Universitat Autònoma de Barcelona

Analysis of applications and outcomes of minimally invasive surgical techniques in wildlife

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Doctoral Thesis 2017

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This work is dedicated to all the wondrous wildlife patients that I have had the remarkable privilege of working with, and to my amazing wife Yolanda and our beautiful children Nuria and Luca, who have had the patience and understanding to let me do this

“People have forgotten this truth," the fox said. "But you mustn’t forget it. You become responsible forever for what you’ve tamed.”

- Antoine de Saint-Exupéry, The Little Prince

ACKNOWLEDGEMENTS

My most sincere and heartfelt thanks go to my supervisors Laila Darwich Soliva and Rafael López for all their kindness, encouragement, help, support, and perhaps most of their patience with me. Thanks also to my wife Yolanda for her support, and carrying an unfair share of the household burden and care of our children during this project.

Many thanks to Nic Masters, Michelle Barrows, Jonathan Cracknell, Simon Girling, and Iain Valentine for sharing the zoological collections surgical data with me for this study. Many thanks to Donna Brown and Eve Smaller for their administrative help. Many thanks to Peter Sedman for his advice and direction, and the many human and veterinary surgeon colleagues who have shared experiences and information with me, and taught me much of what I have used in this project.

To you all, my sincere thanks.

"UNLESS someone like you
cares a whole lot,
nothing is going to get better.
It's not."

- Dr Seuss, the Lorax

SUMMARY

Minimally invasive surgery (MIS) is currently regarded as the gold standard for many human surgical procedures, and has also been demonstrated to benefit domestic animal veterinary patients for several procedures. Many of the benefits of MIS, well established in the evidence base for human surgery, could have particular application in wildlife veterinary surgical patients, but despite the fact that the first non-domestic animal MIS procedures were performed almost 50 years ago, demonstration of its advantages over open surgery remains fragmented and mainly low-level evidence.

The first objective of this doctoral thesis was to establish the quality and scope of published peer-reviewed literature abstracts forming the current evidence base for all types of surgery in wild animals, as well as establish published complication rates. A total of 635 abstracts, containing a total of 6582 individual animals were included. The majority were single case reports at 59.69%, with only 15.19% of publications contained 10 or more animals. The complication rate calculated from summation across all papers was 5.67% (95% confidence interval [CI] 5.12-6.24%, standard error [SE] 0.28%).

The next objective was to compare the outcomes between MIS and open surgical procedures in wildlife in the current peer-reviewed published literature. A systematic review, with indirect comparison meta analysis, evaluated complications between open surgery and MIS in wildlife. 243 individual studies met the search criteria for open or MIS surgery of the abdomen or coelomic cavity in wildlife species, of which only 50 studies included 10 or more individuals. Only two publications directly compared MIS and open surgery, and the direct meta analysis results, while appearing to favour MIS, were not statistically significant. Individual patients and reported complications were summated, to estimate total published complication rates. Across all wildlife species a 6.54% absolute risk reduction (95% CI of the difference 5.08-8.14%, SE 0.78, $p<0.001$) was evident in publications of MIS surgery compared to open abdominal or coelomic surgery. There was a statistically significant lower complication rate across all analysed taxonomic groups, but the evidence was at high risk of bias.

Another objective was to compare the outcomes of open abdominal and MIS surgical procedures in captive wildlife species. Surgical records for a 25 year period, were analysed from four zoological collections. Out of a total of 1633 surgical procedures, 361 animals underwent abdominal or coelomic cavity surgery via open surgery or MIS. Across all species, open surgery carried a major complication rate of 26.35%, while MIS only carried a major complication rate of 5.16%; an absolute risk reduction of 21.19% (95% CI of 13.69-29.14%, SE 3.93%). Published complication rates were notable lower, indicating likely positive publication bias and outcome reporting bias. This needs careful consideration when wildlife veterinarians attempt evidence based surgical decisions.

The last objective was to evaluate innate cognitive biases that may predispose to poor surgical decisions in veterinarians operating on wildlife species, and result in adverse surgical outcomes. 57.14% (95%CI 50.01-63.99%, SE 3.6%) of pre-clinical veterinary students, when self-predicting their surgical skills 5 years after graduation, believed they would be above average, while only 3.7% (95% CI 1.81-7.45%, SE 1.37%) believed they would be below average. Untrained veterinary surgeons appeared to have an illusory superiority bias, when self-evaluating their surgical aptitude and future surgical performance. Further, only 3.17% (95% CI 1.46-6.75%, SE 1.28%) ranked clinical auditing as the most important of six suggested options, to improving their personal surgical outcomes once qualified veterinary surgeons. This indicated an innate lack of appreciation or understanding of its value in improving surgical skills and performance.

RESUMEN

La cirugía mínimamente invasiva (CMI) se considera actualmente el estándar recomendado en un número considerable de procedimientos quirúrgicos en medicina humana y algunos de sus beneficios están ampliamente reconocidos por la evidencia existente. Las ventajas de este tipo de cirugía también están reconocidas para determinados procedimientos en animales domésticos, aunque no existe una evidencia convincente sobre las ventajas de la CMI sobre la cirugía convencional.

El primer objetivo de esta tesis fue revisar la calidad y amplitud de las publicaciones revisadas por pares que forman la evidencia actual para todos los tipos de procedimientos quirúrgicos en animales salvajes, así como establecer el índice de complicaciones quirúrgicas publicadas. Se incluyeron 635 resúmenes con 6582 individuos de fauna salvaje. La mayoría de las publicaciones se basaban en casos individuales (59,69%) y un 15,91% incluían 10 o más animales. La frecuencia de complicaciones quirúrgicas calculada en base a la suma de las publicaciones fue 5,67% (95% Intervalo de Confianza [IC] 5,12-6,24%, error estándar [ES] 0,28%).

El segundo objetivo fue evaluar las complicaciones entre la cirugía convencional y la CMI en fauna salvaje con los datos obtenidos de las publicaciones existentes a través de una revisión sistemática, con comparación indirecta de meta-análisis. Un total de 243 estudios cumplieron el criterio de CMI o cirugía convencional del abdomen/cavidad celómica en estas especies, de las cuales sólo 50 comprendían 10 individuos o más. La tasa total de complicaciones se calculó sumando los pacientes individuales y el número de complicaciones publicadas. Del total de especies, se observó una reducción absoluta del riesgo de complicaciones del 6,54% (95% IC de la diferencia 5,08-8,14%, ES 0,78, $p<0,001$) para la CMI en comparación a la cirugía convencional de la cavidad abdominal/celómica. A pesar de obtener una menor tasa de complicaciones quirúrgicas con la CMI en todos los grupos taxonómicos analizados, esta evidencia presentaba un alto riesgo de sesgo.

El tercer objetivo fue comparar los resultados de la cirugía abdominal convencional (abierta) y la CMI en especies de fauna salvaje en cautiverio. Se analizaron los

registros quirúrgicos de cuatro colecciones zoológicas en un período de 25 años. De un total de 1633 procedimientos quirúrgicos, 361 animales fueron sometidos a cirugía de cavidad abdominal/celómica mediante cirugía abierta o CMI. En todas las especies, la cirugía abierta tuvo una tasa de complicaciones mayor de 26,35%, en comparación con la CMI que fue del 5,16%, representando una reducción del riesgo absoluto del 21,19% (IC del 95%: 13,69-29,14%, SE 3,93%). Las tasas de complicaciones publicadas fueron notablemente más bajas, lo que indica un posible sesgo de publicación y de notificación de resultados positivos. Esto debería tenerse en cuenta para la formulación de decisiones quirúrgicas basadas en la evidencia por los veterinarios de fauna salvaje.

El último objetivo fue evaluar los sesgos cognitivos innatos que pudieran predisponer a los veterinarios que realizan intervenciones quirúrgicas en animales salvajes a la toma de decisiones erróneas. El 57,14% (95%IC 50,01-63,99%, ES 3,6%) de los estudiantes de nivel pre-clínico encuestados, al predecir sus habilidades quirúrgicas 5 años después de su graduación, creían estar por encima del promedio, mientras que sólo el 3,7% (95%IC 1,81-7,45%, ES 1,37%) creía que se encontraría por debajo, demostrando un sesgo de superioridad ilusoria a la hora de evaluar su propia aptitud quirúrgica y futura destreza. Además, sólo el 3,17% de los encuestados (95% IC 1,46-6,75%, ES 1,28%) clasificó la auditoría clínica como una de las opciones más importantes para mejorar los resultados quirúrgicos una vez sean veterinarios cirujanos calificados, indicando una falta de apreciación innata o de comprensión de su valor para poder mejorar las habilidades quirúrgicas y el rendimiento.

