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1 CLINICAL RESEARCH

Comparison of capillary microsampling with conventional sampling for measuring cefazolin concentrations in the plasma of critically-ill pediatric patients

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Introduction

- Pharmacokinetic research in pediatric intensive care unit (PICU) patients is currently limited, leading to suboptimal dosing of antibiotics and therefore poorer outcomes in these patients.
- Microsampling with capillary tubes (CMS) is a more efficient method to obtain clinical samples for pharmacokinetic studies, allowing for smaller volumes of blood to be taken.
- Following Federal Drug Administration (FDA) criteria, a laboratory-based validation and then a correlative bridging study were performed to determine if CMS produces results comparable to conventional sampling in detecting cefazolin concentrations in plasma in PICU patient

Methodology

- Laboratory-based validation demonstrated the validity of the method in measuring concentrations of cefazolin in plasma across the clinically-relevant concentration range of 1 to 500 μg/mL with precision (<5.4%), accuracy (-2.7 to 2.5%), as well as ensuring stability of samples over time (1).
- Next, plasma from seven critically-ill PICU patients receiving cefazolin was collected as a CMS via heel prick and a conventional sample over varying time points of administration.
- Clinical samples were then extracted using acetonitrile and analyzed with high performance liquid chromatography with mass spectrometry (Shimadzu LC-MSMS 8030+) along with quality-control samples of known cefazolin concentrations from healthy volunteers.

Results

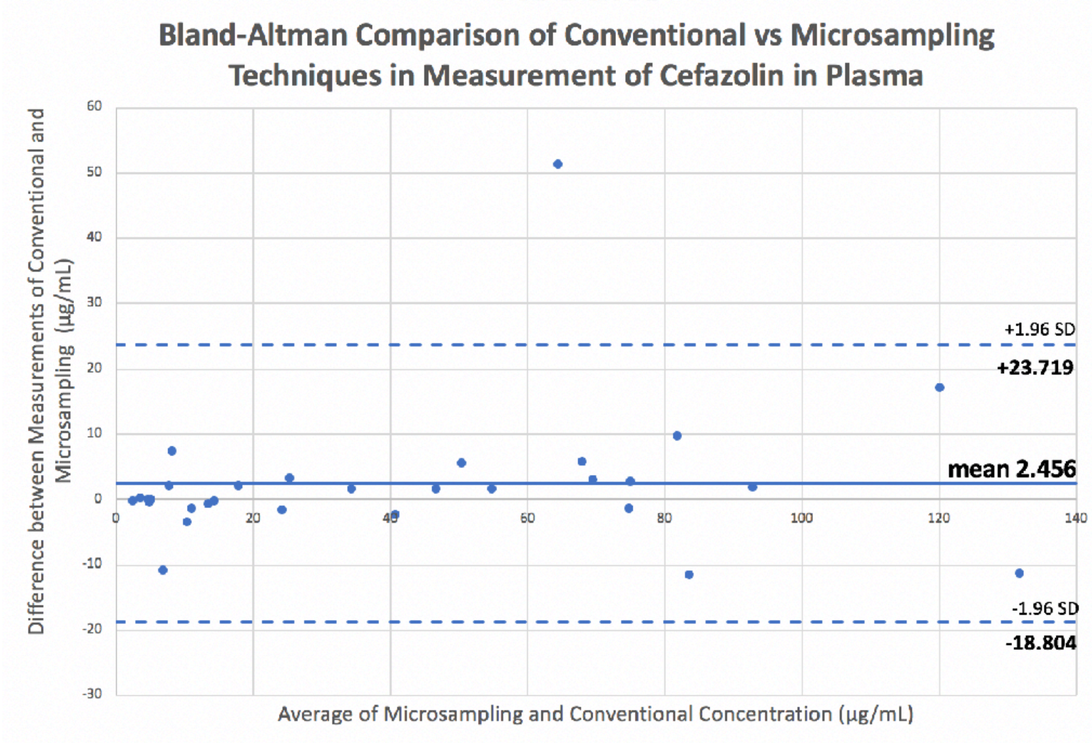

Figure 1: A bias of 2.456 was calculated, with all data points except one falling within an upper limit of agreement (ULoA) of 23.719 (+1.96 S.D.) and a lower limit of agreement (LLoA) of -18.804 (-1.96 S.D.).

Conclusion

These findings provide an improved method to facilitate future pharmacokinetic studies and therefore improve outcomes by optimizing the dosing requirements of cefazolin in PICU patients.

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Classical Music in Cardiac Prevention and Rehabilitation

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Cheng & Grove. ***Classical music in cardiac prevention and rehabilitation.*** British Journal of Cardiac Nursing. 2017; 12(12).

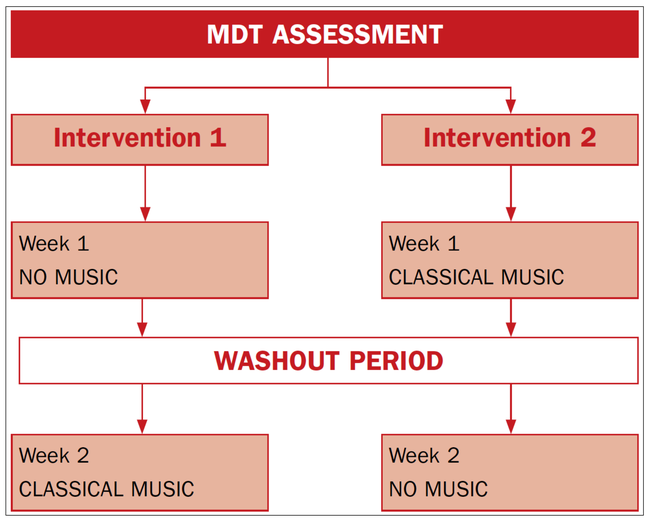
Introduction

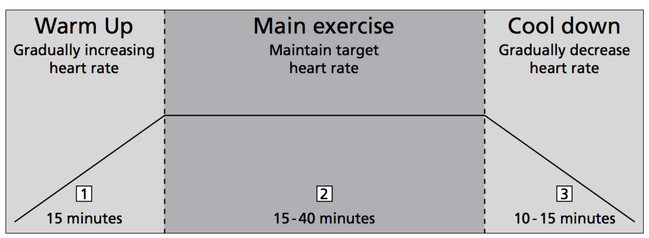
Cardiovascular diseases (CVD) are the leading global cause of death, responsible for over 31% of total mortality.[1] Currently, CVD prevention programs incorporate a multifaceted approach using risk modification, cardioprotective therapies, medical risk-factor (RF) management, and targeting of psychosocial health. Physical inactivity (PA) has been identified as one of the main modifiable RFs of CVD; increasing PA and exercise has been shown to correlate with a 33% relative risk reduction in CVD incidence.[2] As a result, individuals undergoing secondary prevention focus on increasing their exercise levels while in cardiac rehabilitation. Music is utilized during the conditioning phases of these programs, when patients undergo the main exercise circuit. As it currently stands, CV rehabilitation programs across the United Kingdom (UK) do not have regulations on the musical genre played during exercise sessions.[3] While studies have outlined classical music's positive impact on the psychological aspects of cardiovascular patients, current literature lacks its impact on exercise intensity.

Objective

A service evaluation was conducted within the Imperial College Healthcare NHS Trust in order to understand how classical music affects exercise intensity. The main objective of this pilot study was to **identify whether classical music could successfully increase physical activity intensity**.

