD both at individual and community levels not to mention health care systems and policies. We explore the causes and potential preventive measures in this brief overview.

Cardiovascular disease in persons of South Asian descent prevention is better than cure Introduction:

Cardiovascular disease (CVD) is the leading cause of healthcare cost, morbidity and mortality <sup>(1)</sup>. The incidence of CVD in persons of South Asian (SA) descent (defined as: at least 3 grandparents of Indian, Pakistani, Bangladeshi, Nepali or Sri-Lankan origin) is much higher than in other ethnicities <sup>(2)</sup>.

The SA population cohort also has a higher incidence of myocardial infarction along with a 3 to 5 fold increase in cardiovascular mortality  $^{(3)}$ .

Why do South Asians have a higher incidence of CVD and cardiovascular events?





The biology of coronary artery disease is considered to be no different in the SA population compared to others <sup>(4)</sup> although SAs on statins have more calcified atheroma compared to their non-SA counterparts as seen in a study by Ahmadi et al <sup>(5)</sup>. They compared CT coronary angiograms between SA population and a non SA population already on statins and found that statin use was associated with twice the quantity of calcified plaque in the SA compared to the non-SA population (25% vs. 12%, p<0.01) with no difference in mixed and noncalcified plaque<sup>(5)</sup>.

What about traditional cardiovascular risk factors? Out of the traditional "big four" cardiovascular risk factors (hypertension, diabetes mellitus, smoking and hypercholesterolemia), SAs have an increased prevalence of impaired glucose tolerance and a two-fold increase in the prevalence of type 2 Diabetes Mellitus (DM)<sup>(6)</sup>. This was further reiterated in the MASALA study (Mediators of Atherosclerosis in South Asians Living in America) - a prospective study that enrolled South Asians between 40 and 79 years of age without known CVD living in the United States of America. They found that this immigrant SA population cohort had a 23% prevalence of DM compared to other ethnicities <sup>(7)</sup>.

Elevated blood glucose itself has a direct negative effect on vascular endothelium and the progression of atherosclerosis<sup>(8)</sup> – the latter being basically an inflammatory process, driven by hyperinsulinemia, insulin resistance and dyslipidemia <sup>(9)</sup>. This inflammatory process leads to micro and macrovascular damage and its consequences. Elevated fasting glucose is also a component of metabolic syndrome (MetS). Definitions of MetS vary although the WHO definition involves any 3 out of the following 5 factors: elevated waist circumference, elevated triglycerides, reduced HDL-C, elevated blood pressure and elevated fasting glucose<sup>(10)</sup>.

It is interesting to note that waist circumference cut offs for abdominal obesity in non-SA populations are quite high by traditional WHO definitions ( $\geq$ 94 cm in men and  $\geq$ 80 cm in women)<sup>(11)</sup>. Lower cut-offs ( $\geq$ 90 cm for men and  $\geq$ 80 cm for women) have been recommended for Asian populations <sup>(12)</sup> and even lower cut-offs for persons of Indian origin.

This matters because wrongly utilising the higher cut-offs for waist circumference might prevent timely identification of risk factors for MetS. Similarly, accurate ethnicity-specific Body Mass Index (BMI)



cut-offs are essential to identify a population at risk and initiate aggressive primary prevention measures. Caleyachetty et al have described an equivalent risk of type 2 diabetes at substantially lower BMI values (23.9 kg/m2) in the SA population <sup>(13)</sup>. In contrast, the obesity cut-off in the White population is defined as a BMI  $\geq$  30.0 kg/m2 and correlates with the risk of developing DM  $^{(13)}$ .

Awareness of ethnicity specific BMI cut-offs can ensure targeted preventive therapy to reduce the risk of developing and/or early identification of DM and its consequences including CVD.

Is it only a predilection to DM in SAs that results in CVD or are there other factors responsible?

Other factors also play a role in the SA population's risk for CVD. Dyslipidemia patterns in SAs include raised triglycerides and low HDL-C- a component of MetS<sup>(10)</sup>. There is varying data on the increased levels of Lipoprotein a (Lp(a)) as a contributory risk factor to CVD in the SA population compared to non-SA population. However, increased ratios of apolipoprotein B100 to apolipoprotein AI which are

known to predict atherosclerosis have been shown to be more prevalent in the SA population in the INTERHEART study <sup>(14)</sup>. In the INTERHEART study, Yusuf et al established a case-control study in 52 countries and correlated multiple demographics, lifestyle factors and blood tests to myocardial infarction<sup>(14)</sup>.

SAs also have lower adiponectin levels (peptide hormone released by adipocytes with insulin- sensitizing, antiatherogenic, and anti-inflammatory effects), higher visceral fat levels and were physically less active as seen in the cohort taken from the MASALA study and the MESA (Multi-Ethnic Study of Atherosclerosis) study (15). In addition, Shah et al have shown that stress, anxiety and depression in SAs is associated with carotid intima media thickness - an indicator of subclinical atherosclerosis <sup>(16)</sup>. Furthermore, increased consumption of sweets <sup>(17)</sup> and "high-heat food hypothesis" (frying and re-heating oils)<sup>(18)</sup> are thought to be direct and indirect contributors to increased CVD risks.

Although the role of smoking and tobacco as a risk factor for CVD must not be forgotten, studies have not demonstrated increased use in SA compared to non SA population. One must remember smokeless-tobacco use in history taking including chewing tobacco which maybe more prevalent amongst female SA population<sup>(19)</sup>.

#### **Conclusion:**

What can be done about this increased CVD risk in the SA population?

A combination of genetic and lifestyle factors appear to be responsible for the increased CVD risks seen in the SA population. A simplified chain of events would be--reduced physical activity resulting in increased weight gain/waist circumference combined with a poor diet leading to a perfect recipe for metabolic syndrome and/or DM and increased risk for or the actual manifestation of CVD.

Changes in mind-sets are required at individual and community level as well as changes in healthcare systems and healthcare policies. Early identification of SAs at risk by novel screening programs which

include physical examination and blood tests and in the future perhaps also screening CT coronary angiography might arrest the development of and/or prevent of one of the most prevalent diseases.





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MENTAL HEALTH EDITORIAL 🔤

### Swasthya Mental Health



**Chief Editor Dr Santosh Mudholkar** Consultant Forensic Psychiatrist



Associate Editor Dr Fahida Aria Consultant Psychiatrist and Executive Medical Director

### WELCOME MESSAGE

am delighted to welcome you all to mental health section of Swasthya health journal. We are aware that this issue was delayed due to unforeseen circumstances. We sincerely apologize for this delay. After a promising start for 2022 with receding in Omicron cases and easing of lockdown the nation mourned the death of our beloved longest serving monarch, Late, Queen Elizabeth II on 8th September 2022. Swasthya editors paid homage to Her Majesty who stood tall and was a source of inspiration to millions of people in U.K. as well as several more well-wishers from other countries.

In this issue we have developed mental health section which provides an overview of "Neurodevelopmental Disorders", a topic not well covered in previous issues of the journal. It is topic not often reviewed by colleagues from other medical and surgical specialities. It is nevertheless an important issue as it affects around 15-20% of child population. Neurodevelopmental conditions are heterogeneous and include autistic spectrum disorders (ASD), attention deficit hyperactive disorders (ADHD) along with other genetic conditions associated with neurodevelopmental delays in speech, motor or language functions. Some neurodevelopmental conditions are associated with low I.Q. learning difficulties, specific reading or writing disorders. Others such as high functioning autism , Asperger's syndrome are unlikely to be associated with intellectual difficulties. It is not unusual to have an overlap between neurodevelopmental disorders and neuropsychiatric conditions.

