Deep neuromuscular block reduces intra-abdominal pressure requirements during laparoscopic cholecystectomy: a prospective observational study

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Clinical trials registration
ANZ Clinical Trials Registry No ACTRN12612000961842.
URL: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=362991.

Ethics approval
Local Human Research Ethics Committee (TQEH/LMH/MH) protocol approval number: HREC/12/TQEHLMH/130.

Conflicts of interest
R.M.V.W. consulted for MSD and T.L. consulted for and received a small research grant from MSD (not related to this study). For the remaining authors, none were declared.

Funding
This work was supported by the Department of Anaesthesia of The Queen Elizabeth Hospital, Woodville South, South Australia, Australia.

Submitted 19 January 2015; accepted 20 January 2015; submission 4 December 2014.

Citation
Van Wijk RM, Watts RW, Ledowski T, Trochsler M, Moran JL and Arenas GWN. Deep neuromuscular block reduces intra-abdominal pressure requirements during laparoscopic cholecystectomy: a prospective observational study. Acta Anaesthesiologica Scandinavica 2015

doi: 10.1111/aas.12491

Background: Laparoscopic surgery causes specific post-operative discomfort and intraoperative cardiovascular, pulmonary, and splanchnic changes. The CO_2 pneumoperitoneum-related intra-abdominal pressure (IAP) remains one of the main drivers of these changes. We investigated the influence of deep neuromuscular blockade (NMB) on IAP and surgical conditions.

Methods: This is an open prospective single-subject design study in 20 patients (14 female/6 male) undergoing laparoscopic cholecystectomy. Inclusion criteria were 18 years or older, and American Society of Anesthesiologists classification 1 to 3. Under a standardised anaesthesia, lowest IAP providing adequate surgical conditions was assessed without NMB and with deep NMB [post-tetanic count (PTC) < 2] with rocuronium. The differences between IAP allowing for an adequate surgical field before and after administration of rocuronium were determined, as were effects of patient gender, age, and body mass index.

Results: Mean IAP without NMB was 12.75 (standard deviation 4.49) mmHg. Immediately after achieving a deep NMB, this was 7.20 (2.51). This pressure difference of 5.55 mmHg (5.08, $P < 0.001$) dropped to 3.00 mmHg (4.30, $P < 0.01$) after 15 min. Higher IAP differences were found in women compared with men. A modest inverse relationship was found between pressure difference and age.

Conclusions: We found an almost 25% lower IAP after a deep NMB compared with no block in laparoscopic cholecystectomy. Younger and female patients appear to benefit more from deep neuromuscular blockade to reduce IAP.

Acta Anaesthesiologica Scandinavica
AN INTERNATIONAL JOURNAL OF ANAESTHESIOLOGY AND INTENSIVE CARE, PAIN AND EMERGENCY MEDICINE

Editorial comment: what this article tell us
In this observational study of patients undergoing laparoscopic cholecystectomy, establishing a deep neuromuscular block allowed a significant reduction in intra-abdominal pressure as titrated by the surgeon to the lowest pressure allowing acceptable surgical exposure.

Laparoscopic surgery has become more efficient and safer over the years due to reduction in intra-abdominal pressure (IAP), modifications in surgical technique, selection of type of insufflation gas, and improvements in anaesthetic management. Despite this, laparoscopic surgery continues to cause specific pathophysiological effects, such as cardiovascular, pulmonary, and splanchnic perfusion changes, where IAP appears to be the primary determinant.[1–3] Lowering insufflation pressures may also result in a reduction in post-operative pain (including shoulder tip pain) and a better quality of life 5 days after surgery.[4–7]

Commonly IAP is maintained at around 12 mmHg for most laparoscopic procedures. In order to keep intraperitoneal pressures low, neuromuscular blocking agents (NMBA) are frequently used. However, the evidence around the dimension of the impact of muscle relaxation on the abdominal insufflation pressures is sparse.

