ACADEMIC: ABSTRACTS

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Various Authors

Freehand 3DUS measurement of the triceps surae muscle volume in premature infants *in vivo*

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Introduction
Premature birth (gestational age <37 weeks) is a leading cause of childhood morbidity and mortality, associated with significant motor sequelae that have profound implications for health, development, and function. The aim of this study was to investigate the volume of the triceps surae muscle in premature infants at three and six months old, adjusted for prematurity.

Methods
Using freehand 3D ultrasound, the bilateral volumes of the medial gastrocnemius (MG), lateral gastrocnemius (LG) and soleus (SOL) were assessed at three and six months corrected ages in seven infants. Scanning was performed by a single researcher, while two researchers independently digitised the images for volume calculation.

Results
The mean volumes of the MG, LG and SOL were 1.74 mL (1.34–2.23), 0.94 mL (0.82–1.06) and 4.15 mL (3.16–4.88) and 2.58 mL (2.14–3.12), 1.36 mL (1.23–1.64) and 5.14 mL (4.45–6.03) at three and six months respectively.

Conclusions
Muscle volume (MV) determines muscle strength and indicates muscle growth. Reduced growth of the triceps surae during infancy is associated with muscle weakness, motor delays and impairments. As the first study to measure MV in premature infants during their first six months of life, these results provide insight into the effects of prematurity on muscle growth and may assist in establishing a structural basis for milestone attainment, determining the aetiology of motor impairments, and facilitating detection of abnormal development.

Effects of maternal position on placental blood flow and restriction — an MRI study.

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Introduction
Supine sleep position is an independent, modifiable risk factor for late stillbirth, with a disproportionately larger impact on pregnancies with fetal growth restriction (FGR). Magnetic resonance imaging (MRI) has revealed that maternal supine position reduces oxygen transfer across the placenta in healthy pregnancies, but the impact in FGR is unknown.

Materials and Methods
12 women with FGR and 27 women with healthy pregnancies at 34–38 gestational weeks underwent MRI in both left lateral decubitus (LLD) and supine positions. Blood flow in the maternal internal iliac arteries and umbilical vein was assessed using phase-contrast MRI. A combined diffusion-relaxation imaging protocol (DECIDE) was used to measure placental perfusion and oxygenation.

Results
In FGR pregnancies, supine position caused a 20% reduction in total internal iliac arterial flow (p=0.01) and no significant change in umbilical venous flow (5%, p=0.55). During the LLD position, growth-restricted fetuses experienced a 14% lower oxygen saturation, 21% lower placental oxygen transfer, and 32% lower oxygen delivery to the fetus than in healthy pregnancies (p=0.004, p=0.001, and p=0.002, respectively). Supine position caused fetoplacental oxygen saturation to reduce from 65.6% to 61.3% (p=0.004) in healthy pregnancies, while in FGR, oxygen saturation was 56.7% in supine position and 54.5% in LLD (p=0.31).

Conclusion
This is the first study to non-invasively quantify the effect of maternal position on maternal and fetoplacental blood flow and oxygenation in FGR pregnancies. Growth-restricted fetuses are tolerating chronic hypoxaemia which may make them more vulnerable to the reduction in placental blood supply caused by supine position.

The impact of COVID-19 lockdown on Chinese care homes in New Zealand

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Introduction
In response to the coronavirus disease 2019 (COVID-19) pandemic, the New Zealand government implemented nationwide lockdowns in 2020 and 2021. Subsequently, visiting restrictions were enforced in care homes across the country. This placed an already vulnerable population at risk of functional and cognitive decline as well as psychological difficulties due to isolation. There is a lack of evidence on the experiences of vulnerable minority groups during the pandemic. The Chinese community is one of the fastest-growing ethnic groups in New Zealand and faces additional challenges, including language barriers, differing cultural beliefs, and COVID-19-related discrimination. This study aims to explore the experiences of Chinese care home residents in New Zealand during the COVID-19 lockdowns.