Study Design





Stratification Level		CV Exercise	Active Recovery
RED	Beginner	18 mins	6 mins
AMBER	Intermediate	21 mins	3 mins
GREEN	Advanced	24 mins	0 mins

Inclusion

- ST-segment elevation myocardial infarction (STEMI)
- Non-ST-segment elevation myocardial infarction (NSTEMI)
- Unstable angina (UA)
- Revascularisation
- Percutaneous coronary intervention (PCI)
- Coronary artery bypass graft (CABG)
- Valve repair and valve-repair replacement
- Implantable cardioverter-defibrillator (ICD)
- Cardiac resynchronisation therapy device (CRT)
- Heart failure (HF)

Exclusion

- Transcatheter aortic valve implantation (TAVI)
- Severe cognitive impairment

The Playlist

Allegro	*Vivace*	*Presto*
(120–168bpm) 'fast, quickly, & bright'	(168–178 bpm) 'lively & fast'	(168–200 bpm) 'very, very fast'
• Étude Op.25, No.12 in C Minor – "Ocean" (Chopin) [2:35]	• Étude Op.10, No.1 in C Major – "Waterfall" (Chopin) [1:57]	• Étude Op.10, No.4 in C# Minor – "Torrent" (Chopin) [2:02]
• 'Finale' from The William Tell Overture (Rossini) [3:12]	• Étude Op.10, No.5 in Gb Major – "Black Keys" (Chopin) [1:40]	• Octet Op.20 – IV: Presto (Mendelssohn) [5:39]
• Hungarian Dance No.5 in G Minor (Brahms) [3:08]	• Étude Op.10, No.12 in C Minor – "Revolutionary" (Chopin) [2:42]	• Tritsch-Tratsch-Polka, Op. 124 (Strauss II) [2:43]
• Piano Sonata No.11 in A Major, K.331 – III. Rondo alla turca (Mozart) [3:24]	• Étude Op.25, No.9 in Gb Major – "Butterfly Wings" (Chopin) [0:58]	
• 'Spring' from The Four Seasons (Vivaldi) [3:29]	• Flight of the Bumblebee (Rimsky-Korsakov) [3:24]	

No operatic aria and lyrical songs were used, as words have been shown to elicit mixed emotional effects on the human mind, and this may in turn also alter PA and exercise intensity. The upper end of tempo in all three categories are > 140 bpm.

Results

Intervention	Mean Borg RPE (units)	Standard Deviation (units)	95% Confidence Interval
No Music	11.429	1.372	10.896 ~ 11.961
Classical Music	12.071	1.386	11.534 ~ 12.609
Difference	+0.642		–1.093 ~ –0.192 (p = 0.997)

Borg Rate of Perceived Exertion:
- Paired t-test
- p = **0.997** (non-significant)
- **Classical music has no effect on Borg RPE**

Intervention	Mean HR_{avg} (bpm)	Standard Deviation (bpm)	95% Confidence Interval
No Music	87.821	12.371	83.024 ~ 92.618
Classical Music	88.143	12.456	83.313 ~ 92.973
Difference	+0.642		–3.475 ~ 2.832 (p = 0.582)

Average Heart Rate:
- Paired t-test
- p = **0.582** (non-significant)
- **Classical music has no effect on HR_{avg}**

Intervention	Median HR_{peak} (bpm)	Inter-quartile range (bpm)
No music	107.5	96-123
Classical music	114.5	102-130
Difference	+7.0 (p = 0.009)	

Peak Heart Rate:
- Wilcoxon matched-pairs test
- 6 bpm mean HR_{peak} difference
- 7 bpm median HR_{peak} difference
- p < **0.01** (significant)
- **Classical music may have an effect on HR_{peak}**

Discussion

- Target training zones are prescribed at 40-70% heart rate reserve (HRR), or 11-14 Borg RPE.[4]
- Exercising at a 70% HRR has been validated for exercise prescription in CV rehabilitation setting.
- For a positive correlation between music and exercise intensity, classical music intervention must motivate individuals to be exercising closer to 70% HRR rather than 40% HRR.
- 7 bpm increase in HR_{peak} as a result of exercising with classical music is statistically significant but not clinically significant.
- Future work can incorporate other genres that may be of interest in CV prevention and rehabilitation settings, such as jazz, or participant age-appropriate musical genres, such as rock and roll, disco, and 60's-70's classics.

Conclusions

- HR_{peak} is the preferred objective measure of PA intensity
- Exercising with classical music does not impact Borg RPE, HR_{avg}, or energy expenditure
- Exercising with classical music increases HR_{peak} by 7 bpm
- Classical music is a safe genre for cardiac rehabilitation services
- Classical music is encouraged as a genre to use during exercise circuits

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Five Patient Outcomes Following Neck of Femur Fracture Surgery

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Introduction

- Hip fractures are the most serious and expensive fall related injury in Australia[1-2].
- Each year there are roughly 22,000 hip fractures in Australia and the number is expected to increase to 30,000 by 2022[1]
- Post operative complications are responsible a large morbidity and mortality to the patient[3].
- This project aims to compare types of fractures, surgery types, surgeon training level and general patient demographics of neck of femur surgical repair for the following outcomes:
  - Intraoperative Blood Loss
  - Change in Parker Mobility
  - Acute mortality
  - 1 year Mortality
  - 28 Day Readmission

Hypothesis

- We hypothesised worse outcomes in those who are older, male, those who had a trainee surgeon, and those who had longer surgical times.

Methods

- Using the Neck of Femur Fracture Database from a tertiary medical centre in Australia, patient data (n=783) was collected from 2014 to July 2018.
- Outcomes used: blood loss, change in Parker Mobility score, one year mortality, acute intraoperative mortality and 28 day readmission
- Variables used in the liner and categorical regression were surgical times, types of fracture, type of surgical repair, surgical experience, age, sex, presurgical mobility, and pre-surgical ASA score.
- Significance was determined at $p<0.05$

Results

Outcome	Factor	Odds Ratio	Confidence Interval	Compared Against
12 Month Mortality	Hemiarthroplasty Cemented	7.69	1.88-35.9	Dynamic Hip Screw
	Hemiarthroplasty Uncemented	4.68	1.14-21.66	Dynamic Hip Screw
	Female	0.38	0.23-0.60	Male
	Pre-surgery Mobility Score	0.80	0.72-0.88	All Scores
	ASA 3	1.99	1.09-3.78	ASA1-2
28-Day Readmission	Age	0.96	0.92-0.996	All ages
	Pre-surgery Mobility Score	1.20	1.03-1.41	All Scores
	Subtrochanteric	0.13	0.02-0.99	Intracapsular Displaced

- Hemiarthroplasty and an ASA score of 3 was shown to have a significant increased chance of death in 12 months compared to other surgeries
- Being female and having a higher Pre-surgery Parker mobility were shown to be protective against dying at 12 months
- Being younger and having a subtrochanteric fracture was shown to be protective for readmission
- Having a higher Parker Mobility score was associated with increased readmission

Take Away

- Hemiarthroplasty and an patient ASA grade of 3 was associated with significantly increased risk of death within 12 months of operation.
- Being female, and having a subtrochanteric fracture was associated with better one year mortality and readmission respectively.

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ASPIRIN OVERDOSE: WHAT IS A REALISTIC RISK ASSESSMENT?

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BACKGROUND

Aspirin is a metabolic poison and overdoses cause acid-base disturbance and organ dysfunction. Risk assessment has been based on the recognised severity of chronic poisoning reported over 40 years ago. We investigated the severity of acute aspirin overdose and predictors of toxicity.

METHODS

We undertook a retrospective series of acute aspirin overdoses presenting to two toxicology units from January 2000 to September 2019. Aspirin exposures >3000mg were identified in prospective clinical databases from toxicology presentations. Clinical notes were reviewed to obtain demographic data, clinical effects, investigations, complications and treatment.