Individuals suffering from autism, autistic spectrum disorders tend to have a different communication styles. Often these individuals have difficulty in understanding social cues, are sensitive to even slight change in environment or routine and have stereotypic interests. Children start to show features of neurodevelopmental disorders such as ADHD, ASD in home environment and school. So early diagnosis of these conditions and specialist assessment by educational psychologists to determine if they warrant special educational needs is crucial. Secondly, this group are also at a higher risk of psychiatric comorbidities including psychotic illness, mood disorders, stress and anxiety disorders. It goes without saying that assessment and treatment requires specialist input by multi-disciplinary team. Although it is acknowledged that a large proportions of these case are managed in the community either in home environment or residential setting a small proportion who present risk of serious harm to others or self, require additional support. In addition to environmental adaptations in specialist settings and require assessment regarding their mental capacity, appropriateness of use of Mental Capacity Act 2005, deprivation of liberty safeguards (DoLS) or Mental Health Act 1983 to protect this vulnerable group of individuals with complex mental health needs. Any decisions regarding their care and treatment or restricting their freedom has to be proportionate using the correct legal framework such as Care Act 2014 and keeping in mind the Human Rights Act 1998.

In U.K. in 2011, there was a media spot-light on BBC Panorama programme which highlighted neglect or ill treatment of individuals with severe intellectual disability in Winterbourne View Hospital, near Bristol. Since then failings at other hospital or residential care settings for individuals with intellectual disability has led to increase vigilance regarding management practices, inspection and regulation by Care Quality Commission (CQC). These cases have highlighted that too often individuals with learning or intellectual disabilities are held in hospitals against their will without sufficient therapeutic input and without their rights being upheld. These issues were prominent when considering reforming of Mental Health Act 1983. There is also a debate whether Mental Health Act 1983 is the appropriate tool to detain individuals with neurodevelopmental disorders (some of whom suffer from intellectual disability). Currently, there is provision in Part II of Mental Health Act 1983 to detain individuals with intellectual disabilities who present with a risk of serious harm to others or self for a period of assessment or treatment. It is argued that this has led to exceedingly long periods of detention for this group of individuals with little therapeutic benefits.



A White paper, "Reforming Mental Health Act 1983 was introduced in January 2021 which set out a package of reforms built on 154 recommendations by a review committee in 2018. Following a consultation period a draft legislation was published in June 2022. The reforms are based on four main principles a) choice and autonomy, b) least restrictive c) therapeutic benefit and d) ensuring patients are treated as individuals. The draft Mental Health Bill was introduced on 27th June 2022 by Mr Sajid Javid, then Secretary for Health and Social Care and is currently under pre-legislative scrutiny. It is proposed that in the reformed Mental Health Act individuals with autism or intellectual disability will only be detained if they have a co-occuring psychiatric disorder.

Setting the scene against this backdrop we are lucky to have established clinicians and academics working in the field of Intellectual Disabilities who have contributed to this Swasthya issue. I was fortunate to meet and interview Dr Indermeet Sawhney, Consultant Psychiatrist in Intellectual Disabilities working in Hertfordshire immediately after she was elected chair of Intellectual faculty of Royal College of Psychiatrists in 2022. In her introductory article to Swasthya, Dr Sawhney has described the concept of neurodevelopmental disorders, screening tools for ADHD in ID population in a simple lucid language. I interviewed Dr Sawhney and she has explained various clinical, management issues in neurodevelopmental disorders, Autism, ASD and highlighted recent research and scientific advances in this field.

The second article in this section is by Prof Biswas from Leicester and colleagues which throws a light on temperament, personality characteristics which underpin psychiatric co-morbidity in sufferers from autism and intellectual disability.

Our concluding article in the section is an interesting piece by Prof Jaydeokar, one of the founders of Centre for Autism, Neurodevelopmental Disorders and Intellectual Disability (CANDID). Prof Jaydeokar discusses how CANDID was conceptualised, its humble origins before being developed as a research centre and how it has helped busy clinicians by providing up to date knowledge, improving their skills in assessment of neurodevelopmental disorders. We understand that it is gaining popularity as a professional networking hub for individuals interested and working in this field at regional and national level in U.K.

I hope you will find this section interesting and looking forward to your feedback.

**Dr Santosh Mudholkar** MBBS MD MSc FRCPsych Chief Editor - Mental Health Section





# Screening for ADHD in ID population

### Dr Indermeet Sawhney

Consultant Psychiatrist & Clinical Director Learning Disability Services, Essex & Trust wide IAPT services. Interim Deputy Medical Director, Hertfordshire Partnership University NHS Foundation Trust

Intellectual Disability is a lifelong condition of impaired intellectual functioning associated with deficits in adaptive functioning with onset in the developmental period. The impaired functioning impacts several domains namely cognitive, language, motor social abilities .ID affects approximately 2% of the population. The DSM-5 recommends a standardised IQ assessment, with ID considered to be approximately two standard deviations or more below the population IQ mean: an IQ score of about 70 or below. It is classified into mild, moderate, severe, and profound, based on life skills, the need for support and the results of IQ testing.

The evidence suggest that mental health disorders are more prevalent among people with an ID than in the general population (Cooper and Collacott 1996;). ADHD, ASD, ID, communication disorders, specific learning disorders and motor disorders are categorised as neuro developmental disorders by DSM V. All these disorders share some common clinical characteristics: childhood onset, steady as opposed to a remitting relapsing course, early onset of neurocognitive deficits, high heritability indices, marked overlap of core symptom domains and often co -occur.

Attention-deficit hyperactivity disorder (ADHD) a neurodevelopmental disorder characterised by a persistent pattern of inattention and/or hyperactivity and impulsivity with an onset in childhood that causes significant functional impairment to the individual (American Psychiatric Association, 2013). Depending on the presence of inattentive or hyperactivity/impulsivity symptoms, ADHD can be further categorised into three types: combined, predominantly inattentive, and predominantly hyperactive/impulsive types. Signs of ADHD are evident during the developmental period, causing functional impairment in different domains of life.

Research suggests that ADHD can be difficult to diagnose and may be underdiagnosed or misdiagnosed in people with ID (Perera, 2015). There are several factors that make the diagnosis of ADHD in ID challenging. Comorbid psychiatric, neuropsychiatric and neurodevelopmental disorders are commonly seen in people with ID and ADHD. The presence of these comorbidities may conceal or exacerbate the signs of ADHD. Lack of confidence among clinicians to make a diagnosis of ADHD in patients with intellectual disability due to difficulties in establishing whether their activity and attention levels are consistent with the developmental stage of the individual (K. Xenitidis et al, 2010), patients' inability to articulate symptoms they experience (Perera, 2018) which may be due to patients' diminished comprehension and impaired expressive ability are some of the reasons. Challenges in applying DSM V ADHD criteria for people with severe ID (Perera et al 2020) as it limits the relevance of some of the symptoms e.g., patient forgets where they have put objects such as keys etc may not be relevant for the severe ID population as they are fully supported with their daily activities and may not be in possession of their personal belongings. Additionally, many adults with ID have been raised in long-term mental institutions and/or have lost contact with their families; thus, their medical histories are fragmented, and reliable early developmental history which is pivotal to the diagnosis gets lost. As people with ID often have memory difficulties and they find it difficult to recall their childhood further compounding the problem. There is lack of awareness and training in diagnosing and prescribing amongst practitioners and also ambivalence about the existence of ADHD in ID amongst some professionals, which does not help the cause.

Effective treatment of ADHD has a positive impact on the symptom control and reduction of the core features of ADHD. Evidence suggests that people with ID and ADHD on ADHD medications are less likely to use antipsychotic medications compared to people with ID and ADHD not on ADHD treatment (Al-khudairi et al 2019). This aligns with the national STOMP agenda, stopping over medication of people with a learning disability, autism or both with psychotropic medicines. People with neurodevelopmental disorders can have higher rates of challenging behaviour. Challenging behaviour is not a psychiatric diagnosis but rather a socially constructed and descriptive concept. Challenging behaviour is described as "undesirable behaviour that is of an intensity, frequency, or duration that threatens the physical safety of the person or others or restricts access to community or facilities" (Emerson 1995). ADHD symptoms may present as CB in people with ID. These behaviours can be exhausting for the person with ID as well as carers. Diagnostic overshadowing where there is a tendency to attribute the behaviour to the Intellectual Disability rather than exploring underlying ADHD is another potential cause of missed diagnosis. By treating the underlying ADHD, behaviour labelled as "challenging" may be reduced (Korb, L., 2019)

The Diagnostic Interview for ADHD in adults with intellectual disability (DIVA-5-ID) is a diagnostic tool recommended for use in people with intellectual disability. Using the DIVA-5-ID requires significant resources and time.