Materials and Methods
We performed semi-structured interviews with predominantly Chinese individuals (n=18) across two Chinese-run care homes in Auckland from April to June 2021. Participants included residents (n=6), family members (n=6), and facility staff (n=6). Interviews were conducted and transcribed in either English or Mandarin Chinese. We coded the interview transcripts and performed thematic analysis to synthesise overarching themes.

Results
The preliminary analysis suggests that lockdown led to difficulties for families in fulfilling the obligation of filial piety. Relationships between residents, family, and staff were enhanced by the use of technology. However, Chinese residents with dementia may face barriers to technology use.

Conclusions
The lockdown promoted a sense of unity among residential facilities included in the study. The necessary and rapid adoption of technology during lockdown was beneficial and strengthened relationships between residents, family, and staff.

Evaluation of post-operative outcomes with wearable sensors following robotic-assisted and conventional knee arthroplasty

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Introduction
Traditional patient-reported outcome measures (PROMs) have failed to highlight differences in outcome when comparing knee replacement designs and implantation techniques. Wearable sensors, such as inertial measurement units (IMUs), provide a cost-effective and portable solution for evaluation of post-operative outcome in combination with traditional PROMs. The aim of this study was to demonstrate the feasibility and reliability of using ankle-worn IMUs for remote patient monitoring (RPM) in the early post-operative period for patients with conventional total knee arthroplasty (TKA), unicompartmental knee arthroplasty (UKA), and robotic-assisted TKA (RA-TKA).

Materials and Methods
44 patients undergoing primary knee arthroplasty (19 RA-TKA, 17 TKA, and 8 UKA) for osteoarthritis were prospectively enrolled. Community-based RPM was performed pre-operatively, then weekly from post-operative weeks two to six using IMUs and PROMs. IMU-based metrics included: cumulative impact load, bone stimulus, and impact asymmetry. PROMs scores included: Oxford Knee Score (OKS), EuroQol Five-dimension with EuroQol visual analogue scale, and the Forgotten Joint Score.

Results
Preliminary results showed significant improvements in mean impact asymmetry by 67% (P=0.0055), bone stimulus by 41% (P<0.0001), and cumulative impact load by 121% (P=0.0349) between post-operative week two and six. The mean change scores for OKS were 7.5 (RA-TKA), 11.4 (TKA), and 11.2 (UKA) over the early post-operative period (P=0.144). Interestingly, PROMs scores (OKS) did not always reflect the same trend as IMU-derived limb usage between the different implantation techniques.

Conclusions
We present a quantitative, scalable, and low-maintenance RPM system using IMUs that can supplement traditional PROMs to provide a more holistic overview of post-operative recovery following knee arthroplasty. Furthermore, these data suggest a difference in the functional outcome of TKA and UKA patients that might be overlooked by using PROMs alone.

Qualitative and quantitative analysis of bacterial microcolonies in the tonsils of patients with tonsillar hyperplasia

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Introduction
Tonsillar hyperplasia (TH) can cause a spectrum of clinical presentations, ranging from obstructive sleep apnoea to recurrent tonsillitis. Current treatment options are limited to antibiotics and tonsillectomy. Recent studies have identified bacterial microcolonies in tonsillar tissue, but it is unclear whether they provoke an immune response.

Materials and Methods
Tonsils were collected from 25 paediatric and ten adult patients undergoing tonsillectomy for TH. Tissue sections with microcolonies were stained using fluorescent in-situ hybridization (FISH) targeting *Streptococcus* spp., *Haemophilus influenzae*, and *Fusobacterium* spp. Immunohistochemistry (IHC) was used to identify T and B lymphocytes. Microcolonies from adjacent tissue sections were dissected via laser. The bacterial load of these microcolonies will be determined using Droplet Digital PCR.