RESULTS

There were 170 cases in 143 patients (98 females [69%]) with a median age of 28 years (Interquartile range [IQR]: 20-44 years). Patients presented a median of 3.5 h (IQR: 1.7-7.2 h) post ingestion following a median aspirin ingestion of 7200 mg (Range 3300-86400 mg). Co-ingestions were taken in 131 (77%) presentations. Charcoal was given in 37 (22%) presentations a median of 3.0 h (IQR: 2-4.5 h) post-ingestion.

Common clinical features were tinnitus in 36 patients (21%), vomiting in 45 (26%) and tachypnoea (respiratory rate > 20 breaths per minute) in 61 (36%). Confusion, coma (GCS < 9) and hypotension occurred in 15 (9%), 9 (5%) and 17 (10%) cases respectively, although in most cases these were attributable to co-ingestions. A bicarbonate <20 mmol/L occurred in 38 (22%) presentations.

The median peak aspirin concentration was 276 mg/L (IQR: 168-400 mg/L). There was a strong association between dose ingested and peak concentration (Pearson r=0.55; p<0.0001 [Figure 1]). There was a small negative association between dose ingested and bicarbonate (Pearson r=-0.21; p=0.012 [Figure 2]).

Figure 1

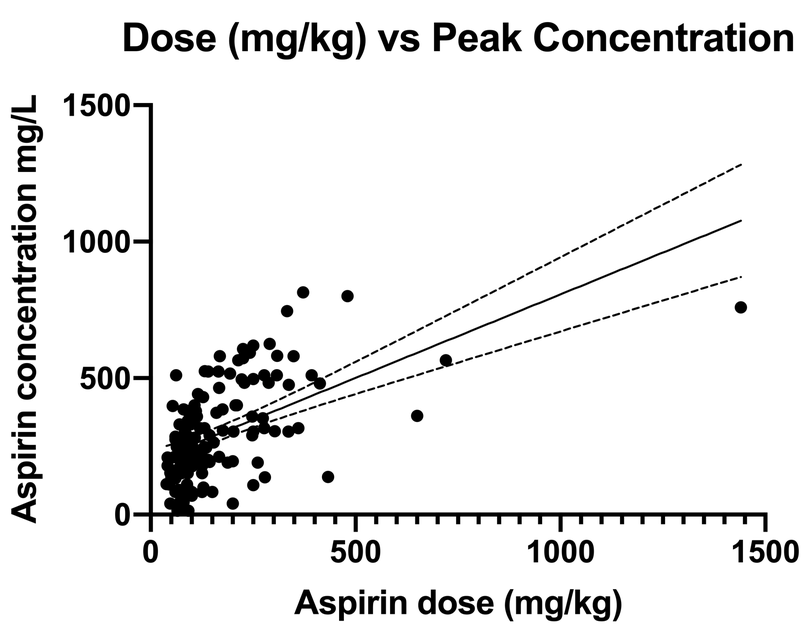
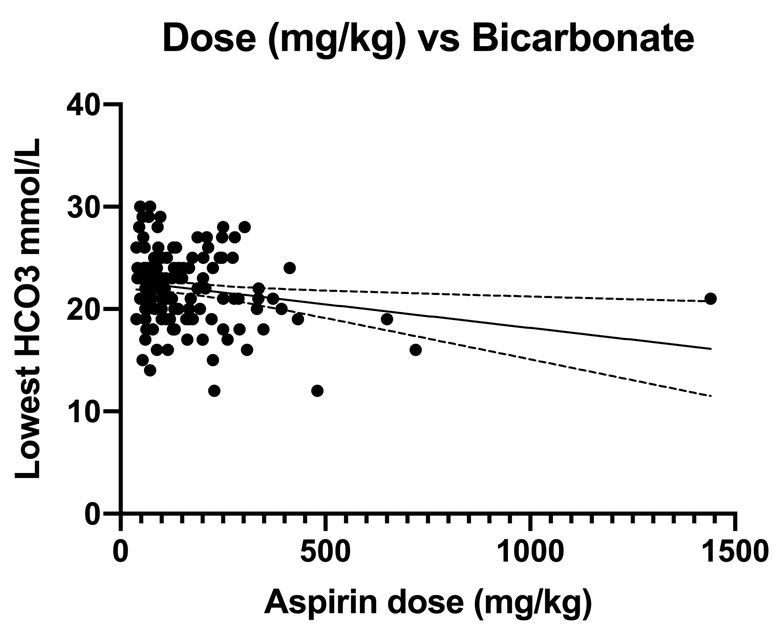


Figure 2



There were four cases of severe toxicity, ingesting 372mg/kg, 480mg/kg, 1440 mg/kg and 333mg/kg. Peak salicylate concentrations were 814 mg/L, 800 mg/L, 759 mg/L and 745 mg/L respectively. Urinary alkalinisation was performed in 35 (21%) presentations. No patient required dialysis and no patient met any of the EXTRIP criteria for dialysis. Twenty one patients were admitted to ICU. The median length of stay was 18 h (IQR: 7-24 h).

CONCLUSIONS

Acute aspirin overdose caused only mild toxicity in most cases. There were few cases of severe toxicity with peak salicylate concentrations >700mg/L, all ingesting doses >300mg/kg. Both salicylate concentration and bicarbonate were associated with dose ingested.

External factors affecting number and composition of presentations to the emergency department

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Background

Multiple factors affect pattern of ED presentations. This study sought to identify all factors affecting ED presentations with a specific focus on the 2011 Brisbane floods.

Methods

1. Literature review
   - Databases: PubMed, Cochrane Library
   - Google Scholar, Embase,
   - Publishing date: 1990 – present
2. Analysis of an ED presentations dataset
   - Princess Alexandra Hospital ED
   - Comparison Dec-Feb 2010, 2011, 2012

Results

1. Literature review
   - 75 articles reviewed for factors affecting presentation numbers and pattern
     - Predictable: weekday, time of day, season.
     - Non-predictable: environmental events of drought, earthquakes, floods
2. Analysis of dataset
   - No significant variation across three periods to number or composition.

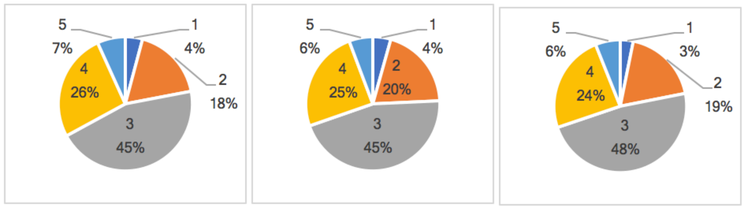

Fig1: Triage category assigned to patients L) 2010, M) 2011, R) 2012

Discussion

- Lack of variation to presentations during Brisbane flood could potentially be because of delayed presentations or injuries that did not require immediate or emergency attention
- Further investigation is needed to fully appreciate the affects of the flooding in Brisbane 2011