It is imperative the diagnosis of ADHD is identified at the earliest with the aid of screening tools and subsequently managed appropriately. Rating scales have been shown to be useful in identifying and screening for ADHD in adults in the mainstream population. There are many screening tools available for ADHD in general population. However, validity of such ADHD screening questionnaires in people with ID can be questionable and there are no validated tools to screen for ADHD in people with ID. Therefore, there is a need to develop easier methods such as screening tools to detect ADHD among people with ID.

### **Quality improvement Project:**

The low rate diagnosis of ADHD in people with ID in our services compared to high prevalence rate reported was recognised. We aimed to identify the predictive ability of specific symptoms of ADHD as applied to people with intellectual disability and develop a screening tool. ADHD screening tool in this QI project consisted of ten questions. Nine questions were based on a previous study which highlighted that certain items used in the process of diagnosing ADHD in general population were not reliable in people with intellectual disability. Screening questionnaire reflected different presentation of ADHD among people with ID (Perera et al 2020). An additional question relating to challenging behaviour was added given that it can be a common presentation among adults with ADHD and ID (Korb et al 2019).

The screening questionnaire was sent to the carers of the patients with instructions to be completed by a person who knew the patient well. Patients within the age group of 18 to 50 years who had an established diagnosis of intellectual disability were included in the QI project. Patients with a diagnosis of dementia were not included. In parallel, the clinicians also assessed all the patients using the semi-structured interview and DIVA- 5-ID. If one or more questions on the questionnaire were answered 'yes', it was considered a positive screening. Comparisons were then made between DIVA-5-ID and the questionnaire results.

#### **Results**:

There were 78 eligible people open to the psychiatric team. Of the 78 questionnaires sent out, 39 (50%) were returned; 26 male (66%) and 13 female (33%) respondents, with a mean age of 38 years. Thirty had moderate-to-profound intellectual disability (77%) and nine had mild intellectual disability (33%). Only one person did not have a comorbid health issue. Of the 38 respondents with comorbid health issues, 14 had one (36%), 14 had two (36%) and ten had three or more (26%) comorbid conditions. Just one person was not on any psychotropic medication. Seven people were on one medication, 15 were on two medications and 16 were on three or more medications.

Of the 39 respondents, 36 (92%) had answered at least one question of the questionnaire positively, with three replying negatively to all questions. The corresponding DIVA-5-ID of all 39 respondents was completed, which identified 24 (61%) as having ADHD. A specialist statistical analysis was undertaken to identify the reliability of each of the questions compared with the gold-standard DIVA-5-ID. Two positive responses to three specific questions (1,2 & 6) had 88% sensitivity/87% specificity for predicting ADHD.

	Question	Yes/No Present in the last months	Tick if this symptom goes back to childhood
Q1	Doeshe/shefindhardtositinoneplaceforlong?		
Q2	Doeshe/shepaceupanddownmostofthetime?		
Q3	Doeshe/sheoftenfidgetwiththeirhands/feet?		
Q4	Ishe/sheveryimpulsive/can'twaitforhisturn?		
Q5	Does he/she often intrude/interrupt others?		
Q6	Is he/she easily distract- ible by busy environments?		
Q7	Does he/she often move from one task/activity to another?		
Q8	Does he/she appear preoccupied and not listening when spoken to directly?		
Q9	Is he/she forgetful in daily tasks and need fre- quent reminders and prompting?		
Q10	Does the patient display any challenging behaviour?	If yes, please tick the following that apply (you can choose one or more) Physical aggression towards others Damage to property	

Appendix 1 - ADHD screening questionnaire for people with intellectual disability (questions identified for final screening in bold)



Final ADHD Screening Tool (with statistical association between questions & DIVA-5-ID results)

Quesstion		Yes/No (Present in last 6 months)	Tickk if symptom goes back to childhood	P-value	
Q1	Does he/she find it hard to sit in one place for long?			<0.001	
Q2	Does he/she pace up and down most of the time?			<0.001	
Q3	Is he/she easily distracted by busy environments?			0.01	

Appendix 2 – Pathway



#### **Discussion:**

There are many barriers to diagnosis ADHD in adults with ID. Using the DIVA-5-ID as a diagnostic tool can be resource-intensive for daily clinical practice and hence, screening tools are of value where ADHD is suspected. However, in a population with a high prevalence of ADHD, there is no screening tool to undertake a full assessment.

This innovation in routine clinical practice is the first evidence-based attempt to develop a screening tool for ADHD in people with intellectual disability. This tool has the potential to influence positive change in supporting the health needs of people with intellectual disability. The obvious benefit is to quickly identify people with intellectual disability with suspected ADHD for further diagnostic workup, i.e., theDIVA-5-ID. Other benefits include reduction of misdiagnosis and, by extension, reduction in polypharmacy, particularly in the prescribing of inappropriate psychotropics in a vulnerable population. Better screening can lead to improved diagnosis, improving both health and quality of life for the patient. Furthermore, it will also have positive implications on clinician resource and time.

In conclusion, there is a significant level of underdiagnoses of ADHD in people with intellectual disability. This QI project delivered three evidence-based screening questions to assist carers and clinicians to consider further ADHD diagnostic work-up. These questions could be easily incorporated into any preliminary inquiry into a referral for a psychiatric or behavioural assessment of a person with intellectual disability, to help consider ADHD and provide better clinical formulation and bespoke treatment of their needs. Further development and national adoption of the screening tool could help with better recognition and effective treatment of ADHD in this vulnerable population.

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# A Special interview with Dr Inder Sawheny with a career in neurodevelopmental disorders and learning disabilities

- an interview by Dr Santosh Mudholkar

# Q1) Can you inform our readers regarding your current professional roles? What are your priorities as RCPsych chair of ID faculty?

I am a consultant psychiatrist specialising in Intellectual Disability (ID) and work with adults with ID in the community. I also have a managerial role within my Trust and am the Clinical Director. I have recently been elected as the Chair for the Faculty of Psychiatry of Intellectual Disability, Royal College of Psychiatry. I feel it is such a privilege and great honour to be elected to this role, which is at a national level. The Royal College of Psychiatry is a professional medical body that sets and raises standards for psychiatry and supports psychiatrists.

One of my key priorities is to address the physical health of the very vulnerable population we serve, who are known to have a reduced life expectancy. More must be done to bridge this gap and championing their physical health. The profound health inequalities that exist have, once again, been raised in the recently published LeDeR report.

Secondly, workforce is a huge challenge across all specialities, and we are not immune from it either. Recruitment for us is a pressing issue so we really need to do more to attract talented trainees to this speciality by innovation, ensuring they receive a good experience, and more importantly retaining them. This will help train specialists for the future.

I am mindful of the paucity of research within our speciality and I am really keen to engage more colleagues in academic work. Research should not be seen as the remit of purist academics, so need to engage "jobbing clinicians" to participate in it at varying levels. Expanding research will benefit patients and also help to attract and support doctors with an interest in research, which will inevitably help with the recruitment.

Finally, we will be looking to explore new pathways and models too, for neurodevelopment disorders, in particular Autism and ADHD.

# Q2) How long have you been working in mental health? What inspired you to follow a career path in neurodevelopmental disorders and learning disabilities?