Results
In a preliminary dataset including 18 children and five adults, 91% of patients had at least one microcolony, with a mean of 4.3 identified per patient. *H. influenzae* was detected in 86% of microcolonies, followed by *Fusobacterium* spp. (43%) then *Streptococcus* spp. (33%). Bac-

teria-lined crypts were detected in 48% of patients, with *Streptococcus* probe-positive cells accounting for the greatest area. Lymphocytes were found co-localized with microcolonies within the crypt lumen in 81% of patients.

Conclusions
We have successfully developed a combined FISH-IHC protocol that allows simultaneous visualization of clinically relevant bacteria and immunocytes within tonsillar tissue. The consistent co-localization of lymphocytes with microcolonies does not match typical lymphocyte behaviour, and we hypothesize this may contribute to TH pathogenesis. Further studies comparing TH to normal tonsil tissue are required to determine the pathogenic effect.

Genetic relationships between alcohol consumption, serum urate and gout.

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Introduction
Alcohol consumption is a risk factor for elevated serum urate and gout. Several single-nucleotide polymorphisms (SNPs) have been associated with both alcohol consumption and serum urate or gout in separate genome-wide association studies (GWASs). The aim of this study was to systematically assess the relationships between these SNPs and alcohol consumption in influencing serum urate levels and gout.

Materials and Methods
Candidate SNPs were identified by comparing serum urate, gout, and alcohol consumption GWASs for overlap. These were tested for association with each phenotype among >450,000 European individuals from the UK Biobank using multivariable-adjusted regression analyses. Interaction terms were used to quantify SNP-alcohol interactions in influencing serum urate and gout. The nature of these relationships was evaluated using genotype-stratified or mediation analyses.

Results
35 SNPs were assessed. Most SNPs were associated with alcohol consumption and serum urate or gout in opposing directions. Only SNP rs11940694 at the *KLB* gene demonstrated consistent directions of association with each phenotype. The direct effect of *KLB* accounted for most of the total observed effect on serum urate and gout, with smaller, indirect effects mediated through alcohol consumption. SNPs at *LOC100507053* (rs11733695), *ADH1B* (rs1229984) and *ADH1C* (rs141973904) showed non-additive interactions with alcohol consumption for serum urate. *ADH1B* (rs1229984) additionally showed a non-additive interaction for gout.

Conclusion
The study findings are strongly indicative of pleiotropic effects at each SNP on serum urate levels and gout that are independent of their effects on alcohol consumption. Novel interactions were identified between *ADH1B* and alcohol intake to influence serum urate and gout.

Neuroinflammatory pathways in the midcingulate cortex in Huntington's disease.

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Introduction
Huntington's disease (HD) is a genetic neurodegenerative disorder that can result in motor, mood, and cognitive symptoms. HD pathophysiology has been linked to the process of neuroinflammation — the presence of inflammatory mediators and reactive glial cells in the brain parenchyma. Many signalling pathways likely interact to propagate neuroinflammation in the brain. Neuroinflammation is thought to cause cell loss, and in the anterior cingulate cortex, cell loss has been correlated with HD mood symptoms. The presence of neuroinflammation and cell loss in the HD midcingulate cortex (MCC) has not been investigated yet.

Materials and methods
This project investigated the presence of neuroinflammatory pathways in 14 HD and nine control post-mortem human MCC samples using next-generation sequencing. HD cases were split into the symptom profiles of motor, mood, and mixed. These data were analysed using Gene Ontology (GO) enrichment analysis. These results were validated with Nanostring nCounter gene assays and western blotting experiments.

Results
We have found 24 upregulated inflammation-related genes including Toll-like receptors, classical complement, AQP4, CHI3L1, P2X7R, S100A9, and SPP1 across HD cases. However, 13 inflammation-related markers, including chemokines, were downregulated. GO enrichment analysis reflected this, with multiple inflammation-related GO terms being upregulated and downregulated in all HD mood and motor groups. In mood HD cases, seven inflammation-related genes were upregulated and none were downregulated.