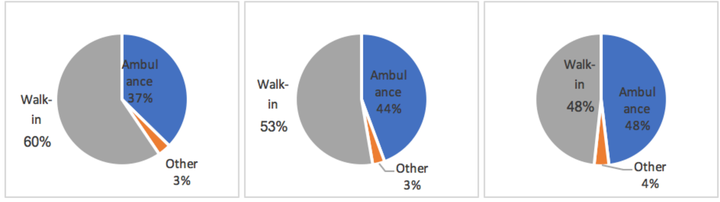

Fig2: Mode of presentation to hospital L) 2010, M) 2011, R) 2012

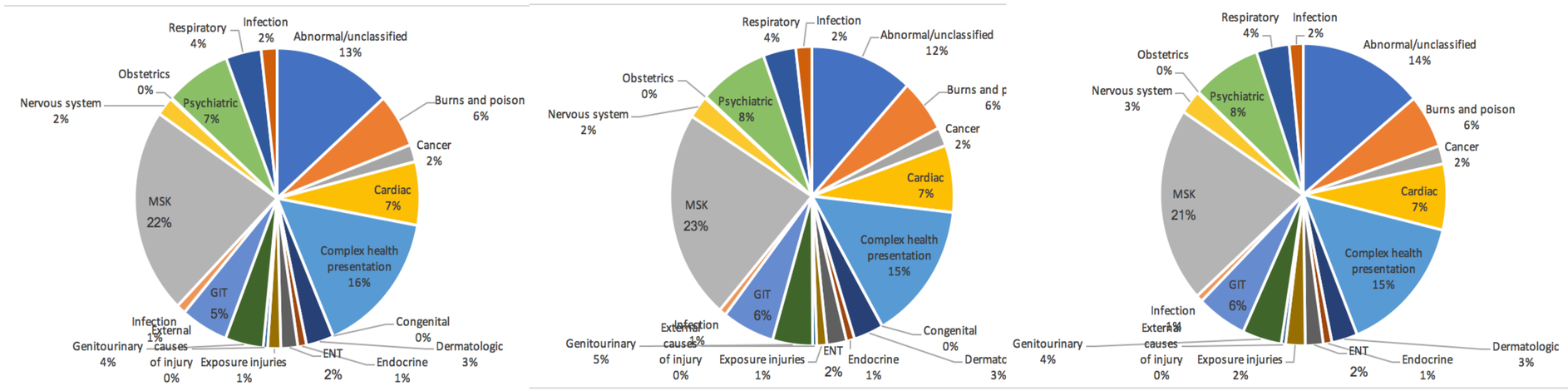

Fig3: ICD-10 diagnosis for patients L) 2010, M) 2011, R) 2012

More Than Just OSA: Non-respiratory Sleep Disorders in Australian Down Syndrome Children

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Introduction

• Sleep Disorders are common in children with Down Syndrome (DS), with most studies evaluating obstructive sleep apnoea (OSA)[1]

• Prevalence estimates for OSA in this group range from 24 to 59%[1]

• Current literature reports that non-respiratory sleep disorders also occur more frequently than in typically developing (TD) children[2]

• Existing studies of non-respiratory sleep disorders in children with DS have assessed either community or referred children, not both [3,4]

• Many of these studies have used the Children's Sleep Habits Questionnaire (CSHQ) [3,4]

• No Australian studies have been undertaken to date.

Aims

•Using the CSHQ:

1) Assess the prevalence of non-respiratory sleep disorders in a community group of Australian children with DS (DS_{comm})
2) Compare Australian children with DS from the community with those referred to a sleep physician (DS_{ref})

Methods

• CSHQ disseminated by Down Syndrome Queensland and DS Australia (DS_{comm}) or completed at first sleep clinic visit (DS_{ref})

• Additional questions:

- DS_{comm}: previous attendance to a sleep clinic and parental concern regarding sleep problems
- DS_{ref}: reason for referral to sleep clinic

Results

• DS_{comm} n=76 (57% male; median age 9.7 yrs)
• Ds_{ref} n=42 (50% male; median age 7.0 yrs)

Prevalence of sleep disorders:

• DS_{comm} 90.9% DS_{ref} 85.7% (p = 0.54)

Mean total CSHQ score:

• DS_{comm} (57.13 ± 9.54) DS_{ref} (52.76 ± 9.48) **(p = 0.023)**

• DS_{comm} group scored higher on the *Night Wakings* subscale **(p = 0.00021)**

DS_{comm} Group:

• 45.1% of children in had been seen before in sleep clinic

• 73.7% parents had concerns about a sleep disorder

DS_{ref} Group:

• 91.9% of children referred for snoring or OSA

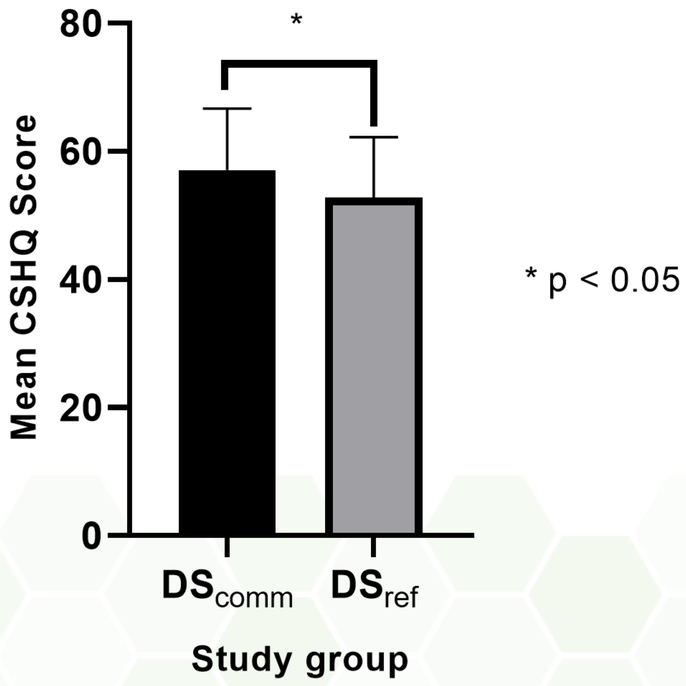

Fig. 1. Comparison of mean total CSHQ score between the DScomm and DSref groups

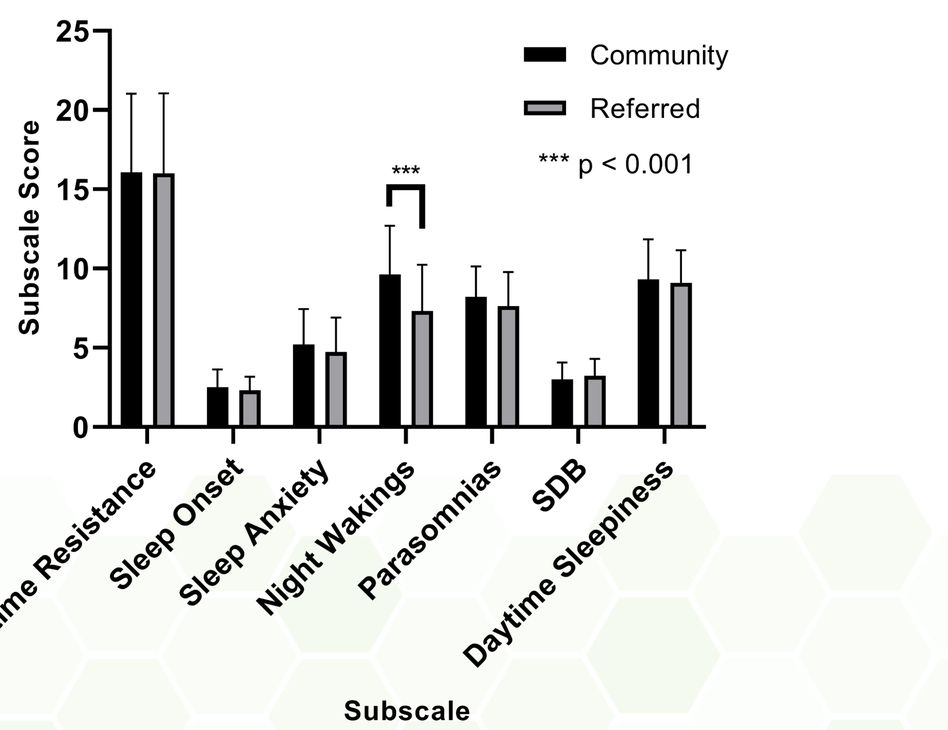

Fig. 2. Comparison of mean percentage subscale scores between the DScomm and DSref groups

Discussion

- The prevalence of sleep disorders was found to be just as high in a community sample of Australian children with DS as it is in those referred to the sleep clinic.
- 92% of those children referred to the sleep clinic were referred with a complaint of snoring or symptoms of OSA.
- A large number of parents of community children were concerned about their child having a sleep disorder (73.7%), however less than half of the children had ever attended a sleep clinic
- This high prevalence is of concern due to recent findings of worsened cognitive and behavioural outcomes in children with DS who are impacted by sleep disorders[5]
- This study suggests there are large number of children with DS in the community who are experiencing sleep problems but are not being seen in the clinic, only those with OSA are being referred.
- In order to improve outcomes for children with DS, greater awareness is required amongst parents and primary care physicians regarding these problems, with a low threshold to refer to tertiary services.