Neuromuscular blockade (NMB) has recently been shown to improve surgical working conditions significantly, although these trials did not focus on IAP reductions.[8,9] Also, in a recent study, deep NMB was associated with marginally better surgical conditions compared with moderate NMB during low-pressure pneumoperitoneum in laparoscopic cholecystectomy.[10]

It was the aim of the current project to (1) investigate the difference between achievable IAP reduction with deep muscle relaxation, as defined by a post-tetanic count of less than 2 (PTC < 2),[11] compared with no NMB and (2) investigate which patients may benefit most from this. Data from this study are meant to assist in the design and power assessment of an appropriately sample-sized prospective future study.

Methods

Ethical approval for this study (Ethics Committee reference HREC/12/TQEHLMH/130) was provided by the Human Research Ethics Committee of The Queen Elizabeth Hospital, Woodville South, South Australia (Chairperson A/Prof Timothy Mathew) on 23 November 2012. Site-specific authorisation (SSA/12/TQEHLMH/133) was also obtained. The study was registered with the Australia New Zealand Clinical Trials Registry (Ref: ACTRN12612000961842). A single-subject design was chosen, where essentially each patient acted as their own control, to limit the number of patients required for this study (see flowchart in Fig. 1). It also eliminated the need for any stratification. After obtaining written informed consent, 20 patients undergoing laparoscopic gallbladder surgery were recruited. Inclusion criteria were 18 years or older and American Society of Anesthesiologists classification 1 to 3. Exclusion criteria included lack of English language skills, psychiatric or mental issues precluding proper informed consent, pregnancy, muscle relaxant medications, and/or neuromuscular disease.

Quantitative neuromuscular transmission (NMT) monitoring was applied before induction. Although the international guidelines for clinical research in studies of NMBAs were followed as much as possible,[12] the quantitative acceleromyography NMT monitor we had available was rather limited (Stimpod NMS450; Xavant Technology Pty Ltd; Silverton, Pretoria, South Africa). Proper calibration of the signal was not possible. We used a current of 50–60 mA with a pulse width of 0.02 ms. The ulnar nerve/adductor pollicis muscle was used every time. Effort was put into correct positioning of the arm/hand to ensure a free movement for the thumb. Clear PTC and train of four (TOF) ratio stimulus readings were obtained in all patients. Patients received a standardised anaesthesia with induction with fentanyl (2 μg/kg lean body mass), propofol (titrated to effect), and succinylcholine (1.2 mg/kg). Depth of anaesthesia was monitored with bispectral index analysis (BIS; Covidien; Boulder, CO, USA; range 40 to 60). Following intubation sevoflurane was titrated to the BIS and fentanyl was titrated to effect. Volume-controlled ventilation, adjusted to an end-tidal CO_2 target of 35–40 mmHg, was used with 50% oxygen in air, an inspiration/expiration