CONTENTS **PAGES**

1. INTRODUCTION

1.1. Minimally invasive surgery

Minimally invasive surgery (MIS), such as laparoscopic cholecystectomy, is performed routinely in human surgery in the developed world, and is currently regarded as the gold standard for many human surgical procedures (Sica and Biancone 2013; Ruffolo and others 2013; van Dijk and others 2014; Küper and others 2014; Antoniou and others 2015; Coccolini and others 2015b; Mandrioli and others 2016). MIS is generally used to refer to any procedure that is less invasive than open surgery used for the same purpose (Wickham 1987). Although this has most often been used to refer to rigid endosurgical procedures such as laparoscopy, the term can also be applied to percutaneous interventional techniques. Laparoscopy, thoracoscopy, and arthroscopy are also alternatively referred to as minimal access surgery, video surgery, endosurgery, and endoscopic surgery, and, by lay persons and professionals alike, as “keyhole surgery.”

Multiple individual studies, as well as systematic reviews and meta analysis have demonstrated benefits for human patients over open abdominal surgery for surgical procedures such as cholecystectomy (Laurence and others 2012; Cheng and others 2012; de Goede and others 2013; Coccolini and others 2015a; Sedaghat and others 2017), and appendectomy (Meynaud-Kraemer and others 1999; Garbutt and others 1999; Temple and others 1999; Aziz and others 2006; Markides and others 2010; Ciarrocchi and Amicucci 2014), and a myriad of other surgical procedures across different surgical disciplines (Khan and others 2003; Li and others 2012a; Antoniou and others 2014; Sajid and others 2016; Sathya and others 2017; Xiong and others 2017). These advantages include reduced post-operative hospitalisation and care requirements, rapid post-operative recovery and return to normal activity levels, reduced post-operative pain, lower risk of developing post-operative complications such as reduced abdominal adhesions, less wound dehiscence and lower wound infection rates, when compared to traditional open surgery.

Despite these advantages, there was considerable initial resistance to the use of the MIS or endoscopic surgery in human medicine. While the first laparoscopic examination in a live patient was demonstrated in a dog in 1901 by Georg Kelling (Spaner and Warnock 1997; Vecchio and others 2000), and Hans Christian Jacobaeus performed the first human laparoscopic examinations in 1910 (Hatzinger and others 2006), it was a prolonged period before the mainstream medical profession accepted these MIS techniques, aided by the later eventual development of supporting technology such as video cameras. Gynaecologists were the first to adopt laparoscopic procedures in the 1970's (Spaner and Warnock 1997; Vecchio and others 2000; Antoniou and others 2015). Kurt Semm then performed the first laparoscopic appendectomy in 1980 (Litynski 2017b; Antoniou and others 2015), and Erich Muhe the first laparoscopic cholecystectomy in 1985 (Litynski 2017a,b; Reynolds 2017; Blum and Adams 2011; Antoniou and others 2015), but it was only after Phillipe Mouret performed the first video assisted laparoscopic cholecystectomy (Polychronidis and others 2017; Spaner and Warnock 1997; Vecchio and others 2000; Blum and Adams 2011), that human laparoscopic surgery entered the mainstream medical profession. The rapid uptake in general surgery was partly patient driven, as the public became aware of "keyhole" or "band-aid" surgery. It then progressed so rapidly, that by 1993, only 6 years later, the National Institutes of Health (NIH) held a consensus conference that declared laparoscopic cholecystectomy the treatment of choice for uncomplicated gallstones (Neugebauer and others 1995; Lhermette and Sobel 2008).

Similar to the earlier acceptance of MIS in human gynaecology, reproductive studies constituted the majority of the earliest applications in animals, with laparoscopic examinations of ovarian activity and reproduction. Studies with a variety of non-human primates were performed in the 1960's and early 1970's (Balin and others 1966; Dierschke and Clark 1976; Graham 1976; Mahone and Dukelow 1978; Harrison 1980) and in the 1970's endoscopic sexing of birds was developed (Bush and others 1978a; Harrison 1978; Bush 1980). The late 1970's also saw laparoscopic reproductive studies, including attempts at laparoscopic artificial insemination and other assisted reproductive techniques, in a variety of captive wildlife species such as large felids, bears, deer, and reptiles (Bush and others 1978c, 1980; Wildt and others 1978). The first veterinary multiple authored book on

"Animal laparoscopy" was published in 1980, and included chapters on zoo and exotic animal species, as well as birds and reptiles (Harrison and Wildt 1980). All the more remarkable, considering procedures were still largely done by eye while holding the endoscope, and that at this stage laparoscopy was still very much on the fringe in human surgery.

After these initial reproduction studies veterinary uptake of MIS techniques stalled somewhat, and largely remained limited to research centres, for use in human surgical training, and laboratory animal study models for human surgery, until a gradual resurgence of interest in and development of veterinary applicable operative procedures and training in the last two decades (Dupré and others 2017, 2009; Soria-Gálvez and others 2017; Masero and others 2000; Rawlings and others 2000; Van Goethem and others 2003; Usón Gargallo and others 2006; Sánchez-Margallo and others 2007; Kim and others 2011; Pader and others 2011b; Tapia-Araya and others 2016b, 2015b, 2016a). Currently veterinary MIS literature includes reports covering advanced techniques such as single incision laparoscopic surgery (SILS) and natural orifice transluminal surgery (NOTES) procedures (Sánchez-margallo 2007; Alford and Hanson 2010; Pader and others 2011a; Manassero and others 2012; Tapia-Araya and others 2015b; Hartman and others 2015), and now extends to MIS reports in unusual or difficult species such as fish and elephants (Boone and others 2008a; Stetter 2010; Marais and others 2013c; Rubio-Martínez and others 2014; Sweet and others 2014a).

Veterinary research use of MIS techniques advanced at the same rate as in human surgery (Balin and others 1966; Harrison 1980; Wildt and others 1981), and in common with human surgery, veterinary MIS techniques in domestic animals have also been demonstrated to hold benefits for veterinary patients, such as reduced post-operative pain and morbidity, reduced wound infection or dehiscence, shorter post-operative recovery to function, shorter hospitalisation periods, and reduced post-operative care requirements, while yielding adequate diagnostic biopsy samples (Devitt and others 2005; Walmsley 2007; Culp and others 2009; Parkinson 2012; Mayhew and others 2012; Shariati and others 2014; Case and others 2015; Gauthier and others 2015; Collins and others 2016; McDevitt and others 2016), although it has been highlighted that findings between different studies can be inconsistent

(Mayhew 2014). MIS further carries the potential advantage of good visualisation and magnification, especially useful in locations that are difficult to visualise in open surgery (Freeman 1999; Rijkenhuizen and others 2008; Pizzi and others 2010; Mayhew 2014). This offers the potential for achieving safe, atraumatic and physiological surgery.

The hurdles to the uptake of MIS in mainstream veterinary surgical practice, as well as more specifically in wildlife species, appear somewhat different to human surgery. One hurdle is that MIS has a significant initial learning curve, even for simple procedures such canine laparoscopic ovariectomy (Pope and Knowles 2014), which has been estimated as having an initial learning curve of 80 procedures. This learning curve may be accelerated by good veterinary training programs and realistic training models (Usón-Gargallo and others 2014), just as demonstrated in human surgery (Usón Gargallo and others 2006; Toledano Trincado and others 2014; Beyer-Berjot and others 2014; Tsai and others 2016; Jung and others 2016; Ibrahim and others 2016; Terzi and others 2016). With experience the learning curve for more advanced and technically demanding procedures becomes shorter (Runge and others 2014a). The hurdle provided by the initial learning curve is exacerbated in veterinary surgery by the fact that most private veterinary practitioners do not have the mentoring experienced in human specialist surgical training by being an assistant for a large number of cases undertaken by an experienced senior surgeon. Instead once qualified, many veterinary private practitioners do not specialise, and learn on the job, often being largely self taught and working in relative isolation.