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Bovine Jugular Vein Conduits vs. Homografts for Pediatric Pulmonary Valve Replacement

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Introduction

- Repair of congenital heart defects often requires relief of right ventricular outflow tract obstruction
- Several options exist for pulmonary valve replacement, including prosthetic valves and right ventricle to pulmonary artery conduits, but the optimum choice has been unclear
- This study compared long-term performance of bovine jugular vein (BJV) conduits and cryopreserved homografts

Methods

Inclusion Criteria

Patients undergoing pulmonary valve replacement:

- With a cryopreserved pulmonary homograft, aortic homograft, or bovine jugular vein conduit;
- Under 20 years of age at time of operation;
- Operation between 1 Jan 2000 and 31 Dec 2018;
- At Queensland Children's Hospital (Brisbane), Royal Children's Hospital (Melbourne), and the Prince Charles Hospital (Brisbane).

Exclusion Criteria

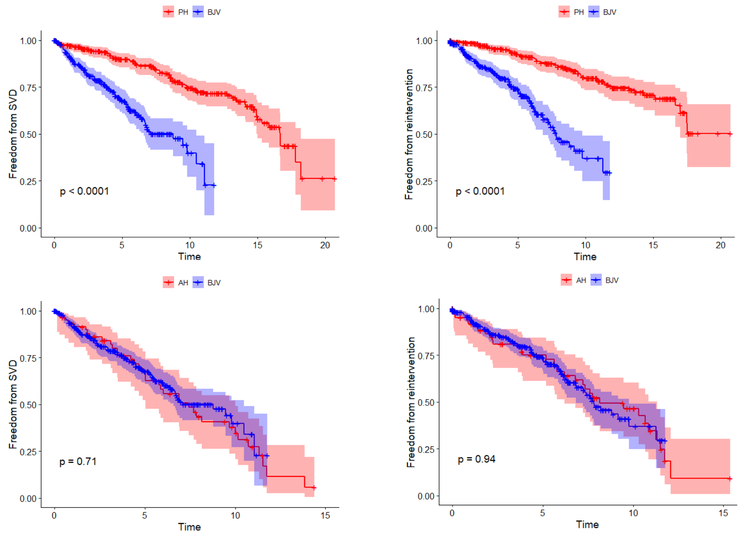
- Acquired (non-congenital) heart disease;
- All other valve/conduit types.

Performance Measures

- Freedom from structural valve degeneration (SVD; peak trans-pulmonary gradient ≥50 mmHg or moderate or greater pulmonary regurgitation);
- Freedom from re-intervention (surgical or catheter);
- Incidence of infective endocarditis

Variable	Pulmonary Homograft (n=305)	BJV Conduit (n=302)	Aortic Homograft (n=66)
Small conduit (≤15mm)	5.2%	35.1%	30.3%
Oversized conduit (z-score ≥ 2)	15.7%	25.5%	42.4%
Median follow up	9.4 years	4.7 years	10.1 years
Incidence of infective endocarditis	1%	10%	1.5%

Selected characteristics of the three study groups by conduit type (above).



Kaplan-Meier curves comparing: freedom from SVD in BJV conduits and pulmonary homografts (top left), freedom from reintervention in BJV conduits and pulmonary homografts (top right), freedom from SVD in BJV conduits and aortic homografts (bottom left), and freedom from reintervention in BJV conduits and aortic homografts (bottom right).

Results

- Pulmonary homografts significantly outperformed both BJV conduits and aortic homografts in freedom from structural valve degeneration (SVD) and reintervention; these differences persisted with propensity-matching
- No difference was found between the performance of BJV conduits and aortic homografts
- Small conduits showed significantly higher risk of SVD and reintervention, as did oversized conduits
- Infective endocarditis occurred in 10% of BJV conduits, compared to 1% and 1.5% in pulmonary and aortic homografts

Limitations

- Differences between study group characteristics resulted in propensity-matched samples of only about half the original sample, though the results remained similar
- Median follow up time was much shorter for the BJV group
- IE prophylaxis could not be accounted for

Conclusion

- Pulmonary homografts result in better outcomes than BJV conduits or aortic homografts when implanted in the pulmonary position

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Year 4

Incidence of diabetic ketoacidosis in children with newly diagnosed type 1 diabetes presenting to QCH

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Introduction

Pediatric diabetic ketoacidosis (DKA) is associated with significant mortality and morbidity.[1] Risk factors for DKA in newly diagnosed patients include younger age (<2 years), delayed diagnosis, lower socioeconomic status, and residing in a country with a low prevalence of T1DM. The aim of this study was to determine the incidence of DKA in children with newly diagnosed type 1 diabetes (T1DM) presenting to Queensland Children's Hospital (QCH) and compare the cohorts presenting in DKA and non-DKA.

Results

A total of 355 children were admitted to QCH with a new diagnosis of T1DM. The 5 year incidence of DKA was 42.8%. There was no significant change in DKA incidence over the 5 years. There was an even distribution of children presenting with mild, moderate, and severe DKA. Females and those from low SES areas were found to have a higher risk of presenting with DKA at T1DM diagnosis. There was no significant difference in age at diagnosis between the two cohorts.

Methods

Inclusion criteria consisted of children:

- ❑ Newly diagnosed with T1DM
- ❑ Between January 1 2015 to December 31 2019
- ❑ Aged 0 to 16 years
- ❑ Treated at QCH

A retrospective chart review was performed to ascertain gender, age, DKA status and severity, and socioeconomic status.

Discussion

There are high rates of DKA at first presentation of T1DM in Brisbane and the incidence has increased since last studied in 2001 to 2011.[2] Given the consistently high rates of DKA over the last two decades, public awareness campaigns are warranted.