I started off as a clinical attachment to get a flavour in psychiatry and have never looked back. This is going back over two decades, gosh that is very telling of how long I have been around!

The speciality of psychiatry of ID offers so much diversity and richness in clinical settings. There is so much breadth in clinical work ranging from epilepsy, neurodevelopmental disorders, forensic issues, dementia, interface with legal aspects etc. We get to explore the complex interface between mental, physical health, social and environmental factors work and its impact on behaviour. There is a great opportunity to work in a holistic way in this speciality. In ID psychiatry we work across an MDT with different knowledge and skill sets and are always learning something new, making it challenging, very exciting and stimulating. Serving some of the most vulnerable people and making a positive difference to their lives makes it very gratifying and extra special.

# Q3) What are neurodevelopmental disorders and what is their impact on individual sufferers psychosocial functioning?

Put simplistically, as the name suggests in neurodevelopmental disorders there is impairment in the development of the central nervous system, which unfolds during the development of the child. NDD includes Attention-Deficit/ Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), Tourette syndrome (TS), Intellectual Disability (ID), Speech Language Disorder (SLD) and Developmental Coordination Disorder (DCD). All NDD share some key common characteristics, such as childhood onset, male preponderance, a steady rather than remitting and relapsing course, early onset of neurocognitive deficits and high heritability indices. They also tend to co-occur and have a marked overlap between their core symptom domains.

People with ID often face discrimination and rejection this can lead to loneliness, low self concept, trauma and leading on to significant impact on their mental well being. It is well established people with learning disability are more likely to experience mental disorders as compared to the general population. They also have a higher risk of exploitation and abuse The lack of understanding of social context, inability to manage their emotions, impulsivity, could all have a consequence of them being socially isolated, stigmatised, low selfesteem and a poor quality of life. Patients may present with challenging behaviour which can place a huge burden on their carer / families and in some cases can even lead to breakdown of the placement and in some extreme cases ultimately leading to hospital admissions. Simple things like inability to stick to a routine, change in their environment could lead to a display of challenging behaviours and this may inadvertently lead to more prescribing of psychotropic medication.

### Q4) Can you explain Autism or autistic spectrum disorders?

Essentially ASD is one of the neurodevelopmental conditions and it is characterised by difficulties in reciprocal impairments in social interaction and communication. For example, the individual is unable to appreciate someone's emotional ques and have an inability to moderate behaviour according to a social context. They also display restrictive repetitive interests and behaviours and are associated with rigidity with a preference for stability and routine. Change to routine can be very distressing for autistic people and make them very anxious . Autistic people may experience over- or undersensitivity to sounds, touch, tastes, smells, light, colours,

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temperatures or pain. There are many simple reasonable adjustments that can be made to make environments more autism-friendly. In keeping with other NDD's, autism is a lifelong condition and it has its onset in childhood. However, there may be a delay in the diagnosis and may only come forth when there is a crisis or there is an increase in demand later in life. A correct diagnosis is vital as it helps to explain both to the autistic person and to others, their strengths and areas of support and need which inform care planning. There is a great variability how these symptoms come together to make autism; they may be present as a spectrum ranging from being traits in certain individuals to being very severe and obvious disability in others.

Autism itself is not a mental illness but it does significantly raise the risk of physical health problems. Additionally, autistic people are also at a higher risk of co morbid mental illness and other NDD, which has an impact on the presentation and management. Mood and anxiety disorders are particularly frequent and most notably generalised anxiety disorder.

# Q5) What do you mean by the term learning/intellectual disability? How common are intellectual disabilities and Autism?

Learning/Intellectual disability has been known by a number of terms which are used quite interchangeably. In the past some rather unsavoury terminology was used which has now been dropped. LD is characterised by significant degree of cognitive impairment together with deficits in adaptive behaviour which has an onset before the age of 18. The disability can impact different domains; cognitive (language, reading, writing), social (social judgment, interpersonal communication) and practical (personal care, money management) domains. As a result of this disability, individuals find it difficult to adapt with daily demands of the normal social environment and need support in day to day everyday life depending on the severity of ID.

ID is considered to be approximately two standard deviations or more below the population IQ mean of a standardised IQ assessment: an IQ score of about 70 or below. It is important the time of assessment, the person is not experiencing mental health, social, or other turmoil in their life as that could affect their performance in tests The global IQ score cannot be used as a concrete measure to define ID; a global IQ score is a summation of various subdomains of verbal and performance scores . It is important to use both clinical assessment and standardised testing of intelligence. The level of severity of ID can be divided on the basis of IQ; Mild (IQ 50–69), moderate (IQ 35-49), severe (IQ 20–34) and profound (IQ less than 20).

Among those with a diagnosis of ID, about 85% have mild ID, 10% have moderate ID, 4% have severe ID, and around 1% have profound ID. ID as a group is quite heterogeneous as there is a large variability in their impairments and support needs. Many live independently in the community with minimal support from family or services. Others may require more of a care home environment or supported living services. There is significantly higher mental and physical comorbidity in ID populations when compared with the general population. The trend of comorbidities is also related to the intensity of ID. Learning disability can often get confused with specific learning difficulties such as dyslexia. The key difference here is specific difficulties versus global difficulties in learning.

Autism is present in about 1% of the general population, it's prevalence is higher, 3-5% in mental health service users

and approximately 10% in PWLD. Conversely, around 40-50% of autistic people have a learning disability, compared with just 2% of people without autism. The prevalence of autism increases with greater severity of learning disability.

# Q6) Can you give us some examples of recent advances, innovations in the field of neurodevelopmental disorders?

There are several promising new areas of research for example, genetics now provides new insights into neurodevelopmental disorders. Most of the known NDDs genes belong to few common frequently affected molecular pathways. Molecular studies have provided a better understanding on how different mutations can disturb the converging pathways and lead to the identification of potential targets, thereby opening perspectives for future treatment. This knowledge could lead to the development of targeted drugs and to a shift from the current paradigm of symptomatic treatment toward more resolutive curative treatments.

Pharmacogenomics is another upcoming frontier that provides insights to medication response based on unique individual characteristics and work is ongoing to identify and validate biomarkers in various domains. There is research underway around technological advances in improving diagnosis, providing bio-feedback responses and engaging individuals into vocations.

Dr Indermeet Sawhney, consultant psychiatrist and clinical director for learning disability services at Hertfordshire Partnership University NHS Foundation Trust was interviewd by the Chief Editor Dr Santosh Mudholkar for Swasthya Journal.

Dr Sawhney is known for her pioneering work in Herts and Essex to support people with learning disabilities and autism.



Pharmacogenomics is another upcoming frontier



# Impact of temperament and character on psychiatric co-morbidity in people with autism and intellectual disability

### Asit Biswas<sup>1,2</sup> & Frederick Furniss<sup>3</sup>

AUTHORS and AFFILIATIONS

\*Asit Biswas MD, FRCPsych 1,2, Consultant Psychiatrist and Honorary Professor 3 Frederick Furniss, MA, PhD, Clinical Psychologist & Honorary Clinical Psychology Teach

- 1 Leicestershire Partnership NHS Trust
- 2 Department of Health Sciences, University of Leicester
- 3 School of Psychology, University of Leicester

### Abstract

People with autism spectrum disorders (ASDs) show unmistakable temperament and character, as also experience high rates of internalizing psychiatric disorders including depression. Aetiologically, the possible role of temperament and character in determining susceptibility and resilience to psychiatric disorders has received little study in people with ASD, intellectual disabilities (ID), or both. Children and adults with ASDs show a pattern of lower Surgency/Extraversion, higher Negative Affectivity/Harm Avoidance, and lower Effortful Control/Self-Directedness compared with typically developing persons, which may account for their susceptibility to developing internalizing problems associated with experiencing social adversity. A similar pattern of personality characteristics may explain the increased susceptibility to depression in persons with IDs. Children with Down syndrome (DS) show an unusual pattern of low levels of Effortful Control together with low levels of Negative Emotionality/Harm Avoidance, which may account for the lower rates of mental ill-health experienced by people with DS by comparison with others with IDs. Clinical implications and directions for future research are discussed.

