New additions to publications by NALHN Staff 15/11/18

Dr Rajinder Singh, Department of Gastroenterology, who co-authored the attached article which was published in the *Gut*. (Paper 1)

Dr K. Oliver Schubert, Mental Health Services, who is a joint author of the attached paper which was published in the journal, *Journal of Psychiatric Research*. (Paper 2)

Dr Gus Dekker, Dr Jemma Wohling, Dr Nicole Edge & Dr David Pena-Leal, Department of Obstetrics and Gynaecology, who co-authored the attached article which was published in the *Australian & New Zealand Journal of Obstetrics & Gynaecology*. (Paper 3)

Dr Gus Dekker and Dr Bernd Froessler, Department of Obstetrics and Gynaecology, who co-authored the attached Letter which was published in the *Archives of Gynecology & Obstetrics*. (Paper 4)

Dr Vishwanath Biradar, Department of Intensive Care, who co-authored the attached article which was published in the *Australian Critical Care* (Paper 5)

The papers are now on display in the Library (Level 2). Please let us know if you or a colleague have had a paper published, and we will add it to our collection and email it out.

**Paper 1**

*An Asian consensus on standards of diagnostic upper endoscopy for neoplasia*

*Gut* (2018); Nov 12

**Abstract:**

**Background:**
This is a consensus developed by a group of expert endoscopists aiming to standardise the preparation, process and endoscopic procedural steps for diagnosis of early upper gastrointestinal (GI) cancers.

**Methods:**
The Delphi method was used to develop consensus statements through identification of clinical questions on diagnostic endoscopy. Three consensus meetings were conducted to consolidate the statements and voting. We conducted a systematic literature search on evidence for each statement. The statements were presented in the second consensus meeting and revised according to comments. The final voting was conducted at the third consensus meeting on the level of evidence and agreement.

**Results:**
Risk stratification should be conducted before endoscopy and high risk endoscopic findings should raise an index of suspicion. The presence of premalignant mucosal changes should be documented and use of sedation is recommended to enhance detection of superficial upper GI neoplasms. The use of antispasmodics and mucolytics enhanced visualisation of the upper GI tract, and systematic endoscopic mapping should be conducted to improve detection. Sufficient examination time and structured training on diagnosis improves detection. Image enhanced endoscopy in addition to white light imaging improves detection of superficial upper GI cancer. Magnifying endoscopy with narrow-band imaging is recommended for characterisation of upper GI superficial neoplasms. Endoscopic characterisation can avoid unnecessary biopsy.

**Conclusions:**
This consensus provides guidance for the performance of endoscopic diagnosis and characterisation for early gastric and oesophageal neoplasia based on the evidence. This will enhance the quality of endoscopic diagnosis and improve detection of early upper GI cancers.

**Paper 2**

*Co-expression network analysis of peripheral blood transcriptome identifies dysregulated protein processing in endoplasmic reticulum and immune response in recurrent MDD in older adults.*


**Abstract:**
The molecular factors involved in the pathophysiology of major depressive disorder (MDD) remain poorly understood. One approach to examine the molecular basis of MDD is co-expression network analysis, which facilitates the examination of complex interactions between expression levels of individual genes and how they influence biological
pathways affected in MDD. Here, we applied an unsupervised gene-network based approach to a prospective experimental design using microarray genome-wide gene expression from the peripheral whole blood of older adults. We utilised the Sydney Memory and Ageing Study (sMAS, N=521) and the Older Australian Twins Study (OATS, N=186) as discovery and replication cohorts, respectively. We constructed networks using Weighted Gene Co-expression Network Analysis (WGCNA), and correlated identified modules with four subtypes of depression: single episode, current, recurrent, and lifetime MDD. Four modules of highly co-expressed genes were associated with recurrent MDD (N=27) in our discovery cohort (FDR<0.2), with no significant findings for a single episode, current or lifetime MDD. Functional characterisation of these modules revealed a complex interplay between dysregulated protein processing in the endoplasmic reticulum (ER), and innate and adaptive immune response signalling, with possible involvement of pathogen-related pathways. We were underpowered to replicate findings at the network level in an independent cohort (OATS), however; we found a significant overlap for 9 individual genes with similar co-expression and dysregulation patterns associated with recurrent MDD in both cohorts. Overall, our findings support other reports on dysregulated immune response and protein processing in the ER in MDD and provide novel insights into the pathophysiology of depression.