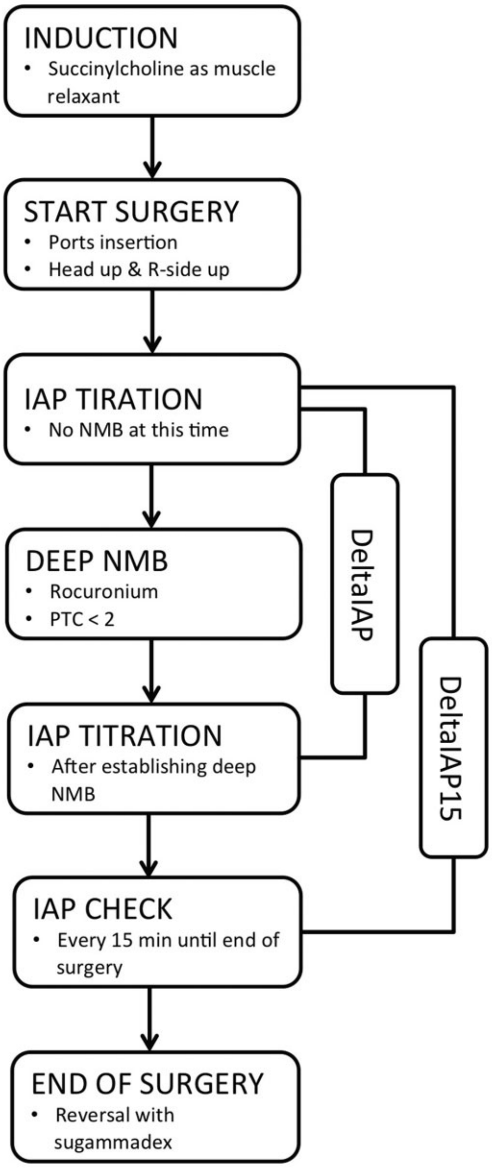

Fig. 1. Flowchart. deltaIAP, IAP difference between no NMB and immediately after obtaining a deep NMB; deltaIAP15, IAP difference between no NMB and 15 min after obtaining a deep NMB; IAP, intra-abdominal pressure; NMB, neuromuscular blockade; PTC, post-tetanic count.

ratio of 1 : 1.5, positive end-expiratory pressure of 5 cm H_2O, and a respiratory rate of 10 to 15/min. After the succinylcholine had worn off, evaluated by visual assessment of the TOF twitches, and after obtaining a head up and right side tilted up position (which was maintained during the surgery), the surgeon titrated to the lowest IAP allowing acceptable surgical exposure, starting at 14 mmHg after placement of all ports (ConMed Linvatec 40L Insufflation System; ConMed Linvatec, Largo, FL, USA) and lowering the pressure setting with 2 mmHg every 2 min, and increasing with steps of 1 mmHg should the surgeon regard the surgical exposure as not acceptable. Subsequently, rocuronium 0.5 mg/kg was administered. Once the target of a PTC < 2 was reached, the surgeon attempted to further reduce the IAP from the earlier achieved setting (while there was no NMB), using the same algorithm as described above, again titrating to the lowest IAP allowing acceptable surgical exposure. During the surgery, the target of PTC < 2 was maintained through titration of a rocuronium infusion starting at the initial rate of 0.5 mg/kg/h. IAP was registered at 15-min intervals for the duration of the surgery. At any time during the laparoscopic procedure, the surgeon could request an increase in IAP. At the end of surgery, the NMB was reversed using sugammadex and adequate reversal was confirmed by a TOF ratio > 0.9. All surgeons were experienced in laparoscopic surgery and in their final year of training or staff specialists. They were not blinded during the study.

As the primary outcome measure, the difference (deltaIAP) between the lowest acceptable IAPs before and after administration of rocuronium was determined. This was repeated at 15-min time intervals until the end of surgery. As secondary outcome measures the effects of patient gender, age, and body mass index (BMI) on deltaIAP immediately after establishing a deep block and after 15 min were determined.

Data were analysed using SPSS (v20; IBM, Armonk, NY, USA). Data were tested for normal distribution using the Kolmogorov–Smirnov and the Shapiro–Wilk test. Due to nonparametric distribution of the IAP data immediately after achieving deep NMB, pressure values before and after deep NMB were tested with the Wilcoxon signed-rank test. Data showing normal distribution were analysed with the paired or independent samples *t*-test as appropriate. Data are displayed as mean (standard deviation). The Pearson's correlation coefficients were calculated for the relationships between the pressure differences, and age and BMI. No formal sample size calculation was performed as this study was planned to quantify the difference between the

Table 1 Patient characteristics.

	Patients ($n = 20$)
Gender (female/male)	14/6
Age (years)	49.2 (18.0)
Height (cm)	166 (9)
Weight (kg)	78.1 (21.5)
BMI (kg/m^2)	28.5 (5.9)
ASA* (I/II/III)	4/13/3
Previous abdominal surgery (Y/N)	2/18
Emergency/Elective	6/14
Acute abdominal inflammation (Y/N)	6/14

Data are mean (SD) or absolute numbers. *Physical status according to the American Society of Anesthesiologists.

lowest acceptable IAPs before and after the implementation of a deep block with rocuronium.