Further hurdles to the mainstream uptake of MIS in veterinary practice include the relatively high initial equipment purchase costs (Mayhew 2014), the ease, familiarity and speed with which the alternative open procedure, such as laparotomy, may be pursued, the increased surgery time generally needed by most practitioners to perform a MIS procedure, and the time and theatre cost implications this may carry in a busy veterinary practice (Arulpragasam and others 2013; Mayhew and others 2013).

Despite numerous notable advantages, MIS techniques such as laparoscopy carry some injury risks specific to this type of surgery that need consideration

(Desmaizières and others 2017; Ragle and others 1998; Staffieri and others 2007; Hendrickson 2008; Buote and others 2011; Marais and others 2013c; Pope and Knowles 2014). The greatest MIS-specific risk is probably in achieving safe access (entry) at the start of MIS procedures, commonly underestimated by novice surgeons (Corson and others 2001; Vilos 2002; Trottier and others 2009; Pizzi and others 2011a; Mayhew and others 2012; Ulker and others 2014; Pizzi 2015; Ahmad and others 2015). Access may be open (a small incision into the abdomen, followed by port placement); blind (blind entry into the abdomen with a sharp trocar, normally after blind insertion of a Veress needle to insufflate the abdomen); or optical (using a laparoscope to assist entry, either with or without prior abdominal insufflation with a Veress needle). Injuries can may occur with any of the techniques, although the incidence and injury type and severity differ. Even supposedly atraumatic cannulas can may cause entry injuries to vascular structures, organs, or the bowel. The merits and risks of different abdominal access techniques remain contentious in both human and veterinary laparoscopy, and continue to be debated. Despite strongly held personal opinions and experiences, a Cochrane collaboration systematic review found no clear evidence for any one technique being safer than another (Ahmad and others 2015). It is recognized, however, that adverse events in surgery are under-reported in the literature. The high incidence and extent of abdominal wall adhesions in species such as chimpanzees (*Pan troglodytes*) and gorillas (*Gorilla gorilla*) makes entry problematic in some individuals, irrespective of the technique selected, although open access appears preferable (Pizzi 2015), and not dissimilar to humans with a scarred abdomen from previous surgery (Ahmad and others 2012; Li and others 2012b; Zhang and others 2013; Mandrioli and others 2016; Sajid and others 2016; Ha and others 2016). Similar to in obese humans (Ciarrocchi and Amicucci 2014) , open access through the caudal umbilical scar can also be safely achieved in large obese animals such as bears (Pizzi and others 2011a; Pizzi 2015), this being the thinnest part of the abdominal wall. This site has the further advantage in many animal species, such as canines, in avoiding inadvertent entry into the often large, fat-filled falciform ligament. There are veterinary species were the technique is anatomically not feasable, such as large adult pinnipeds, in which the blubber layer may simply be too thick, and the use of a Veress needle is still required.

Inadvertent bowel injuries incurred during laparoscopy also carry a specific risk (Corson and others 2001; Vilos 2002; Trottier and others 2009; Ulker and others 2014; Pizzi 2015; Ahmad and others 2015). Due to reduction in surgical trauma in MIS, there is a reduced peritoneal and systemic inflammatory response in comparison to open abdominal surgery (Jakeways and others 1994; Aldana and others 2003). While a benefit of MIS under normal conditions, it is a problem in cases of bowel trauma, as it can result in an important delay in the manifestation of clinical signs, if unrecognised at the time of surgery. This results in a high mortality rate. The most frequent causes of laparoscopic bowel injury in humans are either entry related Veress needle punctures or sharp trocar injuries, or thermal injuries from electrosurgical instruments, and the small intestine is frequently affected (Corson and others 2001; Vilos 2002; Cesario and others 2016).

Unrecognised thermal injuries to the bowel may occur irrespective of the electrosurgical modality employed: whether it is a monopolar, bipolar, tissue feedback bipolar, or ultrasonic scalpel. The tips of all electrosurgical instruments generate heat with use, and may cause inadvertently bowel thermal injuries. These injuries may result in delayed perforations 24-48 hours later (Aldana and others 2003; Trottier and others 2009; Ulker and others 2014). Monopolar surgery carries further risks related to insulation failures, as well as poor contact with the ground plate leading to patient burns. In veterinary surgery this is a particular risk in small mammals with thick fur, that which acts as an insulator, as well as in birds with their insulating feathers (Hernandez-Divers 2008; Pizzi 2012b).

Another MIS specific injury risk is from “"out of sight" injuries that occur in the body cavity behind the tip of the endoscope, and are hence unseen. In addition to inadvertent thermal injuries from electrosurgical instruments, trauma can may occur from non-visualised instrument entry through ports. This is a particular risk in thoracoscopy with resultant lung puncture, which if missed can may result in life-threatening post-operative pneumothorax developing (Pizzi 2012c; Usón-Casaús and others 2014; Wormser and others 2014; Radlinsky 2015; Case 2016).

Despite growing evidence for the advantages of MIS in domestic animals (Parkinson 2012; Mayhew and others 2012; Shariati and others 2014; Tapia-Araya and others

2015a; Case and others 2015; Gauthier and others 2015; Collins and others 2016; McDevitt and others 2016), there is still a paucity of data regarding MIS related complications and adverse outcomes in veterinary patients (Desmaizières and others 2017; Hendrickson 2008).

1.2. Wildlife Surgery

Wild animals were maintained in captive collections in ancient history by various cultures, yet there are almost no records of what veterinary care may have been given to these animals. In ancient Egypt the female Pharaoh, Queen Hatsheput, in 1500 BC had the first large collection of wild animals that may be called a zoo, however there are no remaining records of any veterinary care, and if this was available, or provided (Fowler 2006). The earliest records of veterinary care for wild animals or non-traditional animals were kept for the Indian King Asoka, 250 BC, who ordered the construction of veterinary hospitals to care for all animals, including elephants. The first recorded modern zoo veterinarian was Charles Spooner, who was appointed at London zoo in 1829, the year after it was founded (Fowler 2006). The first textbook of zoo and wildlife medicine, including small amounts of surgery, was only published in 1978 (Fowler 1978). Zoo and wildlife veterinary medicine and surgery as a recognised discipline was established relatively late in comparison to the veterinary care of horses (important due to their role in transportation and the military), agricultural animals, and companion animals, but occurred at a similar time to the establishment of the field of Conservation Biology, which was concerned with the conservation, management, and protection of vulnerable species, populations, and ecosystems (Soule 1985).

While wildlife surgery is a small specialty niche, inside the discipline of zoological veterinary medicine, it has the potential to play a role in the conservation of endangered wildlife species in captive breeding programs and rescue centres. In critically endangered species, optimal treatment, should it be needed, of each remaining individual may be essential if a species is to survive. Some species, such as the Socorro dove (*Zenaida graysoni*) are extinct in the wild (IUCN 2000), with only a small population of birds in captive breeding programs. Surgery has been performed on Socorro doves, and a successful outcome in this type of situation could help maintain maximum genetic diversity, important in maintaining a minimum viable population (Shaffer 1981).

Wild animals that need to be returned to the wild also demand the highest levels of surgical outcomes, as animals have to be 100% fit to survive in the wild, avoid predators, or catch prey. An athletic species such as the peregrine falcon (*Falco peregrinus*) will almost certainly not survive when returned to the wild, if not completely returned to normal function. Even a very small decrease in flight ability and manoeuvrability will make the difference between catching enough birds to survive and starving to death.

Even though captive wildlife in zoological collections are more protected, they still pose challenges compared to domestic animal surgery. There is a great variety in body sizes, even in the same taxonomic group. As an example, primates can range in size from a 100gram pygmy marmoset (*Cebuella pygmaea*) to a 200kg gorilla (*Gorilla gorilla*), and can also have notable anatomic differences of surgical importance, even in the same taxonomic group. Differences in anatomy and physiology may require different surgical techniques with different speeds of healing (Divers 2015). Many wildlife species not only have very different anatomy from humans and domestic animals, but also suffer from completely different diseases, resulting in the potential for novel applications of MIS techniques, that are not required in humans or domestic animal species (Campbell-Palmer and others 2012, 2015; Pizzi 2015).