Conclusion
These results present a complex picture of potential inflammation priming in the HD MCC, rather than overt neuroinflammation.

Sleeve gastrectomy for weight loss impacts the gastric conduction system

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Introduction
While sleeve gastrectomy is an effective treatment for obesity and type 2 diabetes, it can be complicated by gastro-oesophageal reflux, nausea, and food intolerance. The stomach's greater curvature is removed, including the normal gastric pacemaker region. This thesis aimed to evaluate the impact of sleeve gastrectomy for weight loss on gastric electrophysiology using body surface gastric mapping (BSGM).

Method
Patients at least three months post sleeve gastrectomy were recruited (n=21) and compared to healthy controls (n=25). The patient group was recruited from all patients who had a sleeve gastrectomy at Auckland District Health Board in the five years prior to study commencement. The control group was taken from a previous study. Gastric myoelectrical activity was measured using BSGM comprising 64 electrodes on a conformable array and a wearable reader (Alimetry, Auckland). Recordings were a 30 minute fasted baseline and four hours post-meal. Gastrointestinal symptoms were measured and quality of life questionnaires were employed.

Results
Sleeve gastrectomy patients reported low symptom burdens. Gastric slow wave frequencies were consistently lower in patients compared to controls (mean 2.36 vs 2.93 cycles per minute, p<0.001). Gastric myoelectrical amplitude was lower in sleeve gastrectomy patients (19.1 vs 42.2 μV; p<0.001), although this difference may be due to patients having a greater body mass index causing signal attenuation. The power ratio was comparable (1.42 vs 1.71; p=0.85). Analysis of slow wave conduction direction patterns were not significantly different between groups (p=0.64).

Conclusion
This thesis suggests most patients following sleeve gastrectomy develop a stable gastric pacemaker at a lower intrinsic frequency. It did not indicate that the altered electrophysiology correlated with gastrointestinal symptoms. Application of BSGM in other and more symptomatic cohorts may provide new insights into the impact of alteration of normal gastric anatomy on gastric conduction.

Neuromelanin distribution with T1 mapping, histology and OCT

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Introduction
Neuromelanin-sensitive magnetic resonance imaging (MRI) has the potential to provide a means for early detection of neurological degenerative diseases such as Parkinson's disease. This project was aimed at developing a method of quantifying neuromelanin distribution to allow correlation with MRI T1 maps, as a proof of principle toward more generally using T1 MRI maps to determine in-vivo neuromelanin distribution. A good method to quantify neuromelanin is elusive, and this was our challenge.

Materials and Methods
Four neurologically normal ex-vivo human brains were obtained from the University of Auckland Human Anatomy Laboratory. These were extensively imaged using a variety of preparation techniques and MR imaging sequences including T1 mapping. This tissue was then carefully dissected for neuromelanin quantification. Several histological techniques were investigated. Optical coherence tomography (OCT), a technique which uses lasers to measure the attenuation of tissue, was investigated and optimised for neuromelanin quantification.

Results
Ex-vivo brains were successfully scanned with a variety of MRI sequences, providing quantitative maps. Histological quantification of neuromelanin with or without staining is semiquantitative. We have had some success in developing OCT as a method to quantify neuromelanin.

Conclusions
The absolute quantification of neuromelanin is difficult. Several histological methods can provide semiquantitative data. OCT seems to be a promising novel approach.

Optimising perioperative pain management: short-term inpatient use and long-term opioid prescribing following surgical procedures at Counties Manukau Health

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Introduction
Opioid analgesics are commonly prescribed following total knee arthroplasty (TKA) to manage pain and improve recovery. Prolonged opioid use following surgery can lead to short- and long-term adverse effects.