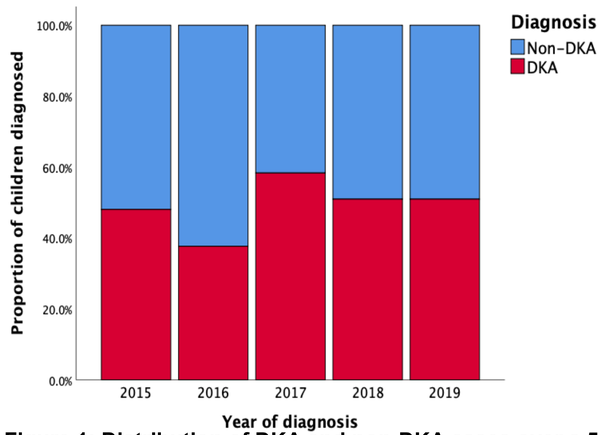

Figure 1: Distribution of DKA and non-DKA cases over a 5 year period

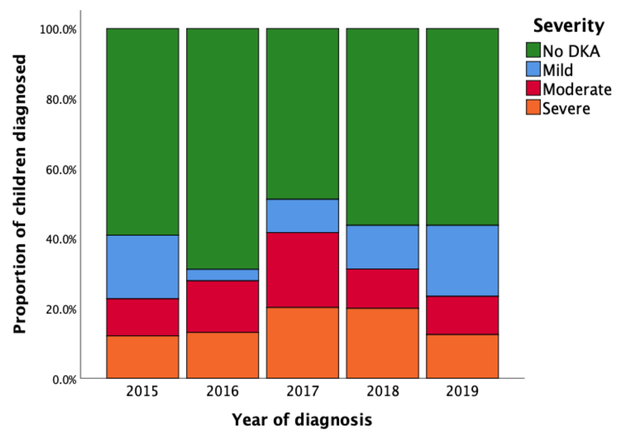

Figure 2: DKA severity by year

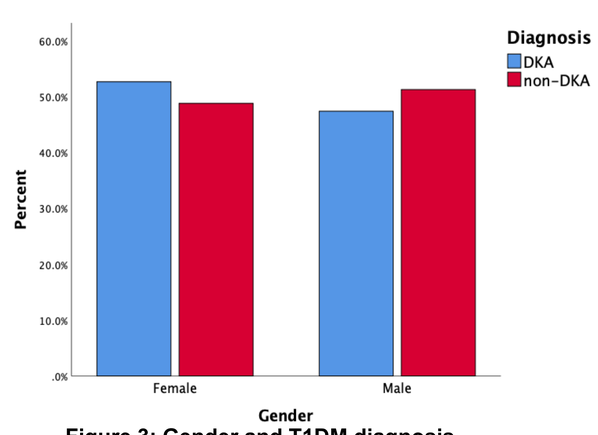

Figure 3: Gender and T1DM diagnosis

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Development of a photonumeric scale using 3D total-body photography to train artificial intelligence algorithms towards an objective assessment of melanoma risk

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Background

Melanoma

- >13000 New Cases and >1800 Deaths Annually in Australia.
- Most common cancer affecting Australians aged 15-39.
  - Third most common cancer in Australia across all age groups. (1)

Risk Factors

- Age, Hair Colour, Skin Phototype, Skin Cancer History, Atypical Naevi, Number of Naevi, Freckle Density, Sun Exposure History.
  - Reliance on self-reported and subjective clinical measures.
  - Assessment is cost-intensive and clinician-dependent. (2)

Aims and Methods

Aims

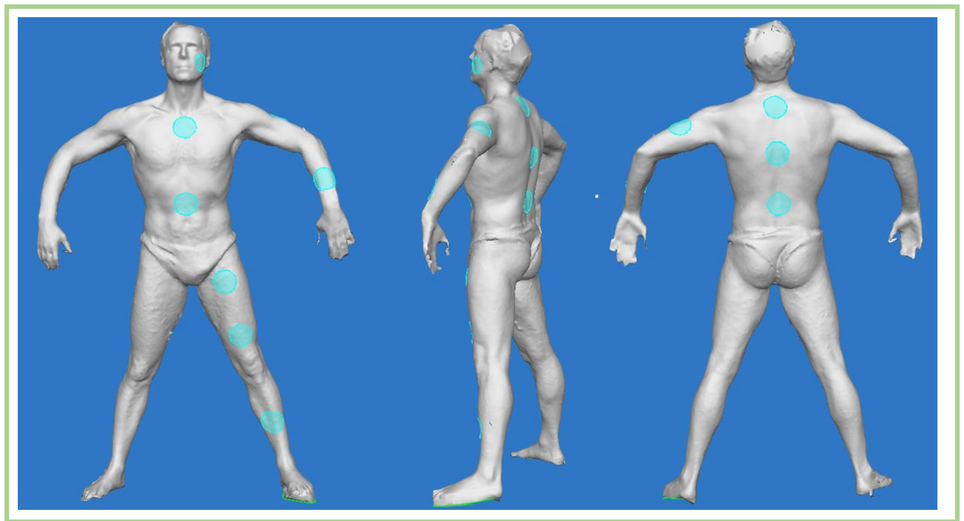
1. Develop a photonumeric scale of eleven body regions to quantitatively grade freckling density and solar-damage.
2. Train a deep-neural artificial intelligence algorithm to apply the photonumeric scale for an automated and objective assessment of melanoma risk.

Objective: An Objective and Automated Phenotypic Risk Assessment

- Number of Naevi
- Freckle Density
- Solar-Damage, to Replacing the Sun Exposure History

VECTRA WB360 Whole Body 3D Imaging

- 92 cameras instantly capture white and cross-polarised light images.
- Rendering of a 3D patient avatar.
- Blind-Spots
  - Skin clefts, Scalp under hair, Soles of feet.
- Existing AI Algorithm
  - Automated count of naevi greater than 2mm (3)

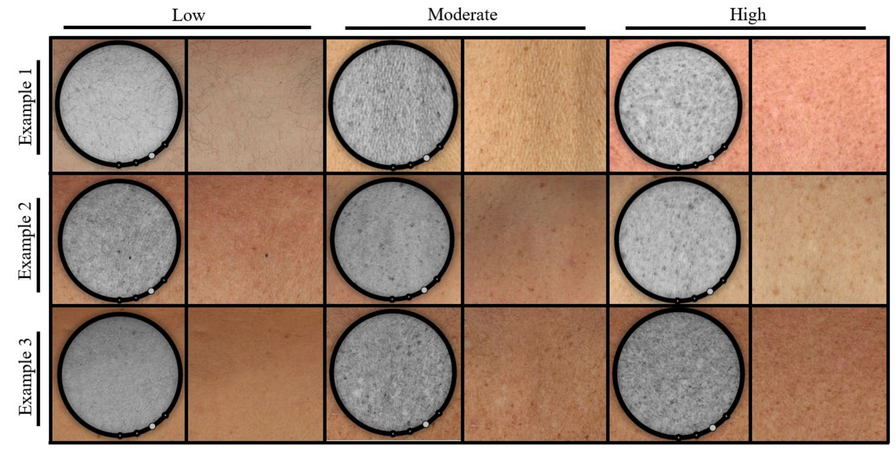


Body Regions for Assessment

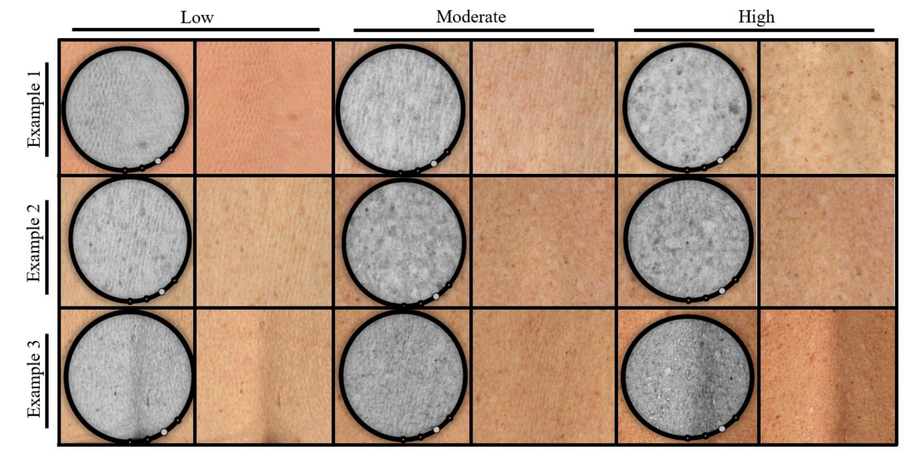
- Face, Chest, Back, Upper and Lower Arm and Leg.
- Solar Exposed and Non-Exposed