1.3. Minimally invasive surgery in wildlife species

It stands to reason that MIS is likely to hold advantages in captive or free free-ranging wildlife just as in domestic animals, although the current evidence base is still limited, and there is a paucity of studies addressing safety, techniques, and specific applications relevant to wildlife veterinary patients (Divers et al, 2010; Hernandez-Divers et al, 2005; Hernandez-Divers et al,2009; Maclean et al, 2006; Pizzi et al, 2010; Pizzi et al, 2011; Pizzi et al, 2012). Reporting of clinical outcomes and complication rates, with comparisons between MIS and traditional open surgery, is still almost non-existent in the wildlife surgical published literature (Boone and others 2008b; Pizzi 2012b, 2015; Steeil and others 2012a).

Emphasis is commonly placed on the small wounds and reduced post-operative pain in veterinary MIS. However, the enhanced magnified visualisation, access to parts of the body and structures difficult to visualise visualize in open surgery, provision of excellent illumination, and ability to perform less traumatic and more physiological surgery in MIS are also of considerable value to the wildlife surgeon. Reducing the invasiveness of surgical procedures through different MIS techniques should not, however, be accomplished at the cost of increased risks to the patient (Pizzi 2015).

While MIS techniques potentially hold even greater advantages in the veterinary treatment of captive and free ranging wildlife species, their application also faces specific challenges not encountered in either human surgery, or domestic animal surgery. In these veterinary patients post-operative care and monitoring is difficult, and it may not be possible to restrict post-operative activity at all (Cook 1999; Pizzi 2012a, 2015; Llano Sanchez and others 2016). In primates, separation from the group for any length of time can adversely affect social group stability and behaviour, and result in fighting and serious injury or death, on reintroduction of the operated individual. Individual primates undergoing MIS procedures can be more rapidly returned to their normal outdoor enclosures and groups, resulting in minimal social disruption of the group (Pizzi 2012d). Aquatic species such as seals or beavers undergoing MIS may need to be allowed an early post-operative return to water and swimming, so small water proof wounds are required (Campbell-Palmer and others 2015). Intelligent and dextrous primates, such as chimpanzees (*Pan troglodytes*) can manually remove sutures, and open and interfere with wounds. Using small 3-5mm diameter MIS instruments holds potential for limiting wound interference, and hence reducing post-operative complication rates in these animals (Graham 1976; Pizzi 2015). Small MIS wounds help reduce the risks of wound contamination and infection both intra operatively- and post-operatively, especially when operating under less than ideal conditions such as in animal enclosures, outdoors, or in makeshift theatres in the field (Pizzi and others 2011a,b; Campbell-Palmer and others 2015; Llano Sanchez and others 2016)

Laparoscopy encompasses MIS procedures in the abdominal cavity, while coelioscopy, is endoscopy of the coelomic cavity in non-mammalian species. This is the most widely recognized and the best reported MIS technique in the zoo and wildlife surgical field. It has been applied in mammal species ranging from mice (Shapira and others 2009) to elephants (Marais and others 2013a; Rubio-Martínez and others 2014; Sweet and others 2014b), as well as in birds, reptiles, amphibians, and fish (Stetter 2010; Pizzi 2012b; Chai 2015; Divers 2015). It has applications in diagnostic and operative surgery, as well as assisted reproduction applications in wildlife. The emphasis in this thesis is on laparoscopy and coelioscopy, as there are still relatively few published reports on the application of other MIS modalities in wildlife.

Diagnostic, or exploratory, laparoscopy and organ biopsy is are especially useful in captive wildlife, considering the limitations of other diagnostic modalities in wildlife species, and the limited availability and high cost of advanced imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI).

The reports of both elective and emergency laparoscopic operative procedures, other than reproduction related, are still relatively few in wild mammals (Wildt and others 1978; Bush and others 1978b, 1980; Cook 1999; Fauquier and others 2003; Jeffery R Zuba 2004; Pizzi and others 2011a; Campbell-Palmer and others 2015). Many wildlife species not only have differing anatomy from humans and domestic animals, but also suffer from very different pathology and surgical diseases requiring surgery. Available instrumentation and techniques for humans may not be directly applicable to wildlife patients. Differences in pathology and anatomy also results in the potential for novel applications of MIS techniques, that are not indicated in humans or domestic animal species. Applications may even be unique to a particular location (Campbell-Palmer and others 2015; Pizzi 2015)

The use of laparoscopy in assisted reproductive techniques and sterilisation has been the most reported application in wildlife (Bush and others 1978a,b; Wildt and others 1978; Cook 1999; MacLean and others 2006; Steeil and others 2012b; Marais and others 2013b), although advances in fields such as ultrasonography and endocrinology have reduced its application in more recent times, with the advent of less invasive alternatives, such as transcervical and ultrasound-guided needle techniques for insemination and oocyte and embryo collection (Hermes and others 2009). Sterilization via MIS has increased in scope and range of species, with laparoscopic vasectomies having been performed in mammal species ranging from mice (Shapira and others 2009) to elephants (Marais and others 2013a; Rubio-Martínez and others 2014). Laparoscopic tubal ligations and laparoscopic vasectomy have useful advantages in controlling reproduction in captive wildlife reproduction. Preservation of gonadal production of hormones results in maintenance of normal behaviour and no disruption of social hierarchy, which is particularly useful in large primate groups. Gonadal hormones also maintain normal desirable secondary sexual characteristics, such as the mane in male lions, and the fur colours of gibbon species. This may be altered or lost if animals are castrated or ovariectomized. Laparoscopic vasectomy in primates carries the further advantages of being rapid to perform as the vas is easily visualized in the abdomen, in contrast to open vasectomy; and wound interference is minimal, in contrast to the frequent post-operative wound interference and complications that can occur with open vasectomy (Pizzi 2012a,d). Laparoscopic, or laparoscopic-assisted, castration may be performed in cryptorchid males (Pizzi and others 2011b; Runge and others 2014b), as well as species with intra-abdominal testes, such as rock hyrax (*Procavia capensis*), while retraction of testes into the abdomen for castration is possible in species such as pinnipeds, that do not have a true scrotum.

1.4. Evidence-based medicine and surgery

Evidence-based medicine (EBM) refers to the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients (Sackett and others 1996). It encompasses a systematic process of integrating professional expertise, critically appraised research evidence and patient values to formulate the best possible patient related decisions (Sackett and others 2000). EBM was introduced in human medicine in the early 1990's, but evidence-based veterinary medicine (EBVM) (Cockcroft and Holmes 2008) is a more recent development, with the increasing volume and quality of veterinary research studies now available.

The application of EBM to veterinary surgery can be challenging (Vandeweerd and others 2012). Systematic reviews and meta analysis of randomized clinical trials (RCT's) are regarded as the gold standard basis for practicing EBM (Sackett and others 1996). However, limited funding, a wide variety of species, lack of a central national patient database or health care insurance directory, small case numbers, lack of involvement of primary care veterinary practitioners, and legislation such as the Animals (Scientific Procedures) Act of 1986 in the United Kingdom and similar legislation in other countries all hamper large randomised controlled trials in veterinary medicine. Despite these limitations, there are an increasing numbers of veterinary systematic reviews and meta analysis now published (Evans and others 2008; Schmidt and others 2013, 2016; Charalambous and others 2016; Munsterman and others 2016; Langerhuus and Miles 2017).

Developing EBVM is even more challenging in the zoo and wildlife medicine and surgery field. There is a very wide variety of taxonomic groups and species, suffering from a host of differing conditions, and having differing physiological responses and healing. Animals are also often held in small numbers in different independent zoological collections or wildlife rescue centres. Well designed and adequately powered observational cohort or case-control studies can also make a meaningful contribution to EBVM, and are preferable to poorly organised RCTs (Parkin 2010; Vandeweerd and others 2012), but even these can be difficult to achieve in the field of zoological medicine. Wildlife surgery may be particularly problematic, due to the low case volume encountered, and for many species the experimental setting required for a randomised controlled trial would be very difficult to achieve due to the species specialised natural history and specific husbandry, care, and space requirements.