Methods
A series of retrospective cohort studies were completed to review current opioid prescribing practices at Counties Manukau Health following selected orthopaedic and general surgical procedures, including TKA. Various perioperative factors were investigated for associations with postoperative short- and long-term opioid use. These included inpatient consumption of sustained-release (SR) opioids and Quality of Recovery-15 scores (QoR-15) following TKA. Patients were stratified into two groups by inpatient use or avoidance of SR opioids, and three groups by QoR-15 score: low (<25th), medium (25–75th), and high (>75th percentile).

Results
SR opioid use was associated with increased inpatient and outpatient opioid use. Total inpatient opioid consumption between postoperative days zero and three was not significantly different between the SR groups (157.5 mg vs 167.5 mg oral morphine equivalent [OME], p=0.14). Dispensing of oxycodone was significantly greater in the SR opioid group at one and two months following discharge (p=0.01 and 0.03 respectively). Lower QoR-15 was associated with continued outpatient opioid dispensing. In the low QoR-15 group, 87.9% were dispensed either morphine or oxycodone within 30 days following discharge, compared to 56.3% in the high QoR-15 group (p=0.005).

Conclusion
Numerous patient-related and perioperative factors can impact on postoperative opioid use. The avoidance of SR opioids and the identification of patients with low quality of recovery may be important components of opioid-sparing postoperative pain management.

How good is the visually enhanced vestibulo-ocular reflex at identifying combined cerebellar and vestibular dysfunction

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Introduction
The visually enhanced vestibulo-ocular reflex (VVOR) can help iden-

tify combined cerebellar ataxia and bilateral vestibulopathy (CABV). The participant's head is passively rotated while they are instructed to fixate on a stationary target. A reduced eye movement response indicates a positive (abnormal) result. However, there is yet to be a verified method for conducting the VVOR. The sensitivity and specificity of the test for neurological disorders has not been determined either.

Materials and methods
Testing was conducted at five frequencies of rotation while gain (ratio of eye to head movement) was measured using video-oculographic goggles. Four groups of participants were tested: healthy controls, cerebellar ataxia (CA), bilateral vestibulopathy (BV), and CABV. Results from the patient groups were compared with the 95% reference range of healthy controls.

Results
Use of a metronome achieved good control of the head rotation frequency. Control group analysis showed no effect of frequency ($p=0.146$) nor age ($p=0.981$) on VVOR gain. Compared with controls, gains of CABV participants were decreased at all frequencies. In the CA and BV groups, gains were mostly within the normal range. Some BV patients exhibited a decreased gain at frequencies above 0.50 Hz, but never over the lower frequencies.

Conclusion
The metronome is a validated tool for controlling the frequency of manual head rotation. The gain findings are consistent with the theoretical framework that considers VVOR as an additive process between vestibular and cerebellar eye movements. An abnormal VVOR at or below 0.5 Hz appears to be a specific indicator of CABV.

Use of Computational Fluid Dynamics in Assessment of Aortic Valve Disease

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Introduction
Aortic stenosis (AS) is one of the most prevalent types of valvular heart disease, costing more than $30 million annually in New Zealand. AS is an active process whereby the aortic valve becomes calcified, stiffening the leaflets, which impairs its ability to open normally. It is believed that the pathophysiology of AS is triggered by mechanical and adverse haemodynamic shear stress.

This study piloted the use of computational fluid dynamics (CFD) — a branch of applied mathematics that specialises in modelling fluid movement — to simulate these stresses. We aimed to develop an analysis pipeline for clinical use, whereby cardiac magnetic resonance imaging (MRI) images could be used with CFD to generate more patient-specific aortic valve shear stress results.

Methods
The complex equations governing fluid dynamics can be solved using programs called CFD solvers. We used cardiac MRI images to provide the valve geometry and velocity inlet boundary conditions to enable estimation of the aortic valve shear stress.