### 1. Introduction

Some models of personality distinguish dimensions of temperament (e.g. Harm Avoidance and Persistence) believed to originate in differential sensitivity to conditioning processes, from dimensions of character (e.g. Self-directedness and Cooperativeness) emerging through verbal and propositional learning <sup>[1, 2, 3]</sup>. Others assume continuity of underlying mechanisms for temperamental and character traits <sup>[4, 5, 6]</sup>. There is clear overlap of concepts in both



approaches (see Table 1) which have demonstrated associations between personality dimensions and susceptibility versus resilience to development of internalizing disorders in children, and depressive disorders in adults.

In children, low "Effortful Control" <sup>[7]</sup>, i.e. ability to self-modulate affective state, is associated with both internalizing and externalizing psychopathologies, with depression additionally specifically associated with high levels of a trait labelled Withdrawal or Negative Affectivity and low levels of Approach or Positive Affectivity <sup>[5]</sup>. In adults, current depressive symptomatology is positively associated with Harm Avoidance, and inversely correlated with Self-directedness, Cooperativeness, and, less consistently, with low Reward Dependence, with both positive and negative associations occasionally reported for Novelty Seeking and Persistence <sup>[8, 9]</sup>. High Harm avoidance and low Self-directedness predict future depressive symptomatology [8, 10], and in patients with major depressive disorders both are associated with depression severity <sup>[11, 12]</sup>.

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This paper reviews research on personality and depression with people with intellectual disabilities (IDs) and people with autism spectrum disorders (ASDs), first noting some methodological challenges involved, and suggests future research directions.

Model	Buss & Plomin, 1984 [36]	Rothbart et al., 2001 [41]	Cloninger et al., 1994 [29]	Costa & McCrea, 1995 [17]	Factor summary	Possible relevance to depression
Factor 1	Emotionality	Negative Affectivity	Harm Avoidance	Neuroticism	High reactivity and sensitivity to aversive situations/emotions	Tendency to react to social/emotional challenges by withdrawal/avoidance
Factor 2	Activity	Extraversion/Surgency	Reward Dependence	Extraversion	Activity, impulsivity,	High motivation for social interaction and activity
	Sociability		Persistence		sensitivity to social and other positive	
			Novelty Seeking		reinforcement	
Factor 3		Effortful Control	Self-directedness	Conscientiousness	Ability to modulate emotion and/or maintain goal- directed behaviour despite emotional challenge	Ability to cope with negative emotion and maintain-goal- directed behaviour in face of social/emotional challenges
Factor 4			Cooperativeness	Agreeableness	Helpfulness, trust, high level of empathy	Reduced tendency to interpret social challenges as motivated by hostility in others
Factor 5			Self- transcendence	Openness-to- experience	High level of imagination and strength of values	High degree of optimism and hopefulness

# 2. Methodological challenges in investigating personality and psychiatric disorders in people with intellectual disability.

Self-report measures of depressive symptoms and

personality generally used with nondisabled adults and older children may be difficult to complete for many persons with

IDs. Novel self-report scales, adaptations to scales designed for nondisabled people, and diagnostic criteria extended

to encompass observed behaviours possibly indicative of

depressed affect, can be used with people with mild and moderate IDs, but for people with severe IDs assessment of depression relies largely on rating scales completed by (or

Even with persons with mild/moderate IDs, researchers

often rely on third-party informants to complete personality assessments <sup>[14, 15]</sup>. Lindsay, Rzpecka and Law <sup>[16]</sup> rephrased

some questions, read questions aloud to participants, used

a visual aid to assist participants to answer, and provided

breaks during assessment when using the self-rating form of the NEO-PI-R<sup>[17]</sup> with adults with mild/moderate IDs,

requiring 3-4 hours to complete each assessment, and found

significantly different mean scores for self and observer

(keyworker) ratings on the Extraversion, Agreeableness, and

There are therefore substantial methodological challenges in measuring depression and personality in people with IDs. Some persons with an ASD however have intellectual abilities

within the normal range and can complete conventional assessments independently. Given the frequent comorbidity

with information from) third-party informants [13].

of ASD and ID  $^{\rm [18,\ 19]}$  , research with such persons may have some relevance to those with IDs.

## 3. Temperament and psychopathology in persons with autism spectrum disorder

Children with ASDs experience high rates of emotional and behavioural difficulties <sup>[19-22]</sup> although whether adults with ASDs do so when severity of ID is controlled for is less clear <sup>[23]</sup>. Parent reports with younger children suggest that compared with typically developing (TD) children, children with ASDs show lower adaptability and persistence and lower Effortful Control but often not lower Extraversion/ Surgency or higher Negative Affectivity. <sup>[24-26]</sup>. Failures to find differences in Extraversion/Surgency between children with and without ASD may result from the fact that whereas in young TD children Extraversion/Surgency factors typically include a "level of activity" component, in children with ASDs level of motor activity may be negatively associated with other traits involving sensitivity to positive social reinforcement typically measured by Extraversion/ Surgency scales <sup>[24]</sup>. Caution should therefore be exercised when applying measures of temperament factor-analytically developed from work with TD children to assessment of temperament in children with ASDs. Studies including older children have found both higher levels of Negative Affectivity and lower levels of Surgency in children with ASDs than in TD children but disagreed on whether Effortful Control is lower in children with ASDs <sup>[27, 28]</sup>. In children with ASDs Internalizing problems correlate negatively with Surgency and positively with Negative Affectivity; studies differ as to whether Effortful control correlates with Internalizing

Conscientiousness domains.



symptoms within groups of children with ASD but concur that it correlates with this factor in combined groups of children with and without ASDs. Children with ASDs show high variability in scores on personality measures <sup>[27]</sup>.

Two studies have compared Temperament and Character Inventory [29] scores of adults diagnosed with ASDs <sup>[30, 31]</sup>, with scores from a large gender- and age- matched general population reference group; the groups of participants with an ASD scored significantly higher on Harm Avoidance and Self-transcendence and lower on Novelty Seeking, Reward Dependence, Self-directedness, and Cooperativeness than the reference group. High variability in scores, across personality domains, was again noted for participants with ASDs <sup>[31]</sup>. Kanai et al. <sup>[32]</sup> found significantly higher scores on the Neuroticism and Psychoticism, and significantly lower scores on the Extraversion and Lie, scales of the Eysenck Personality Questionnaire, for adults with ASDs than adults without a psychiatric diagnosis.

By comparison with persons without ASDs, older children and adults with ASDs therefore show a pattern of lower Surgency/Extraversion, higher Negative Affectivity/Harm Avoidance, and lower Effortful Control/Self-directedness, which may account for their susceptibility to developing Internalizing problems.

### 4. Temperament and psychopathology in persons with intellectual disability

The prevalence of psychopathology in children with IDs is between 35% and 49%, an approximately three-fold increase by comparison with TD children <sup>[33]</sup>. The proportion of the variance in Internalizing symptoms accounted for by factors such as ability and various family and social factors drops from 36% when these factors and symptoms are measured concurrently to only 5% when such factors are used to prospectively predict psychopathology while controlling for baseline levels <sup>[33, 34]</sup>. However, other than earlier studies of the concept of "difficult temperament", few studies have examined individual temperament and personality factors in children with IDs and their possible role in the development of emotional and behavioural difficulties <sup>[35]</sup>.