Adequate case numbers (sample size) may be problematic, even in human surgical trials. It has been demonstrated that a large number of human surgical trials and observational studies are underpowered, due to insufficient numbers of participants, and are at risk of type II statistical errors, where a study fails to statistically demonstrate a real difference between two groups (Bailey and others 2004; Walter and others 2007; Chang and others 2013a). This may lead to the erroneous conclusion that there is no difference between the compared groups. Despite this, human and veterinary prospective trials and observational studies frequently neglect to perform power calculations before initiating their research (Bailey and others 2004; Walter and others 2007; Ayeni and others 2012; de Goede and others 2013; Chang and others 2013b; Greenland and others 2016)

Pre-emptive power calculations highlight how difficult it would be to perform a randomized controlled trial to demonstrate the reduced complication rates in wildlife MIS compared with open surgical techniques. Demonstration of a 50% reduction in baseline risk from 20% to 10%, would require a total study group of 438 individuals. Demonstration of a more modest improvement, or a lower frequency event, requires even larger numbers: Demonstration of a 50% reduction in baseline risk from 2% to 1%, would require a study group of 5,030 individuals; while to demonstrate a 10% reduction in baseline risk from 20% to 18%, would require a study group of 12,278 individuals (Chang and others 2013b).

It appears likely that the bulk of the future evidence base for wildlife surgery, including MIS, will continue to be based on small feasibility trials, small observational studies, case series, and case reports.

1.5. Cognitive biases and surgical decisions

Cognitive biases result in systematic thinking errors, that cause irrational judgements and decisions. Different types of cognitive biases have been reported (Kahneman and Tversky 1996; Kahneman 2003; Sunstein and others 2003). Cognitive biases are believed to be the result of mental "shortcuts or heuristics, used to make decisions and judgements efficiently (Newell and others 1957; Simon and Newell 1958; Simon 1977). These cognitive "shortcuts" may function by focusing on one, or limited, aspects of a complex problem, and ignoring other aspects. Some heuristics are believed to have had evolutionary advantages, in adaptations where speed may be more important than accuracy, or they may be the results of neural processing limitations, limited mental capacity for processing information, or from where there is a lack of appropriate mental mechanisms, so-called "bounded rationality" (Simon 1972; Kahneman 2003). While heuristics commonly govern automatic and intuitive judgments and decisions, they can also be used as mental strategies when presented with limited information.

The impact of cognitive biases has been particularly well investigated in the field of behavioural economics (Tversky and Kahneman 1975; Griffin and Tversky 1992; Kahneman and Tversky 1996; Kahneman 2003), but research has also demonstrated their influence in poor clinical decision making in human medicine, and their role in surgical errors, even when a good scientific evidence base is available for clinical decision making (Bernstein and Khu 2009; Mittal and Perakath 2010a,b; MacDermid and others 2017).

Certain cognitive biases are of particular relevance to surgery, and potentially increase the risk of adverse outcomes and complication. Confirmation bias is seeking or interpreting evidence in ways that are partial to existing beliefs and expectations, and is a well recognised source of medical errors (Pines 2006; Stiegler and others 2012; van den Berge and Mamede 2013; Jager and others 2014). Confirmation bias in surgery can reinforce anatomic misidentification during surgery, with catastrophic results, such as in the incorrect identification of biliary anatomy during laparoscopic cholecystectomy, resulting in bile duct injury, with potentially fatal consequences for the patient (Buddingh and others 2011).

Illusory superiority bias, or the "above-average effect" is where an individual overestimates their own qualities and abilities, in comparison to the same qualities and abilities of others, despite evidence to support this (Hoorens 1993; Odean 1998; Alicke and Govorun 2005; Krizan and Suls 2008; Beer and Hughes 2010; Brown 2012), and manifests itself in multiple professions, including medicine (Tan 2011; Jager and others 2014) and academia (Cross 1977; Zuckerman and Jost 2001). In one university survey, 68% of academics rated themselves as in the top 25%, and more than 90% rated themselves as above average (Cross 1977). In what is likely the best know example of illusory superiority bias, 93% of American drivers rated themselves as better than the median (Svenson 1981). This bias may hence result in increased risk taking by affected surgeons, and appears to increase with age, likely linked to self-perceived experience (Abdullah 2014).

The Dunning-Kruger effect (Kruger and Dunning 1999) is another cognitive bias relevant to human and veterinary surgeons, or those in training. This cognitive bias occurs when inexperienced, unskilled or incompetent individuals mistakenly asses their ability as much higher than is accurate. This bias is encountered either with simpler tasks, or where success is common, or people feel competent (Simons 2013; Pennycook and others 2017). This makes it of special significance for surgery performed or seen by trainees or inexperienced surgeons, where in some fields of simple routine surgery, adverse outcomes or complication rates may be low (Tan 2011; Abdullah 2014). It may result in surgeons undertaking procedures beyond their skill and competency level, with a resultant increase in the risk of patient harm.

Cognitive biases may result in unrealistic surgical outcome expectations by surgeons and human patients, or in the veterinary field by animal owners, and an expectation that some conditions must have a surgical solution. This is consistent with Maslow's statement that “"If the only tool you have is a hammer, everything looks like a nail.” (Maslow 1966). A recent study found across a variety of human elective surgical procedures not only were a significant number of human elective surgery patients not better a year after elective surgery, 17% actual suffered worse pain than before surgery, and 14% had less function than before surgery (Peters and others 2010). This indicates that approximately 1 in 7 human elective surgery patients were in fact, worse off a year later after having undergone elective surgery. No comparable veterinary data are available, but it is uncertain whether veterinary surgical patients fare markedly better.

Cognitive biases are well recognised as being problematic in multiple facets of medical and veterinary medicine (van den Berge and Mamede 2013; Msaouel and others 2014; Park and others 2014; Fargen and Friedman 2014), and training of medical students to recognise and avoid cognitive biases has been demonstrated to reduce errors in clinical decision making (Hershberger and others 1995; Stiegler and others 2012; Msaouel and others 2014). Interestingly, the act of supervising medical students has also been found to be somewhat protective in preventing senior clinicians committing cognitive bias errors, and causing them to consider alternative treatment options (Roswarski and Murray 2006).

Clinical auditing of an individual surgeons surgical outcomes can help mitigate against cognitive biases and poor clinical decision making, by providing a positive feedback loop, if performed correctly. Clinical auditing is an upward spiral of appraisal and improvement (Viner 2005, 2006). In the veterinary field, the Royal College of Veterinary Surgeons (RCVS) code for professional conduct in the United Kingdom states that clinical governance is a continuing process of reflection, analysis and improvement in professional practice for the benefit of the animal patient and the client owner, and that veterinary practitioners should audit the results of clinical procedures of interest to the practice team and use the results to improve patient care (RCVS 2017).

It is only by measuring their own surgical outcomes and complications that a surgeon can judge their performance, and any improvement, over time. This may help highlight and mitigate against some of the cognitive biases that medical and veterinary surgeons are prone to.

2. HYPOTHESIS AND OBJECTIVES

Hypothesis:

- According to the evidence in human and veterinary surgery, minimally invasive surgical (MIS) procedures in wildlife species would carry similar benefits and advantages over open surgery: a lower risk of developing peri-operative complications and a better post-operative survival.

- The role of clinical audit is not innately understood to contribute to improving surgical outcomes by veterinary surgeons.

Objectives:

The general objective of this project is to contribute to the initial establishment of a basic evidence base for safe and effective minimally invasive surgical techniques in wildlife, and determine suitable applications for these techniques in captive and free-living wildlife species.

Accordingly, the specific objectives and the related studies have been designed as follows:

- **Objective 1:** To establish the quality and scope of published peer-reviewed literature forming the current evidence base for surgery in wild animals.
    - Study 1: *Cutting through a jungle of evidence: assessing the evidence base in wildlife surgery by systematic review of abstracts*.

- **Objective 2:** To compare the outcomes between minimally invasive and open surgical procedures in wildlife in the current peer-reviewed published literature.
    - Study 2: *Complications of open versus MIS in wildlife: A systematic review and indirect comparison meta analysis.*

- **Objective 3:** To determine an overall surgical complication rate in captive wildlife in zoological collections.
    - Study 3: *Captive wildlife surgery complication rates in zoological collections in the United Kingdom over a 25 years period*.