Results

The 20 patients were recruited between December 2012 and October 2013 (Table 1). All procedures could be completed laparoscopically. Mean required IAP for adequate surgical exposure after initial full recovery post-succinylcholine and before deep neuromuscular block with rocuronium was 12.75 (4.49) mmHg. Immediately after achieving a deep neuromuscular block (deep NMB) with rocuronium, this could be reduced by 5.55 mmHg (5.08, $P < 0.001$). After 15 min, almost invariably this difference dropped to 3.00 mmHg (4.30, $P < 0.01$). Subsequently the IAP difference seemed to be maintained, although based on an increasingly reduced number of patients due to progressive completion of the surgery (Table 2). In regards to the secondary outcomes (Fig. 2), higher values of the difference between before and after deep NMB pressures were found in women compared with men, but were only statistically significant 15 min after establishing deep NMB (Fig. 2A–B). A moderate inverse relationship was found between both pressure differences and age (Fig. 2C–D). Despite being statistically significant, in view of the correlation coefficients, hardly any relationship was found between both pressure differences and BMI (Fig. 2E–F). Given the relatively low numbers, further multivariate analysis was deemed inappropriate.

Table 2 Primary outcomes.

	n	IAP (mmHg)	DeltaIAP (mmHg)
No NMB	20	12.75 (4.49)	
Deep NMB at T0	20	7.20 (2.51)	5.55 (5.08)‡
Deep NMB at T15	20	9.75 (2.69)	3.00 (4.30)§
Deep NMB at T30	16*	10.38 (2.90)	3.38 (3.77)§
Deep NMB at T45	11†	11.00 (3.26)	2.91 (4.25)#

Intra-abdominal pressure (IAP) and pressure difference (DeltaIAP) at time of no neuromuscular block (No NMB; T4/T1 > 0.9), and 0, 15, 30 and 45 min after establishing deep neuromuscular block (Deep NMB at resp. T0, T15, T30 and T45; PTC < 2). Data presented as mean (SD). *No data on four patients due to end of surgery; related No NMB IAP value of 13.75 (4.30). †No data on nine patients due to end of surgery; related No NMB IAP value of 13.91 (4.66). Statistically significant differences indicated as ‡$P < 0.001$, §$P < 0.01$ and #$P < 0.05$.

Discussion

We found a significant reduction in surgically required IAP after deep NMB with rocuronium. Though the initial reduction of required IAP was dramatic (40%), this effect decreased to approximately 23% in the early time course of surgery, correlating with the almost consistent request by the surgeon to slightly increase IAP within 15 min after initial paralysis. It is not clear why this reduction in effect occurred during the first 15 min of establishing deep NMB, despite maintaining a PTC < 2. It could be that during progression of surgery, a better exposure is required compared with the start. It is unclear how a pneumoperitoneum could result in a reduction in compliance over time as there appears to be a linear pressure volume relationship in most patients.[13] Notably there were no position changes during this period that could account for the reduction in deltaIAP.[14]

Our result is consistent with recent findings of improved surgical conditions during deep neuromuscular block in laparoscopic retroperitoneal and hysterectomy surgery.[8,9]

It is not obvious to what extend our findings can be extrapolated to a moderate NMB, but a recent study found better surgical conditions in deep compared with moderate NMB.[8] A recently published randomized controlled trial found that surgical conditions in low-pressure (< 12 mmHg) laparoscopic surgery were marginally better with deep compared with moderate NMB.[10]