Results and conclusions
This study compared a general-purpose CFD solver, "ANSYS," and a cardiovascular-specific solver, "CRIMSON." We successfully generated aortic valve shear stress measurements for three patients and succeeded in generating a pipeline by which shear stress measurements can be obtained from cardiac MRI. However, the pipeline was time-consuming, and the results generated from our patients were highly variable. We conclude that the current pipeline is unlikely to be feasible for clinical use for patient-specific aortic valve shear stress estimation. Future research and numerous improvements are required before this pipeline can be clinically applied.

Modelling the Effect of Inflammation on Chitinase 3-like 1 Expression.

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Introduction
Chitinase 3-like 1 (CHI3L1) is a protein believed to play a role in activating immune cells, tissue remodelling, and blocking cell death. CHI3L1 is increased in several inflammatory conditions, such as inflammatory bowel disease (IBD). Accordingly, measurement of CHI3L1 levels shows potential as a novel biomarker, or possible drug target. However, further research is required to determine the role of CHI3L1 in inflammation and the underlying mechanisms involved.

Methods
Caco-2 (epithelial) and THP-1 (macrophage) cell lines were cultured for 48 hours before stimulating with TNF-α, IL-1β and IL-6 at 10 or 100 ng/ml for one, three, six, and 24 hours. Changes in CHI3L1 gene and protein expression were measured by real-time PCR and ELISA, respectively. As a control, the expression of IL-8 (gene and protein) was measured in the same samples. Treated cells were immunostained to visualize whether CHI3L1 expression is cell surface-associated and/or cytoplasmic.

Results
In Caco-2 cells, CHI3L1 gene expression increased after three hours of exposure to IL-1β and TNF-α, but not IL-6, when compared to the control. Surprisingly, this was not followed by a measurable increase in CHI3L1 levels in the same cell culture supernatants or cell lysates. Measurement of IL-8 gene expression and protein levels confirmed cell responsiveness to the stimuli. Preliminary results from THP-1 cells show higher CHI3L1 protein levels compared to the Caco-2 cells. The immunostaining technique used failed to detect CHI3L1 protein in Caco-2 cells, and demonstrated CHI3L1 is predominantly cell surface-associated in THP-1 cells. Further optimization of methods may be required to confirm these findings.

Conclusion
These results suggest that epithelial cells may not be the primary source of the high levels of CHI3L1 reported in individuals with IBD. Instead, it remains a possibility that macrophages responding to proinflammatory cytokines may instead contribute to this response.

Lung Function and Cardiovascular Risk at Age 45 in the Dunedin Multidisciplinary Health and Development Study

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Background
This study aimed to investigate associations between lung function and cardiovascular risk in a general population sample of men and women aged 45.

Methods
The relationship between lung function and cardiovascular risk score was assessed using linear regression among 863 participants of the Dunedin Multidisciplinary Health and Development Study cohort. Lung function was determined by spirometry, body plethysmography, gas diffusion tests, and airway conductance. Log-transformed cardiovascular risk scores determined using two multivariable cardiovascular risk algorithms (Predicting Risk of Death in Cardiac Disease Tool (PREDICT) and Framingham Risk Score (FRS)) were used as the dependent variables. The association was investigated cross-sectionally and longitudinally using changes in lung function between ages 32–45 as the predictor.

Results
Cross-sectionally, low lung volumes were associated with a greater cardiovascular risk score (both log-PREDICT and log-FRS). This association was stronger in women than in men. The association was independent of body mass index (BMI) and smoking history, and was present in never smokers. Associations were not found between cardiovascular risk and measures of airway function (forced expiratory volume over one second/forced vital capacity ratio and specific airway conductance (sGaw)) or gas transfer (diffusing capacity for carbon monoxide/alveolar ventilation). Similar associations were observed in the longitudinal analyses between changes in lung function between ages 32–45 and cardiovascular risk score at age 45.

Conclusion
Low lung volumes at age 45 and accelerated pulmonary function decline between ages 32–45 are associated with a higher estimated cardiovascular risk score. This association is stronger in women, is independent of smoking and BMI, and is present in those who have never smoked.