- **Objective 4:** To compare the outcomes of open abdominal surgery and MIS procedures in captive wildlife.
    - Study 4: *Comparison of outcomes and complications between open surgery and MIS in zoological collections.*

- **Objective 5:** To evaluate the innate cognitive biases that may predispose to poor surgical decision making in veterinarians working with wildlife.
    - Study 5: *Preclinical veterinary students manifest a illusory superiority bias when self-evaluating surgical aptitude and future surgical skill, and do not innately perceive the value of clinical audit.*

3. STUDIES

<u>3.1. Study 1:</u> *Cutting through a jungle of evidence: assessing the evidence base in wildlife surgery by systematic review of abstracts.*

Cutting through a jungle of evidence: assessing the evidence base in wildlife surgery by systematic review of abstracts

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ABSTRACT

A search of captive and free-ranging wildlife surgery abstracts was performed using MEDLINE, CAB Abstracts, Scopus, and Zoological Record, and reading all abstracts from the main journals covering the field, until 31 December 2016. Studies were evaluated for inclusion using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart. A total of 635 abstracts were suitable for inclusion in the analysis, containing a total of 6582 individual animals. The majority of publications were single case reports 59.69% (95% Confidence Iinterval [CI] 55.82-63.43%, SE 1.95%), with only 15.19% (12.54-18.11%, SE 1.42%) of publications contained more than 10 animals. The complication rate calculated from summation across all papers was 5.67% (95% CI 5.12-6.24%, SE 0.28%). The highest published summated complications rate was in single case reports at 25.33% (95% CI 21.21-29.94%, SE 2.23%), with a highly statistically significant difference above studies including more than 10 animals of 21.16% (95% CI of the difference 17-25.8%, SE 2.25, $p<0.001$, $Z=9.39$). Neurosurgery and ophthalmic surgery had the highest reported complications, while reproductive surgery had the lowest. Papers that reported surgical novelty had low reporting of complications, with only a 2.21% (95% CI 1.6-3.04%, SE 0.36%), a significant difference from the general publication complication rate ($p<0.001$). Journal abstracts are possibly the most important part of a published peer-reviewed study. There appears to a likelihood of positive publication bias and outcome reporting bias in current peer-reviewed wildlife surgery abstracts. It is essential that reviewers and journal editors ensure abstracts accurately and adequately detail surgical complications and adverse outcomes in the field of wildlife surgery.

Keywords: *wildlife surgery; systematic review; zoo; zoological; wildlife; surgery*

INTRODUCTION

Wild animals were maintained in captive collections in ancient history by various cultures, yet there are almost no records of what veterinary care may have been given to these animals. While the first large collection of wild animals that may be called a zoo belonged to the female Pharaoh, Queen Hatsheput in ancient Egypt around 1500 BC, there are no remaining records of any veterinary care. The earliest remaining records of veterinary care for wild animals were those kept for the Indian King Asoka, around 250 BC, who ordered veterinary hospitals to be constructed to care for all animals, including elephants. The first recorded modern zoo veterinarian was Charles Spooner, who was appointed at London zoo in 1829, the year after it was founded (Fowler 2006), and the first textbook of zoo and wildlife medicine, including small amounts of surgery, was only published in 1978 (Fowler 1978).

Surgical interventions in wildlife species may play a role in the conservation of endangered wildlife species, whether free ranging, or as part of captive maintained breeding programs. In critically endangered species, successful veterinary treatment of even a single individual may impact the species chance of survival by maintaining a minimal viable genetic population (Shaffer 1981). Optimum treatment in wildlife, as in human and domestic animal veterinary medicine, should ideally be evidence based (Cockcroft and Holmes 2008; Huntley and others 2016). Evidence based medicine is well established in the human medical field, and increasingly recognised to be important in veterinary medicine, with recent systematic reviews for several conditions in domestic animal medicine (Evans and others 2008; Schmidt and others 2013, 2016; Charalambous and others 2016; Munsterman and others 2016; Langerhuus and Miles 2017). Systematic reviews and metanalysis of randomised controlled trials are the desirable level of evidence, but the majority of wildlife medicine literature is a variety of lower level evidence according to classifications in use by the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence (Howick and others 2011a,b).

Wildlife veterinarians may experience a low case load of a specific condition in a species or taxonomic group, especially if rare or endangered, leading to limited experience upon which to base decisions. Due to the wide variety of wildlife taxonomic groups and species, differing pathophysiology, and environments, the wildlife surgical literature is more fragmented and less developed than that for domestic animal species.

Journal abstracts are possibly the most important part of a published peer-reviewed study. Readers frequently rely on the information provided in an abstract when deciding whether to read the full text of an article (Islamaj Dogan and others 2009; Uy and others 2014; Hole 2016; Bigna and others 2016). Veterinary clinicians may only read abstracts due to time pressures when searching for information on a specific case. Many wildlife veterinarians work outside academic institutions, in developing countries, where access to full text articles behind a pay-wall is not easily practical or affordable. Even when using an electronic internet database to search the peer-reviewed published literature, it has been demonstrated that the majority of researchers predominately only read titles and abstracts, rather than consulting full papers (Islamaj Dogan and others 2009). The quality of abstracts in a field is an important consideration when using the infomration to inform to clinical decisions (Beller and others 2013; Uy and others 2014; Bigna and others 2016)

Biases in the published wildlife surgery literature remain an unquantified problem, but are an important problem in all research (Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Kanaan and others 2011; O’Neil and others 2014; Cooper and others 2015). Positive publication bias, where cases or studies with positive or flattering results are more likely to be submitted or accepted for publication, and outcome reporting bias, where some outcomes are reported preferentially, depending on the results, are a particular concern in individual case reports and small case series, such as the majority of wildlife surgery publications, but can affect all study types. Biased literature can lead to sub-optimal decision making, and poorer than expected outcomes, with increased complications, adverse outcomes, and mortalities (Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010).

A systematic review of published peer-reviewed journal article abstracts, available online was performed to assess the current published literature and quantify complication and adverse outcomes rates published.

METHODS AND MATERIALS

A search of the published peer-reviewed veterinary literature was performed using MEDLINE, CAB Abstracts, Scopus, and Zoological Record, as shown to have comprehensive coverage of veterinary journals (Grindlay and others 2012). Search terms used (as in MEDLINE) were: ((((((((((((((zoo[Title/Abstract]) OR wildlife[Title/Abstract]) OR wild[Title/Abstract]) OR zoological[Title/Abstract]) OR exotic[Title/Abstract]) OR exotic animal[Title/Abstract]) OR primate[Title/Abstract]) OR avian[Title/Abstract]) OR bird[Title/Abstract]) OR reptile[Title/Abstract]) OR reptilian[Title/Abstract])) OR herpetolog*[Title/Abstract])) AND (((((((((((((((surgery[Title/Abstract]) OR surgical[Title/Abstract]) OR operation[Title/Abstract]) OR operativ*[Title/Abstract]) OR biops*[Title/Abstract]) OR incision*[Title/Abstract]) OR incise*[Title/Abstract]) OR excision*[Title/Abstract]) OR excise*[Title/Abstract]) OR resect*[Title/Abstract]) OR sutur*[Title/Abstract]) OR endoscop*[Title/Abstract]) OR laparoscop*[Title/Abstract]) OR minimally invasive[Title/Abstract]) OR MIS[Title/Abstract]).

In additional, all journal article titles and abstracts available online as of the 31 December 2016 from the main journals covering the field of zoo and wildlife medicine and surgery were read for any reference or relevance to surgery (see table 1). In two journals, Journal of the American Veterinary Medical Association (JAVMA), and the Veterinary Record, due to the high number of articles with frequent publication, abstracts read for screening were limited to those with the surgery specific half of the keywords, as listed above.

All article titles and abstracts were entered in to an Excel 2007 (Microsoft) sheet and duplicates removed. Duplication was checked by two authors.

Studies were evaluated for inclusion using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart (Moher and others 2009; Beller and others 2013), (see figure 1). Abstracts where no surgery was performed were excluded. Dental procedures were excluded. Abstracts involving small exotic pet rodents, rabbits, ferrets, pot belly pigs as well as those involving farmed South American camelids, water buffalo and deer, where the procedure was not of likely relevance to captive or free ranging wild animals (for example, antler harvesting in farmed deer) were further excluded. Opinionated reviews (non-systematic), letters, non peer-reviewed contributions, and expert opinions were excluded, as level 5 evidence on the Oxford scale of evidence based medicine (Howick and others 2011a,b). Abstracts where no indication of animal numbers were given, were also omitted.