Parental ratings of young (mean age 37.4 months, S.D = 24.1 months) children with intellectual/developmental disabilities (ID/DDs) on the EASI Temperamental Survey [36] have been found to be significantly lower for Activity and Sociability, higher on Shyness and Impulsivity, and not different for Emotionality, than those of a group of TD children matched for age and gender balance <sup>[37]</sup>. As has been observed with children with ASDs, the group with ID/ DD showed higher variance on the temperament scales in comparison to the TD children. For children aged between 9 and 12 years, Zion and Jenvey <sup>[38]</sup> found lower parentrated Sociability, and higher teacher-rated Emotionality, for children with IDs compared with those attending mainstream schools, but no differences in Activity or Shyness. Boström, Broberg & Hwang<sup>[37]</sup> found that children with ID with Down syndrome (DS) were rated as lower in Emotionality than those with diagnoses of ASD or ID/DD of other or unspecified causes, and lower in Impulsivity than children with ID/DD of unspecified cause.

Helles, Wallinius, Gillberg et al. <sup>[57]</sup> examined temperament and character in 40 adult males with a childhood diagnosis of ASD, prospectively followed through over two decades. They reported three distinct temperament and character profiles, (i) high reward dependence was noted in those no longer meeting criteria for ASD, (ii) in those with a stable ASD diagnosis with psychiatric comorbidity, elevated harm avoidance, low self-directedness & co-operativity, and (iii) in those with a stable ASD and no comorbidity, low novelty seeking and somewhat elevated harm avoidance.

The case of DS is of particular interest, since adults with DS have lower overall prevalence of mental ill-health than adults with ID of other causes, and no association between mental ill-health and various factors (e.g. frequency of preceding life events) associated with mental ill-health in the whole population of persons with IDs, suggesting the existence of possible protective biological factors; however incidence of depression (of relatively brief episodic duration) is high compared with other forms of mental ill-health in the DS population [39, 40]. Persons with DS might therefore be hypothesized to show temperament and character characteristics protective of mental ill-health and/or facilitatory to recovery from depression. Comparing parent ratings on the Infant Behavior Questionnaire-Revised<sup>[41]</sup> for 17 infants with DS (age 3-12 months) and an age- and gendermatched control group of TD infants, Gartstein, Marmion & Thompson<sup>[42]</sup> found higher Orienting/Regulatory Capacity factor and lower Negative Emotionality in the children with DS. Nygaard, Smith and Torgersen<sup>[43]</sup> compared parent ratings on the Children's Behavior Questionnaire <sup>[44]</sup> for 55 children with DS aged 4-11 and 91 TD children aged 5-7 years. Children with DS had lower ratings on two dimensions (attentional focusing and inhibitory control) loading on the Effortful Control factor, and lower ratings on the sadness dimension loading on Negative Emotionality. The different findings from these two studies on capacity for orienting attention may represent a developmental effect, with infants with DS exhibiting reduced reactions to novel stimuli, resulting in increased durations of maintained attention <sup>[42]</sup>, with attention to novel stimuli increasing during maturation to reveal reduced ability to effortfully maintain focussed attention. Children with DS therefore appear to show lower levels of factors related to Effortful Control, and also lower levels of Negative Emotionality/Harm Avoidance, than TD children. Whether this unusual direct correlation of two personality factors generally inversely correlated in the general population can account for the relatively low overall risk of mental ill-health, relatively high risk (compared with other disorders) of depression, and relatively brief typical course of depression in people with DS merits further research.

Although epidemiological studies of persons with mild IDs suggest a high prevalence of affective disorder by comparison with that of the general population [45, 46], the relative dearth of investigations of temperament in children with ID extends also to adults, and research with all age groups has often used concepts and instruments with limited convergence with those used with nondisabled adults. Sensitivity theory [47, 48] proposes that unusually high motivation to secure (or avoid) any of 15 "end motivators", 11 positive (e.g. vengeance, food, order), and four negative (rejection, physical pain, anxiety, and frustration) increases risk of developing emotional and behavioural problems. Significantly higher mean motivation for vengeance, food, order and attention, and for avoidance of rejection, pain, frustration, and anxiety, has been reported in children and adults with ID experiencing behavioural or mental health problems compared to participants with ID without such problems <sup>[49]</sup>. Although there appears

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to be some congruence between some of Sensitivity Theory's proposed fundamental motives and dimensions of temperament within other systems (e.g. between the 4 negative sensitivities and Negative Emotionality/Harm Avoidance), Sensitivity Theory proposes no reduction of the 15 motives to higher-order factors, includes no factor corresponding to Effortful self-control, and assumes that the dynamics of behaviour related to persistence and impulsivity will be motive-specific <sup>[47]</sup>. Zigler and his colleagues <sup>[50]</sup> have since the 1960s investigated 5 aspects of personality in individuals with IDs: Positive Reaction Tendency (heightened motivation to interact with/depend on, supportive others), Negative Reaction Tendency (initial wariness in interactions with strangers), Expectancy of Success (on novel tasks), Outerdirectedness (dependence on cues provided by others to guide behaviour in challenging or ambiguous situations) and Effectance Motivation (the degree of pleasure derived from tackling difficult problems). In an initial comparison of scores on the EZ-Yale Personality Questionnaire (EZPQ), a 37-item informant-rated questionnaire designed to measure these traits, Zigler et al. [50] found differences between individuals with IDs and a control group of nondisabled individuals matched for mental age in Positive Reaction Tendency and Outerdirectedness (higher in persons with IDs), and Expectancy of Success, Effectance Motivation, Creativity/Curiosity, and Obedience (lower in persons with IDs; the latter dimensions emerged in addition to factors corresponding to a priori subscales in exploratory factor analysis). Despite the face similarity of several EZPQ scales with personality measures used with the general population (e.g. Positive Reaction Tendency and Reward Dependence, Creativity/Curiosity and Novelty Seeking), relationships between EZPQ scores and measures of psychopathology have yet to be investigated. Studies of personality disorders in persons with IDs in forensic services <sup>[14-16, 51]</sup> have begun to report on the use of contemporary personality assessments with persons with IDs, but investigations of the relationships between personality dimensions and Internalizing problems are at an early stage <sup>[15]</sup>.

#### 5. Temperament, character and depression in people with IDs: summary and future directions for research

Social factors such as socioeconomic status and occurrence of life events are associated with Internalizing psychopathologies and depression in children with IDs and adults with mild IDs, but factors influencing susceptibility and resilience to depression in the face of social adversity are little understood, with research to date having focussed on cognitive factors [<sup>52]</sup>.

Preliminary findings comparing children and adults with ASDs with TD controls show group differences of lower Surgency/Extraversion, higher Negative Affectivity/Harm Avoidance, and lower Effortful Control/Self-directedness in persons with ASDs which may account for their susceptibility to developing Internalizing problems. The limited research with other persons with IDs suggests that a similar pattern of personality characteristics might account for the increased susceptibility to depression in this group also. Since several studies have reported greater variability in personality measures in persons with ASDs and IDs than in nondisabled comparison groups, investigation of the extent to which individual differences in temperament and character might account for inter-individual variability in risk of depression in these populations is clearly of interest.

Further research in this area presents promise in several areas. Conceptually, consideration of temperament and character might help account for variability in susceptibility to depression and provide a link between hypothesized biological factors promoting susceptibility or resilience and the cognitive factors which have been the focus of research to date. In the general population, Harm Avoidance predicts responsiveness to treatment with SSRIs and interpersonal, although not cognitive-behavioural, psychotherapy [53, 54]. Assessment of temperament and character factors in persons with IDs might therefore assist prediction of likely response to treatment with SSRIs, which in this population is highly variable in effectiveness and associated with a substantial risk of serious side effects [55]. If limited Effortful Control is associated with depression in persons with IDs, mindfulnessbased interventions which to date have been used primarily to intervene with Externalising problems in this population might be effective with depression also [56].

Given the potential difficulties with use of self-report measures outlined earlier, the availability of rating scales of temperament and character designed for completion by third-party informants will be important. Early priorities for research should be evaluation of the factor structures and other psychometric properties of such scales when used with persons with IDs and/or ASDs (including measures of agreement between self and third-party ratings), investigation of correlations between factor scores on such measures and those from measures such as the Reiss Profile and EZPQ, and case-control studies of results from such measures in persons with IDs with and without depression.