Results and Discussion

Freckling Scale Example: Mid-Back



Solar-Damage Scale Example: Mid-Back



Future Analysis

- Kappa Coefficient for Photonumeric Scale Reproducibility >0.8
- Freckling Phenotype Comparison to Melanoma-Associated SNPs
- IlluminaCore Exome Chip
  - Significant associations identified elsewhere in 12 SNPS, within 7 genes (4)

Gene	OR (95%CI)[c]	LRTS[d]	P-value
MITF	2.52 (1.28-4.97)	8.3	0.004
TERT	1.87 (1.10-3.17)	6.0	0.014
TERT	1.18 (1.02-1.35)	6.4	0.012
CDKN2A	1.31 (1.14-1.51)	14.7	0.001
CDKN2A	1.22 (1.02-1.46)	5.6	0.018
*MC1R**V92M	1.38 (1.09-1.74)	8.1	0.004
*MC1R**R151C	1.96 (1.58-2.43)	44.2	3e-11
*MC1R**R160W	1.79 (1.41-2.26)	26.9	2e-7
*MC1R**R163Q	1.54 (1.11-2.14)	8.1	0.004
ASIP	1.64 (1.23-2.17)	13.1	0.0003
MX2	1.24 (1.07-1.44)	10.1	0.001
PLA2G6	1.25 (1.06-1.46)	8.5	0.004

(4)

Conclusions and Future Directions

- 3D Total-Body Imaging may enable high-risk screening programs.
  - Require automated, quantitative, and objective measures for risk.
- Shift the paradigm of melanoma from reactive to predictive diagnosis.
  - Early diagnosis, precise interventions, reduced burden of disease.

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Vertebral Body Wedging Significantly Contributes to Coronal Plane Deformity: A Local Morphological Analysis of Adolescent Idiopathic Scoliosis during Growth

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INTRODUCTION

Adolescent Idiopathic Scoliosis (AIS) is characterised by both **lateral curvature and rotation of the spinal column** within patients who present at the age of ten years or older [1-2]. AIS is the most common form of the scoliotic condition, accounting for 85% of all scoliosis cases [3], yet **the exact pathoaetiology of AIS remains largely unknown**. Within the recent decade, there has been a shift toward the analysis of the pathoanatomical variation of the AIS spine with the **three dimensions (3D): coronal, sagittal and transverse planes** (Figure 1). Understanding the anatomical and biomechanical variation between vertebral bodies will elucidate possible pathoaetiological mechanisms of the onset of initial scoliotic deformity [4], while also providing a description of the osseous structures that are commonly utilised within instrumented surgical correction [5].

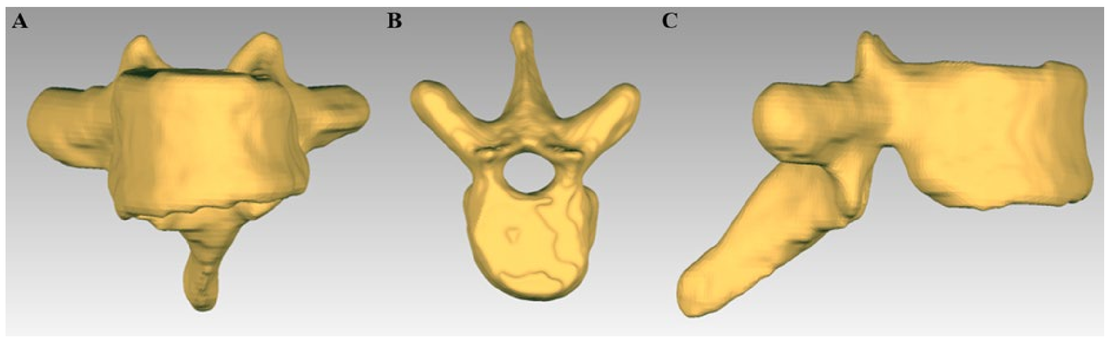

Figure 1: 3D CT Reconstruction of a typical apical vertebrae in an AIS patient (patient age at scan = 15.2 years, Cobb angle = 58°). Typical deformities are represented in the A) coronal, B) axial (with pedicle morphology) and C) sagittal planes. Concave deformities are shown on the right side.

In this investigation, we aimed to begin this 3D vertebral-level approach to AIS research. We provide a **comprehensive, multi-stage investigation of vertebral body (VB) and intervertebral disc (IVD) coronal plane deformities** in main thoracic curve types within AIS patients during growth using a series of sequential MRIs.

METHODS

The study cohort comprised **30 female patients** with Lenke Type I (major thoracic) curves, who were recruited and underwent **three MRI scans**, with a mean time between scans of 8.5 ± 0.7 months.

Datasets were reformatted to produce true coronal plane images of the thoracic spine (T4–L1) (Figure 2). Overall curve morphology, rates of growth, coronal plane IVD and VB segmental deformity were analysed.

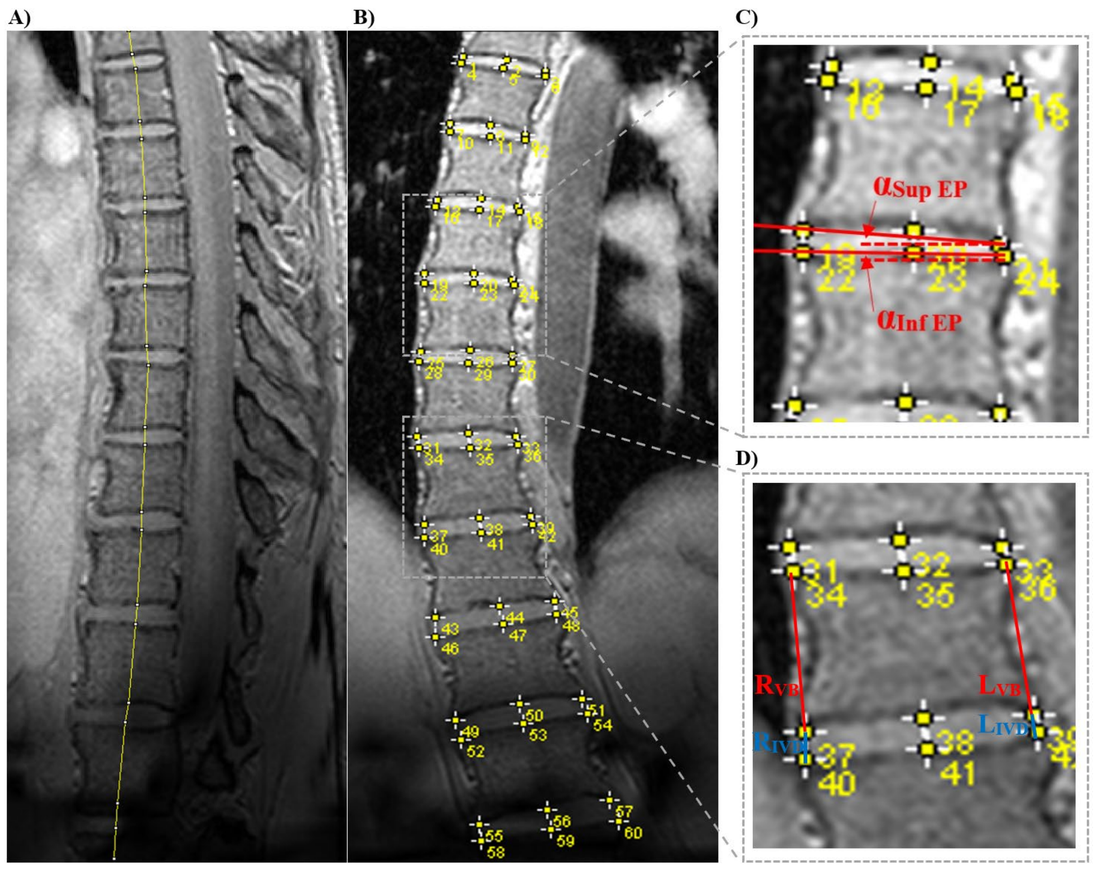

Figure 2: Illustrated technique for measurement of segmental disc and vertebral body wedging angles. **A)** Patient MRI scans were viewed in the sagittal plane. The segmented line tool was used to delineate the mid-points of opposing endplates. Mapping from these central positions, **B)** a pseudo-coronal plane image was produced. Three selected points across each vertebral end plate allowed the demarcation of superior and inferior end plates. **C)** Measurement of the inclination angles between superior and inferior endplates (a_{Sup} EP and a_{Inf} EP, respectively) allowed for the calculation of VB and IVD wedge angles. **D)** Comparison between right and left side heights of VBs and IVDs provided further analysis of coronal asymmetry.