For the purpose of this study surgical complications were defined as 'Any deviation from the normal postoperative course' (Clavien and others 1992). Classification was adopted from (Clavien and others (1992) and Dindo and others (2004), but to include peri-operative complications, and adverse surgical outcomes. Surgical outcome was defined as the result of the surgical intervention. The outcome was deemed as favourable if (1) The aim of the surgical procedure was attained, (2) The patient returned to similar or improved functionality as before the surgery, with no adverse effect on the quality of life, and (3) The patient survived for at least a period of 6months after the procedure, without any major complications arising from the surgery; or the patient died/ was euthanized during the 6 months' post-operative period for reasons unrelated to the surgical procedures. Surgical outcome was considered as adverse if (1) The patient died or was euthanized peri-operatively or postoperatively because of major surgical or anaesthetic complications, or (2) the surgical procedure was unable to fulfil its original aim, or (3) the quality of life of the patient was affected negatively, or (4) surgical intervention was found to be unnecessary, or (5) any major complications arising due to the surgical procedure, such as, repeated surgical interventions because of the failure of the previous surgery.

Summation of all complications (including adverse outcomes) reported and all patient numbers in the abstracts were calculated to yield a publication complication rate, with 95% confidence intervals calculated, for study type, primary article focus, taxonomic group, and surgical discipline.

Statistical analysis was performed with Minitab 17 (Minitab Inc.), Confidence Interval Analysis 2.2 (University of Southampton), and Review Manager (RevMan) 5.3 (The Cochrane Collaboration). Data was examined for normality using Anderson-Darling Normality test. The studies bias was assessed using the Cochrane Collaborations RoB (Risk of Bias) tool (Higgins and Green, 2011). 95% Confidence intervals were calculated for all proportions (rates), medians, and summations.

RESULTS

After removal of duplication and the initial screening for any relevance, a total of 1123 articles were entered into the database, of which 635 were finally suitable for inclusion in the analysis after exclusions (see figure 1 flow chart). The data was non-parametric, as was anticipated.

The majority of publications were single case reports 59.69% (95% CI 55.82-63.43%, SE 1.95, n=379), the same proportion when only considering primary surgical publications (59.47%, 95% CI 53.45-65.22%, SE 3.02, n=157). Only 15.19% (12.54-18.11%, SE 1.42, n=96) of publications contained more than 10 animals, although this rose to 25% (20.16-30.56%, SE 2.67, n=66) when considering only primary surgical publications. The number of animals included in studies are categorised in table 2.

All included studies were level 4 evidence on the Oxford Centre for Evidence Based Medicine scale, except for 2.83% (95% CI 1.8-4.43%, SE 0.66, n=18) of all the papers (n=689) which met the criteria for level 3 evidence. Of these 66.66% (95% CI

43.75-83.72%, SE 11.1, n=12) were on avian surgery, with the majority being columbiforms (66%, 95% CI 39.62-86.19%, SE 13.6, n=8).

Median complication rate for all papers was 0% (95%CI of 0-0%), as it was for all groupings of papers; the median complication rate for primary surgery papers with more than 10 cases was also 0% (95% CI of 0-1.99%). Summation of all complications (including adverse outcomes) reported and all patient numbers are given in tables 2, 3, 4 and 5.

The complication rate calculated from summation across all papers was 5.67% (95% CI 5.12-6.24%, SE 0.28; n studies=635, n cases=372/6582). The complication rate calculated from summation across all primary surgery focused papers was a similar 5.98% (95% CI 5.23-6.83%, SE 0.41; n studies=264, cases n=202/3377).

The highest published summated complications rate was in single case reports (table 2), where this was found to be 25.33% (95% CI 21.21-29.94%, SE 2.23, n=379). There was a highly statistically significant difference between the summated reported complications rate between single case reports and studies including more than 10 animals of 21.16% (95% CI of the difference 17-25.8%, SE 2.25, p<0.001, Z=9.39). This was similar when limited to publications who's primary focus was surgery, with a difference of 17.44% (95% CI of the difference 11.58-24.6%, SE 3.34, p<0.001, Z=5.21).

Amongst major taxonomic groups primates had the lowest summated complication rate, while reptiles had the highest (table 4). There was a statistically significant difference in reported complications between birds and reptiles of 3.95% (95% CI of the difference 1.74-6.7%, SE 1.25, Z 3.16, p<0.005)

Papers focusing on oncology and/or pathology, rather than the surgical aspects of studies reported a statistically highly significant greater rate of surgical complications than papers primarily focusing on surgical aspects of cases or studies, a difference of 13.89% (95% CI of the difference 8.32-20.88%, SE 3.22, Z 4.31, p<0.001). In contrast primarily anaesthesia focused papers reported a lower complication rate than surgically orientated papers, a difference of 4.71% (95% CI of the difference 3.29-5.77%, SE 0.6, Z 7.8, p<0.001) (table 3).

In surgical disciplines neurosurgery and ophthalmic surgery had the highest reported complications, statistically significantly higher than that of soft tissue, or surgery overall, despite having small numbers of published studies and individual cases (table 5). The complications reported were highly statistically significantly higher in orthopaedic surgical studies in comparison to soft tissue surgery, a difference (absolute risk reduction) of 10.23% (95% CI of the difference 7.12-13.89%, SE 1.73, Z 5.92, p< 0.001). Reproductive surgery studies had the lowest reported complications.

Papers that reported surgical novelty had low reporting of complications, with only a 2.21% (95% CI 1.6-3.04%, SE 0.36, n=121 papers) summated complication rate. This differed highly significantly from the general primary surgical publication complication rate by being 3.77% (95% CI of the difference of 2.65-4.82%, SE 0.55, p<0.001) lower (absolute risk reduction).

DISCUSSION

Initial attempts to classify the nature of studies from the abstracts were problematic, and hence studies were simply classified as to levels on the Oxford scale of evidence based medicine (Howick and others 2011a,b), with the majority of publications being level 4. While the majority of small studies (containing less than 9 animals) were best categorised as case series, some studies including 10 or more animals were problematic to categorise, with many unclear as to whether they were retrospective or prospective in nature from how the abstract was written. Further, many abstracts used non-standardised descriptions of the type of study, while failing to meet standard criteria (Grimes and Schulz 2002). It was out with the scope of this study to read all 635 publications fully and in detail to accurately ascertain their precise classification.

It was interesting however, that the taxonomic group best represented with level 3 studies were birds, and particularly pigeons. This is likely because they are a practical and inexpensive experimental model for well designed studies of relevance to other bird species. These studies may not be primarily aimed at free ranging or zoo birds, but rather the large population of pet and breeder birds, that carries financial incentives for optimal treatment by veterinary clinicians in practice and clinical academic hospital.

A major limitation to the interpretation of the results of this study, is that true complication rates in specific wildlife taxonomic groups and species are largely unknown, with even the best published studies focused on specific conditions or procedures.

However, recently Sharma (2016) found an overall surgical complication rate (including adverse outcomes) of 31.6% (95% CI 26.33-37.38%, SE 2.83, n=269) for birds and 40% (95% CI 31.51-49.14%, SE 4.57, n=115) for reptiles, from a comprehensive review of all surgical procedures performed at major zoological collections in the United Kingdom over a 25 year period. In contrast, this study found a statistically significant lower reported rate of complications in the published literature for birds of only 3.71%, a difference between Sharma (2016) and the literature summed complication rate of 27.89% (95% CI of the difference in proportions 22.55-33.72%, SE 2.87, $p<0.001$). In reptiles this study found a statistically significant lower reported rate of complications in the published literature of only 7.66%, a difference of 32.34% (95% CI of the difference in proportions 23.45-41.69%, SE 4.71, $p<0.001$) from Sharma (2016).

Sharma (2016)found complex orthopaedic procedures (fracture repairs) (OR 7.69, 95%CI 1.40 to 42.01, p-value 0.019) were the major risk factors for the an adverse outcomes in birds. While the published avian orthopaedic complication rate was higher than other avian surgical procedures, these are still notably lower than the general avian surgery complication rate found by Sharma (2016).

It hence appears likely that the published peer-reviewed wildlife surgery literature is notably biased. Positive publication bias (Pannucci and Wilkins 2010; Kanaan and others 2011; Richards and Burrett 2013) is likely influencing the literature overall, although it would be expected to particularly affect single case reports and small series. Positive publication bias is the publication or non-publication of research findings, depending on the nature and direction of results (Lacchetti and others 2002; Chalmers 2007; Pitak-Arnnop and others 2010; Richards and Burrett 2013). With limited time and resources, clinicians are likely favouring writing and submitting cases and series with positive outcomes and less complications and adverse effects. Positive outcome cases and case series, may be simpler to write. Review may also have some influence on positive publication bias, with rebuttal and revisions being easier to achieve with straight forward cases without complications or adverse outcomes (Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Kanaan and others 2011; O'Neil and others 2014; Cooper and others 2015).