Research with people with IDs may also contribute to better understanding of the relationship between personality and depression in the general population. Research with people with DS, for example, may increase understanding of the specific contributions of Effortful Control and Negative Emotionality/Harm Avoidance to increasing risk of depression in the general population by offering an opportunity to study the phenomenology of depression in a population demonstrating a reversal of the normal correlation of these factors. The study of temperament, character and depression in people with IDs has made a slow start, but further progress may improve understanding and treatment of depression for people with and without IDs.

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### MENTAL HEALTH 🔤



# Centre for Autism, Neurodevelopmental Disorders, and Intellectual Disability (CANDDID): our journey so far

**Professor Sujeet Jaydeokar** Clinical Director and Chair at CANDDID **Ms Maddy Lowry** Associate Director at CANDDID **Prof Mahesh Odiyoor** Strategic Clinical Director at CANDDID

It started with a conversation on a train back in 2018, that kick-started CANDDID - the Centre for Autism, Neurodevelopmental Disorders and Intellectual Disability, which is hosted by Cheshire and Wirral Partnership Trust in the North West of England. The idea has grown, and this is our journey.

### Why develop a Research Centre?

Our conversation was about how to solve some of our difficult problems:

• How do we improve the health and well-being of people with Autism, Neurodevelopmental Disorder and Intellectual Disabilities – addressing health inequalities and increasing length of life?

• How do we involve people with lived experience (as individuals, families or as carers) in training, education and research, so that they can influence us to address the issues that are important to them?

• How do we attract, develop and retain excellent people to work in this field across health and social care?

• How do we network across the region, nationally and internationally to understand what other people are doing, to learn from their work and together deliver better outcomes?

• How do we develop the range of published evidence around best practice, so that we can influence policy at a national level?

Although, we were trying to do all these things, we didn't have a platform to get engagement with people across our organisation and wider afield. This is when we thought of bringing all those issues together into the concept of a Research Centre. And so, we committed to starting one: CANDDID was born. There was no allocated office, no allocated staff, no allocated budget - just a name, good will, ambition, and tenacity.

### Key points in our journey

Starting our journey with small projects that built momentum



Although, as a research centre, one of our aims was to secure academic research grants through national funding in the UK, we started with time-limited, small grant projects; this allowed us to generate some income to backfill our clinical

staff to be released to undertake the work. Back in 2018, in England, there has been a focus on improving the skills and abilities of staff and unpaid carers across both health and social care. Our first success was a bid to the NHS England and Improvement for some monies to develop co-produced on-line training for families and carers supporting autistic individuals and those with intellectual disability. This project helped us to work with people with lived experience and develop staff across the health and social care field, as well as unpaid carers at home. You can find all the training we developed on this on our website under the headings Better Support, Better Lives.

Success in delivering Better Support, Better Lives kickstarted development of new training initiatives and innovative solutions-based projects e.g our Dynamic Support Tool for Physical Health; income generated through these projects enabled us to consider back-filling posts more substantively. However, with rapidly expanding scope of CANDDID, a number of key individuals continued to work very hard over long hours to deliver on various projects.

In all these projects, we have focused on working with people with lived experience (as patients, carers, or family). We feel that this has kept us grounded in what is important to people's real lives. Four years on, we are now being considered for national funding streams. We have also seen a step change in the way our staff talk about and engage in quality improvement and research. We are developing a learning culture, and CANDDID has helped us do that by being a focal point for people.

### Developing tools to help busy clinicians stratify need

We used population health management principles in



are effective. We would highlight three of our tools here, and you can find out more about them using the links at the end of this article:

- Our Global Mental Health Assessment Tool (GMHAT) can be used in primary and secondary care to screen and manage mental health disorders. To share this more widely, we have developed a relationship with Indian Institute of Health Management Research (IIHMR) and Manchester University in India and Manchester University to deliver training in India. Much of this programme has been delivered through goodwill in the first year, with an aim that course fees can accumulate in India to enable some more structured financing to follow once the course is well-established.
- Across England, we are working with NHS England and Improvement to deliver on-line training in our Dynamic Support Database tool (DSD-ST) which was developed to support identification of people with Intellectual Disability at high risk of admission to mental health hospital. Use of this tool, in conjunction with intensive support in the community, has reduced hospital admission in our local population by between 70%-80% over the last 3 years. We have received some timelimited funding to support this development.
- Another key piece of research for us has been the development of the Dynamic Support Tool for Physical Health (DST-PH) which helps clinicians identify those with intellectual disability who are at risk of premature mortality or preventable death. The tool uses RAG (red, amber and green) ratings to identify levels of risk of

premature mortality or preventable death and allows for systematic response from primary and secondary care services to reduce risks of premature mortality and preventable deaths.

#### Being a "host" for networking opportunities

We were clear we wanted to better network with our peers across the UK and further afield. We wanted to hear what other people were researching, share ideas and learn together.

We decided the best way to do this was to organise an annual conference focusing on clinically led co-produced research. This would enable us to bring people working in this way together, and we could foster those relationships by "hosting" annual conversations about evidence and good practice. Our first conference was held in 2019, with subsequent conferences in 2021 and 2022 Unfortunately the global pandemic affected our 2020 conference but investing in virtual technology meant that we were able to host our 2021 conference. We deliberately set our conference fees to be low and gave a significant discount to people with lived experience to encourage their attendance. Through our networks, we have had some excellent speakers and our technological links have enabled us to attract speakers from overseas, including India.

Building on this success, this year we are hosting our first stakeholder network event - inviting local and national parent/ carer forums and third sector organisations together to help us shape the questions we should be researching solutions for over the next 12-36 months. This will help us to keep our research firmly grounded in providing solutions





to improve the day-to-day experiences of people and their families.

### **Sustainability**

Starting CANDDID with an idea was one thing, sustaining the momentum we have created is another and this has been the hardest part of our journey. It is only in the last 12 months that we have been able to appoint people into substantive roles within CANDDID, as we now have a three-year record of bringing investment into our host Trust. We are delighted to have a part-time Clinical Director, a Business Manager and team of researchers. We have also just moved into a bigger set of offices... we aim to outgrow these in 2 years!

Capacity to deliver against our commitments remains significantly challenging and we continue to seek more substantive funding to help secure more academic time.

### **Closing thoughts**

Creating CANDDID has helped people in our organisation, and wider afield, understand our wide aims

better – people can conceptualise the "Centre" more easily than a set of services in an NHS Trust.

We have been able to use CANDDID to bring people together, identify problems and work to develop and share clinically validated tools that help improve the lives of people with autism, neurodevelopmental disorders and intellectual disability.

Four years on, people are now starting conversations about research, education and training with CANDDID as they recognise that CANDDID can help and has a track record of delivering good quality outputs.

We wish to sustain this momentum and continue our journey. We remain challenged with our core infrastructure. We believe that building a future for research in this field can only be done in partnership with others, like you.

For more information, check out the following

Better Support, Better Lives training: www.canddid.nhs.uk/training GMHAT courses in India: https://iihmr.edu.in/jaipur/gmhatleadership-training-program-on-screening-and-management-ofmental-disorders. DSD-ST online training: https://www.england.nhs. uk/learning-disabilities/dynamic-registers-and-dynamic-systems/



NEWS —

# Cancer Treatment

# NICE recommends 'new'

## skin cancer treatment

In 2022, the National Institute for Health and Care Excellence (NICE) recommended the use of the immunotherapy drug pembrolizumab (Keytruda) as an option for patients with stage 2A and 2B melanoma in England and Wales.

Melanoma is a common form of skin cancer with over 16,000 new cases each year in the UK, and over 2000 deaths. Cancer Research UK emphasised that "86% of melanoma skin cancer cases in the UK are preventable".