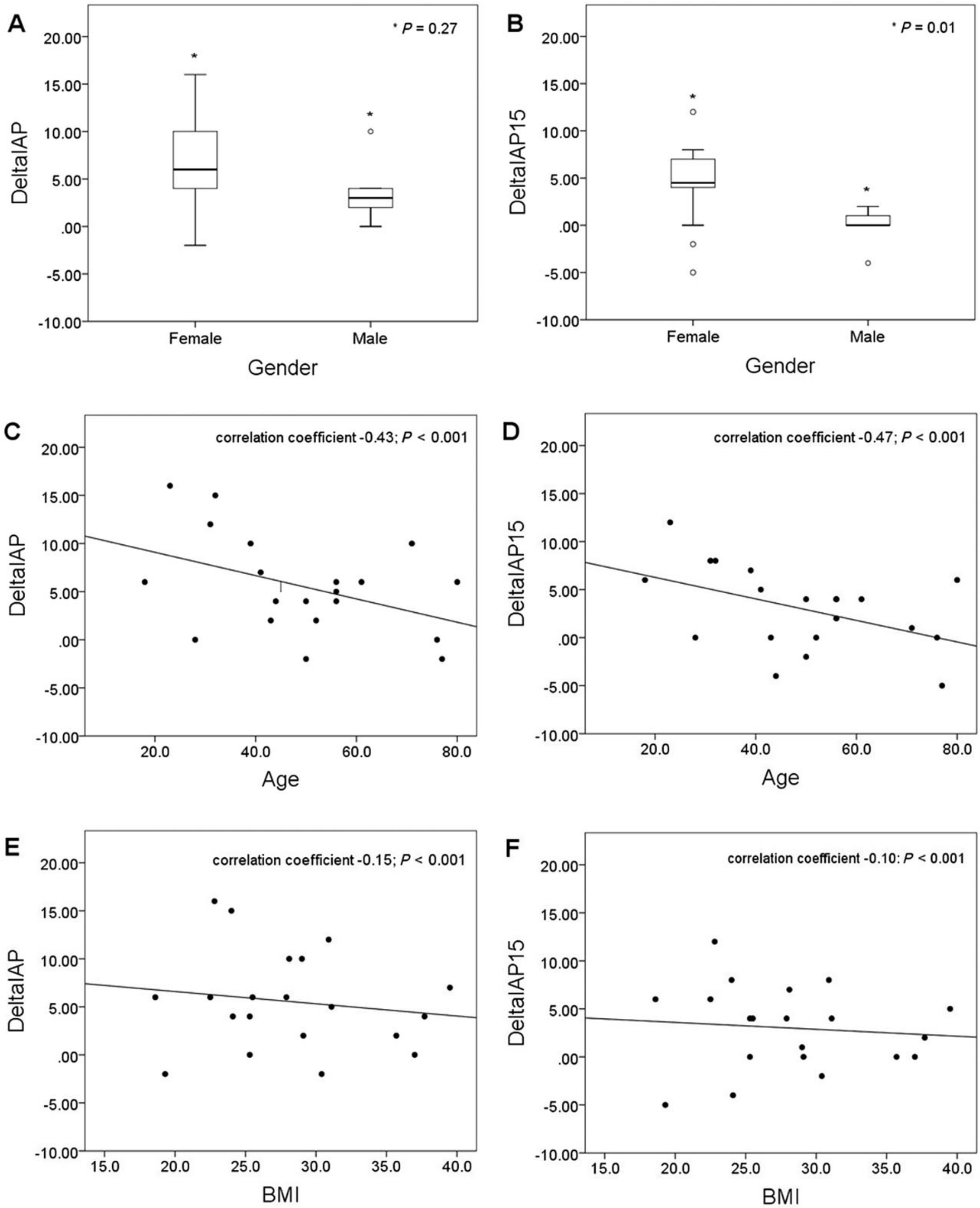

Fig. 2. Effects of patient characteristics on the difference in intra-abdominal pressure between no neuromuscular block, immediately after achieving deep neuromuscular blockade (deltaIAP) and 15 min later (deltaIAP15). (A) and (B) show effects of gender (independent samples *t*-test); (C) and (D) show effects of age (paired samples *t*-test); and (E) and (F) show effects of body mass index (BMI; paired samples *t*-test).