**Paper 3**
Clinical and financial evaluation of carbetocin as postpartum haemorrhage prophylaxis at caesarean section: A retrospective cohort study.

*Australian & New Zealand Journal of Obstetrics & Gynaecology.* 2018 Nov 09

**Background:**
The long-acting oxytocic agent; carbetocin, has been consistently shown to reduce the need for additional uterotonics at caesarean section, but not postpartum haemorrhage (PPH). While promising, current evidence is limited by heterogenicity in study design and findings.

**Methods:**
A retrospective cohort study was undertaken of all singleton caesarean sections at a public tertiary hospital from 2008 to 2010 (n = 2499). From 1 January 2008 to 24 March 2009 all women received prophylactic oxytocin 5-10 units slow push intravenously at delivery, after which all patients received 100 mug intravenous carbetocin. Outcomes were PPH (>=1000 mL) and the requirement of secondary uterotonic treatment. A post hoc cost analysis was also performed.

**Results:**
A total of 1467 and 1024 patients received carbetocin and oxytocin, respectively. Incidence of PPH >=1000 mL was 7.8% for carbetocin compared to 9.7% for oxytocin (odds ratio (OR) 0.79, 95% CI 0.59-1.05). Moderate blood loss >500 mL was significantly reduced with carbetocin; occurring in 27.3% versus 39.4% (OR 0.57, 95% CI 0.49-0.68). There was a 20.0% reduction in secondary uterotonic treatment with carbetocin (OR 0.42, 95% CI 0.35-0.49). Average drug costs were lower with oxytocin at $4.74 versus $36.42/patient. However, the 1.9% reduction in PPH with carbetocin resulted in a $63.46 reduction in cost per patient, with a cost-effectiveness ratio of $1667 to prevent one case of PPH >=1000 mL.

**Conclusions:**
Carbetocin reduced moderate blood loss >500 mL, but not PPH >=1000 mL. Carbetocin conferred a 20% reduction in secondary uterotonic treatment, as well as lowering direct medical costs.

**Paper 4**
Response to letter to the Editor: Treatment of iron deficiency and iron deficiency anemia with intravenous ferric carboxymaltose in pregnancy.


**Paper 5**
Opinions and practices of blood glucose control in critically ill patients with pre-existing type 2 diabetes in Australian and New Zealand intensive care units.

*Australian Critical Care.* 2018 Oct 19.

**Abstract:**

**Background:**
Approximately 9000 patients with type-2 diabetes mellitus (T2DM) are admitted to an intensive care unit (ICU) in Australia and New Zealand annually. For these patients, recent exploratory data suggest that targeting a more liberal blood glucose range during ICU admission may be safe and potentially beneficial. However, the current approach to blood glucose management of patients with T2DM in Australia and New Zealand ICUs is not well described, and there is uncertainty about clinician equipoise for trials of liberal glycaemic control in these patients.
**Methods:**
An online questionnaire of Australia and New Zealand intensivists conducted in July-September 2016.

**Results:**
Seventy-one intensivists responded. Forty-five (63%) used a basic nomogram to titrate insulin. Sixty-six (93%) reported that insulin was commenced at blood glucose concentrations >10 mmol/L and titrated to achieve a blood glucose concentration between 6.0 and 10.0 mmol/L. A majority of respondents (75%) indicated that there was insufficient evidence to define optimal blood glucose targets in patients with T2DM, and 59 (83%) were prepared to enrol such patients in a clinical trial to evaluate a more liberal approach.

**Conclusions:**
A majority of respondents were uncertain about the optimal blood glucose target range for patients with T2DM and would enrol such patients in a comparative trial of conventional versus liberal blood glucose control.