In April this year the British Association of Dermatologists released data showing that between 2013 and 2019 there was a 26% increase in the incidence of skin cancer.

In its final draft guidance, the National Institute for Health and Care Excellence (NICE) has recommended pembrolizumab (trade name Keytruda, MSD) for people aged 12 years and over with melanoma.

Pembrolizumab, sold under the brand name Keytruda, is a humanized antibody used in cancer immunotherapy that treats melanoma, lung cancer, head and neck cancer, Hodgkin lymphoma, stomach cancer, cervical cancer, and certain types of breast cancer.

It is believed to be a step change in clinical management where the standard care for people with stage 2B or stage 2C melanoma is complete surgical excision with wide margins, followed by five years of routine follow-up. However, the NICE pointed out that there are "currently no adjuvant treatment options available" for stage 2 melanoma and highlighted the "unmet need" for treatments after surgery.

According to the NICE the aim of adjuvant treatment is to "remove any residual microscopic disease after surgery to reduce the risk of local relapse or progression to metastatic disease", which, it said, "is currently considered incurable".



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BOOK REVIEW

### **BOOK REVIEW**

### **Clinical Psycho-Oncology**



Clinical Psycho-Oncology: Indian Perspectives and Research by Santosh K. Chaturvedi, one of the international leaders in Psycho-Oncology, drives the reader's attention to the most significant clinical issues in psychosocial oncology: the extremely important topic of communication skills and the need for health care professionals to improve their modalities to relate and empathize with cancer patients and their families; the problem of diagnosis of psychiatric disorders secondary or subsequent to cancer (e.g. anxiety, depression, delirium); the management of psychiatric emergencies and the treatment of the common psychosocial disorders in cancer; the special issues of psychoncology in childhood and adolescence and psychiatry in palliative care; the area of the ethical and spiritual implications in cancer care as well as the problem of stress and burnout among cancer health care professionals.

The work done by the author, as a synthesis of a whole life dedicated to research and clinical care in psychiatry and oncology, will be of extreme help for cancer specialists, general practitioners, nurses and mental health professionals in general, filling a gap relative to the extreme need to have a cross-cultural and social view of cancer, as it is for this book which thoughtfully examines the field from an Indian perspective. Dissemination and application in clinical practice of what the book examines, will help patients and their families to receive a compressive highquality cancer care and to experience a better quality of life as they go through the journey of disease.

Dr Santosh K Chaturvedi, MD, FRCPE [Edinburgh UK], FRCPsych [UK] is a Senior Professor of Psychiatry at the National Institute of Mental Health & Neurosciences, Bangalore, India. Awarded the Indian Council of Medical Research Awards on three occasions, 1989, 1992, 2002; & Awards of the Indian Psychiatric Society – DLN Murthy Rao Oration, Tilak Venkoba Rao Oration, Poona Psychiatric Association awards on many occasions. Dr Chaturvedi is the Editor in Chief of the Journal of Psychosocial Rehabilitation and Mental health, published by Springers Nature. Dr Chaturvedi has more than 500 publications in different International and National journals, with more than 280 citations / listings in PUBMED / MEDLINE; He has edited and / or published Fifteen Books, Manuals or Journals. He also joins the Editorial Team of Swasthya, a helthcare journal published in the United Kingdom. Website https://santoshchaturvedi.in/ Twitter @skchatur

### It happens



A PoeTRY diary about breast cancer Rajan Madhok & Helen Job Denbighshire 2022

### It happens

This is an excellent diary that charts a journey through diagnosis and treatment for breast cancer.

It is Helen's story, recorded, day to day events, she made some personal notes, that is worth reading.

She quotes, "All cancer patients and their circumstances are unique, but what is common is the intense upheaval and the physical and mental toll it takes, despite all the advances in treatments. What gets one through is the focus on living each day, one day at a time. We did it and so can you if you are unfortunate to get a cancer and are reading this. We wish you the very best".



Prof Rajan Madhok and Helen who have together compiled the diary are pictured here with Buddhdev Pandya at the start of the exhibition that Helen held to raise funds for their local cancer charity. Hard copies of the book are available from madhokrajan@gmail.com



### Dr Ranee Thakar elected as the Dr Lade Smith CBE has been President of the Royal College of **Obstetricians & Gynaecologists**



Dr Ranee Thakar is a Consultant Obstetrician and Urogynaecologist at Croydon Health Services NHS Trust and Honorary Senior Lecturer at St George's University of London. She has been elected as the next President of the Royal College of Obstetricians and Gynaecologists (RCOG) and will take up office in December 2022.

Ranee has been Vice President of Global Health at the RCOG since December 2019, is co-chair of the College's Race Equality Taskforce and has been a member of the RCOG Council since 2016. She is past President of the International Urogynecological Association and leads the national obstetric anal sphincter injuries (OASI) Care Bundle Project. Regionally, Ranee leads the Perinatal Pelvic Health Project and Urogynaecology network for South-West London, developing multi-disciplinary collaboration with urologists, midwives, physiotherapists, nurses and GPs.



Professor Mayur Lakhani

# elected as the next President of the RCPsvch



Shubulade Smith CBE is a British academic and consultant psychiatrist at the South London and Maudsley NHS Foundation Trust. She is a senior lecturer at King's College, London and Clinical Director at the NCCMH and forensic services at SLaM. Smith was recently awarded 'Psychiatrist of the Year' in 2019

She is also an RCPsych Presidential Lead for Race and Equality and Clinical and Strategic Director with the College's National Collaborating Centre for Mental Health (NCCMH). Lade will be the College's first Black President and the fifth woman at the helm. orce and has been a member of the RCOG Council since 2016. Lade will become the 18th President of the RCPsych and will replace current President Dr Adrian James when he demits office on 11 July, at the College AGM, which is being held during the RCPsych International Congress in Liverpool.

Former chair and president of the . RCGP Professor Mayur Lakhani has been knighted for services to general practice in the New Year Honours. Professor Lakhani is currently chair of the Faculty of Medical Leadership and Management and a GP at Highgate Medical Centre in Loughborough.

#### Other GPs receiving various lower New Year Honours included:

 London GP Dr Minal Bakhai, the director of primary care transformation at NHS particularly during Covid-19.

- NEW YEARS HONOURS LIST 2022 RCGP treasurer and South London GP Dr *Stephen Mowle,* for services to healthcare.
  - Powis GP Dr Andrew Raynsford, for services to the NHS in Wales.
  - Macmillan chief medical officer Dr Rosemary Loftus, for services to people with cancer.
  - London-based PCN clinical director Dr *Naomi Katz*, for services to the NHS during Covid-19.
  - London GP Dr Sayyada Mawji, for services to healthcare during Covid-19.
  - Dr Wirinder Bhatiani, former chair of NHS Bolton CCG, for services to health and to diversity in Greater Manchester.

CBE is also awareded to Dr Ramesh Mehta England, for services to General Practice, OBE, the President of British Association of Physicians of Indian Origin (BAPIO)



EVENTS

### Dr Sarah Clarke is the new RCP president

Dr Sarah Clarke has been announced as the 122nd president of the RCP, at an extraordinary meeting of RCP Council in 2022. The meeting of the members was called after Professor David Oliver withdrew from the ballot for the election of the president. Dr Clarke assumed the role in September for a 4 years term. Dr Clarke, a consultant cardiologist at Royal Papworth Hospital NHS Foundation Trust in Cambridge, RCP clinical vice president and past president of the British

Cardiovascular Society, said: 'I was delighted to receive the call to serve as president. It is a huge privilege to be the president of the RCP and I want to thank the fellowship and Council who have put their faith in me and will be by my side as we navigate the challenging times ahead for our profession. Professor David Oliver, Former President of British Geriatrics Society, withdrew for health reasons. He said, 'Dr Clarke has the skills, experience and credibility to be a fantastic president".





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### August 2022, Alumni Meeting, Chatsworth

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