Our findings are not consistent with an earlier study by Williams et al. in laparoscopic cholecystectomy comparing spontaneously breathing patients to patients receiving NMBA.[15] They surprisingly found similar qualities of surgical field in both groups with IAPs of 15 mmHg. This may be due to the fact that their target IAP was relatively high with a mean patient BMI of 25.2 kg/m^2, although the fact that the surgeons were not blinded could also have played a role. We found that a mean IAP of 12.75 mmHg was required in patients without NMB with a higher mean BMI of 28.5 kg/m^2. Therefore, a target IAP of 15 mmHg in a patient group of relatively lower BMI would have likely provided a good surgical exposure for all their patients. We would like to point out that 15 mmHg is considered less safe compared with lower pressure settings.[6]

Our patient population had a male/female ratio of 3 : 7. Seventy-five per cent of patients were overweight or obese. This is consistent with known risk factors for gallstones.

The gender difference found in regards to deltaIAP may be partly based on difference in body habitus, with men tending towards centripetal obesity (android or 'apple'; including intraperitoneal fat) and women towards centrifugal (gynaecoid or 'pear') obesity. Centripetal obesity will likely lower abdominal wall compliance.[16,17]

The age-dependent differences may be due to diminishing abdominal wall muscle tissue and related decreased abdominal wall compliance at more advanced age.

The very weak correlation with BMI shows that only about 1–2% of the variance is explained by this. Increased BMI may only occasionally lead to a slight reduction in deltaIAP, likely relating to the increased abdominal wall and intraperitoneal fat ratio affecting abdominal wall compliance. Obviously, neuromuscular block will not influence this.[16] Based on this, one may hypothesize that deep NMB in some cases may not be able to facilitate a better surgical exposure in the morbidly obese patient to the same extend as in patients with a lower BMI.

Pressures above 15 mmHg lead to increased systemic and pulmonary vascular resistance and a reduction in cardiac index and need to be avoided if possible.[6] A target IAP below 12 mmHg is associated with further improved outcomes in regards to post-operative discomfort.[7] Lowering insufflation pressures even more leads to a further reduction in post-operative pain (including shoulder tip pain) and a better quality of life 5 days after surgery.[5,7] Given our finding of a mean IAP requirement of 12.75 mmHg in patients without NMB, this appears to indicate a need for NMB in most of our patients. We have also shown that a deep NMB can realistically improve this with a reduction in IAP of 23%. In view of the significant variability found in required IAP, even with deep NMB, it is clear that any target IAP should be viewed as flexible. The main goal remains adequate surgical exposure. This will be different in each patient and for each type of procedure. Determining factors will be the procedure-type dependent extent of the relevant surgical field, the patient habitus, position, and the abdominal wall compliance.[14,18] Obviously due diligence is required when using a deep NMB to ensure adequate reversal at the end of the procedure.

The power of our study is limited due to the small size and open design, with different (albeit relatively experienced) surgeons involved. However, notwithstanding inter-patient variability in the estimates of adequate surgical exposure, due to the single-subject design, within each patient, the same surgeon assessed the quality of the surgical field both before and after deep NMB exposures and communicated the requirements in regards to the IAP settings. In hindsight, the surgeons should have been blinded.

In conclusion, despite these limitations, we found significantly lower IAPs after the provision of a deep neuromuscular block compared with no block in laparoscopic cholecystectomy in this study that was limited to 20 patients. Younger and female patients appear to benefit more from deep neuromuscular paralysis to reduce IAP during laparoscopic surgery.

Acknowledgements

Assistance with the article: We acknowledge the support of surgical, anaesthetic, and administrative staff at The Queen Elizabeth Hospital during this study.

Authors' contributions

R. M. V. W.: Study design, acquisition, analysis and interpretation of data, drafting and revision of paper.

R. W. W.: Study design, acquisition and interpretation of data, revision of paper.
T. L.: Study design, analysis and interpretation of data, revision of paper.
M. T.: Study design, acquisition of data, revision of paper.
J. L. M.: Study design, analysis and interpretation of data, revision of paper.
G. W. N. A.: Acquisition of data, revision of paper.

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