NEED MORE INFO?

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RESULTS

1. Figure 3 shows 77% of patients demonstrated the majority (>50%) of their coronal curvature was attributed to VB wedging when measured across all three scans. However, the major scoliotic curve can be variably attributed to either the IVDs or VBs.

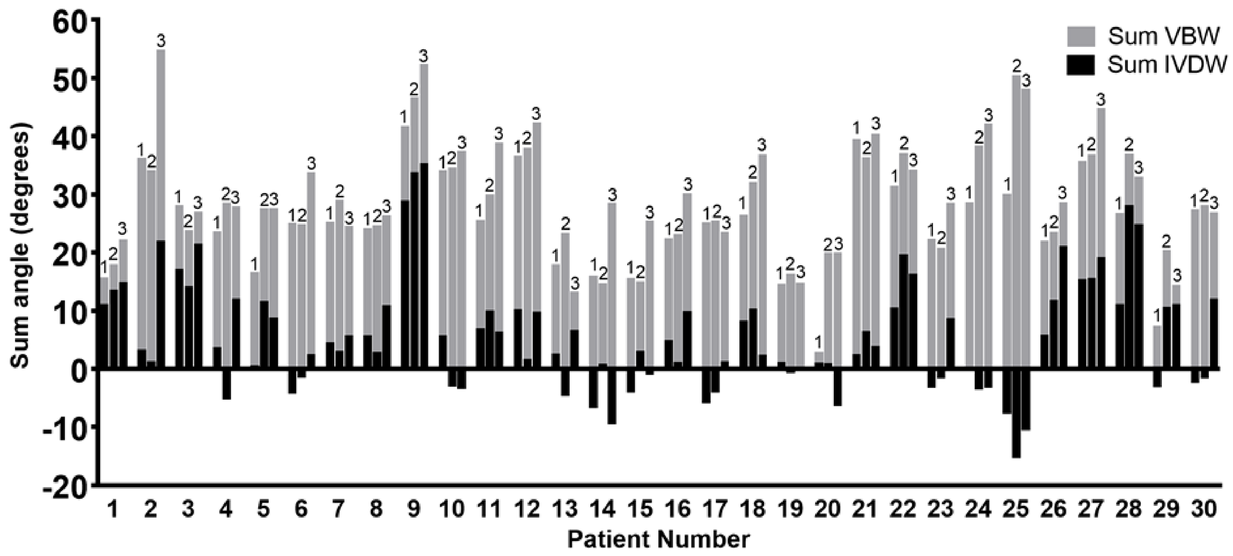

Figure 3: Compiled relative major curve angle contributions of sum vertebral body (grey) and intervertebral disc (black) wedging angles.

2. Both progressive groups (Figure 4) and non-progressive groups (not shown), at all scans, regardless of region, the sum of the VB wedge angle was greater than the sum of the IVD wedge angle (all P≤0.05).

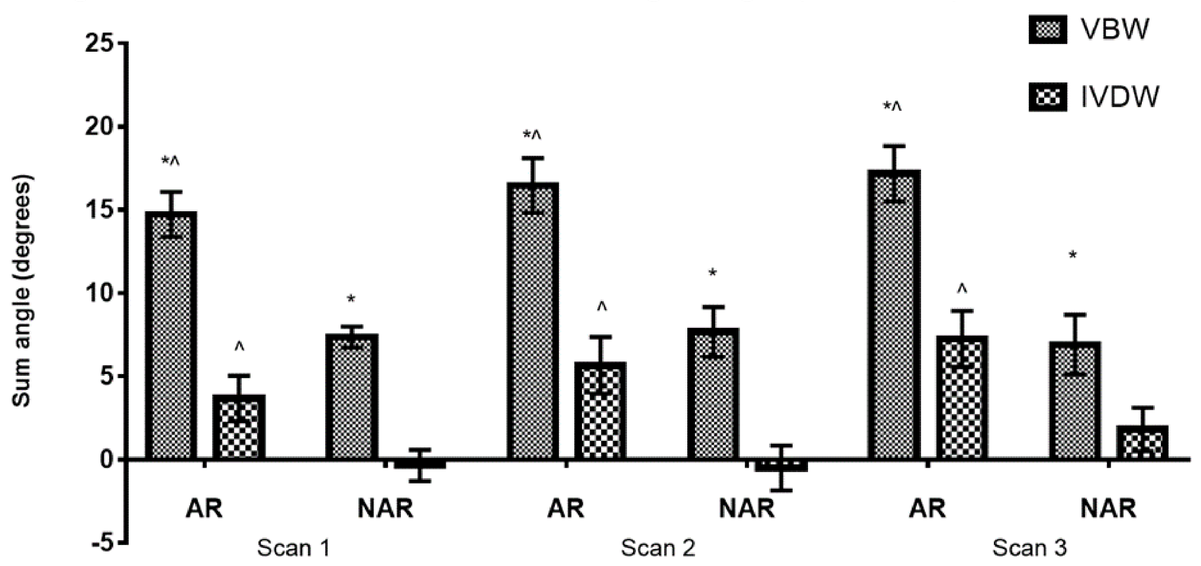

Figure 4: Summated coronal plane wedging angles for vertebral bodies (fine checked pattern) (VBW) and intervertebral discs (large checked pattern) (IVDW) per apical (AR)/non-apical region (NAR) and given scan number. Patients were grouped depending on whether their scoliotic curvature clinically progressed (shown) over the time of study or did not progress (not shown). * Denotes a significant difference (P<0.05) between VB and IVD, and ^ denotes a significant difference (P<0.05) between the same wedging type in AR vs NAR regions, at a given scan number.

3. Notably, when normalised, right-sided asymmetry was greater in IVDs (18.5 ± 23.9%) when compared to VBs (8.3 ± 9.2%) (P<0.05) by third scans.

4. Linear regression analysis demonstrated no correlation between the rate of major curve angle progression and the rate of standing height increase, VB height growth, or IVD height growth (P>0.05).

CONCLUSIONS

- **VB wedging contributed more to the lateral deformity** observed in Lenke Type 1 subtypes of AIS patients than IVD wedging.
- **IVDs did demonstrate the greatest asymmetric deformity**, however, their relatively smaller height resulted in a smaller proportional change in lateral curve angle compared to the VBs.
- MRI can be used as a successful imaging modality to track **segmental changes longitudinally in AIS patients**
- Questions remain regarding the sequence of how these deformities present. Studies which monitor the **bony changes within three dimensions from initial AIS presentation throughout developmental progression** will be a significant focus of continuing investigations.

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