Larger studies should be better powered statistically to detect and determine outcomes and complications accurately, although almost no studies included in this study mentioned power calculations in their abstract, also a notable problem in the human surgical literature (Dimick and others 2001; Bailey and others 2004; Walter and others 2007; Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Ayeni and others 2012; Greenland and others 2016). Interestingly, in this systematic review of abstracts, larger studies with more than 10 animals reported far fewer complications and adverse outcomes than the single case reports. It seems less likely this is due to positive publication bias, and it may be likely that the majority of this is due to outcome reporting bias. Outcome reporting bias is the selective reporting of some outcomes but not others, depending on the nature and direction of the results (Moher and others 2009; Pannucci and Wilkins 2010; Kanaan and others 2011). Larger studies may contain more data, information, and complexity competing within the limited word count of the abstract for inclusion. It appears that complications are likely under reported in abstracts, although the full papers, or ideally the original data, would need to be analysed and compared to confirm or refute this possibility.

There is a risk of readers assuming that larger studies would have more robust evidence, and believing in a false low complication rate gleaned from the abstract. This could adversely impact surgical decision making, with wildlife veterinarians and conservation managers having unrealistically optimistic expectations regarding surgical interventions, and resulting in poorer than expected outcomes, with increased complications, adverse outcomes, and mortalities.

In publications that have a primary focus other than surgery, such as anaesthesia, surgical complications and outcomes may not be judged to be the focus of the study, or of importance to the anaesthesia aspects, hence their omission from abstracts.

It also remains possible that many submitting authors feel it necessary to put as positive a description on published cases or studies as possible for reasons of professional reputation, or even commercial or clinical competitiveness. This possibility appeared to be apparent in the large number of publications that were evaluated to be showcasing surgical novelty. These studies also had a particularly low rate of reported complications and adverse outcomes in comparison to primary surgical publications.

Journal abstracts are possibly the most important part of a published peer-reviewed study, with readers relying on the information provided in an abstract when deciding whether to read the full text of an article (Islamaj Dogan and others 2009). Due to time pressures veterinarians may only read abstracts when searching for information on a specific case (Bigna and others 2016). Many wildlife veterinarians work outside academic institutions, in developing countries, where access to full text articles is not possible, and may only have access to abstracts to inform their clinical decision making. It is essential that reviewers and journal editors ensure abstracts accurately and adequately detail surgical complications and adverse outcomes in the field of wildlife surgery.

CONCLUSION

There appears to a high likelihood of positive publication bias and outcome reporting bias in current peer-reviewed wildlife surgery publications, evident from the results of this study. Complications and adverse outcomes appear to be less likely to be reported in the abstracts of larger studies, even if these are primarily surgical studies. On the basis of these findings wildlife veterinarians using published peer-reviewed abstracts as a basis for clinical decision making are urged to be cautious as to expected outcomes, complication rates, and adverse effects. It should be anticipated that these may be notably higher than reported in peer-reviewed journal abstracts. Reviewers should further ensure that authors adequately report complications and adverse surgical outcomes in publication abstracts.

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Figure 1: Flowchart of the systematic review of wildlife surgical complications reported in peer-reviewed journal article abstracts (Modified from Moher et al, 2009)

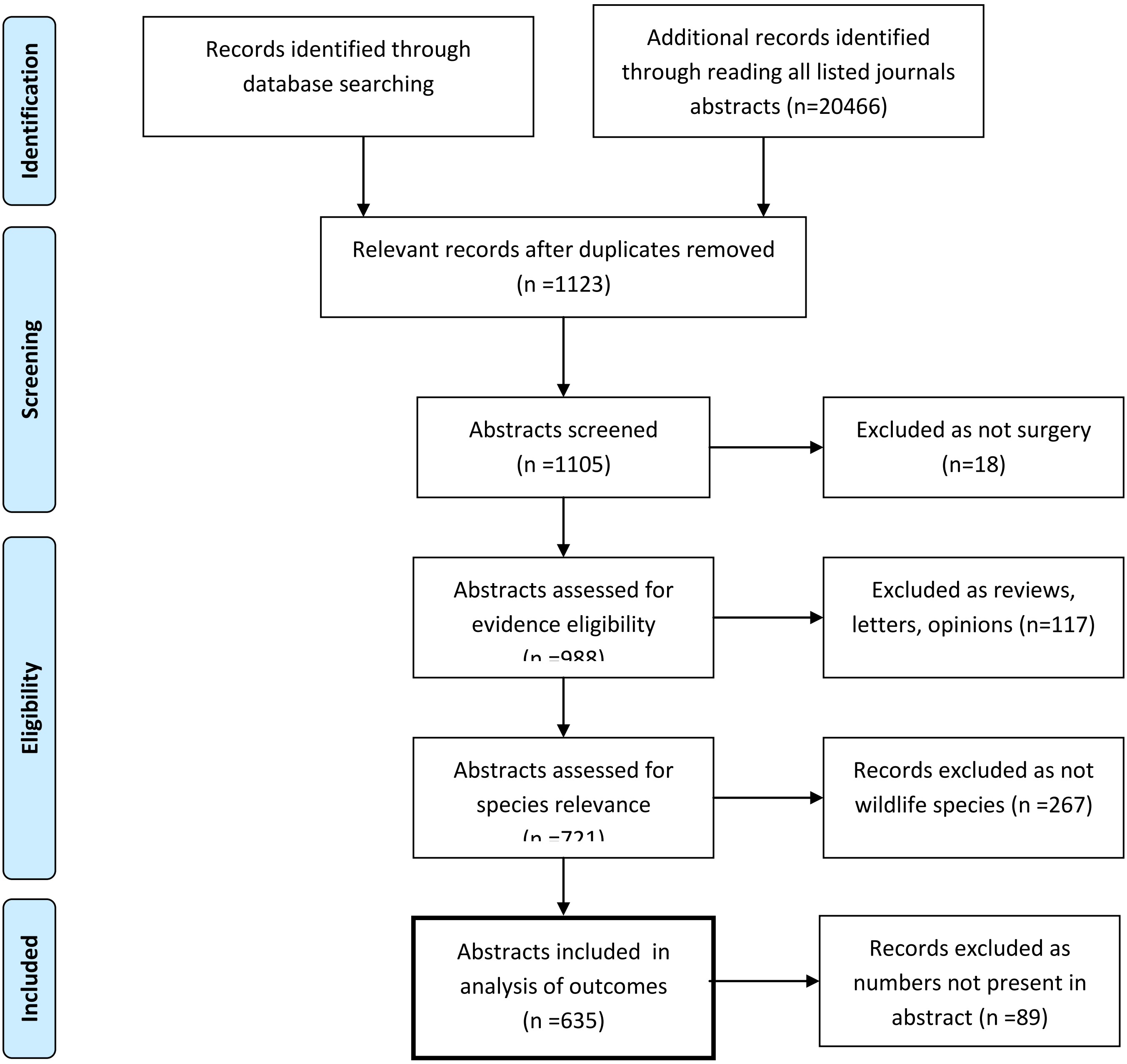

Table 1: Journal abstracts (to 31 December 2016) read for any reference or relevance to surgery. Journal of the American Veterinary Medical Association and Veterinary Record abstracts were limited to those with surgery keywords

Journal	**Dates**	**Journal years**	**Total journal abstracts screened**	**Surgery papers**	**Primary surgical papers**
Journal of Zoo & Wildlife Medicine	1997-2016	19	2100	11.9% (n=250)	32% (n=80)
Journal of Avian Medicine & Surgery	2007-2016	9	386	21.24% (n=82)	48.78%(n=40)
Journal of Wildlife Diseases	1975-2016	41	5004	0.88% (n=44)	25% (n=11)
Journal of Herpetological Medicine & Surgery	2009-2016	5	102	22.55% (n=23)	52.17% (n=12)
Veterinary Surgery	1987-2016	29	2856	0.56% (n=16)	100% (n=16)
Journal of Exotic Pet Medicine	2006-2016	10	395	1.77% (n=7)	71.43%(n=5)
Vet Clinics of North America - Exotic Animal Practice	2001-2016	15	661	0.76% (n=5)	20% (n=1)
Journal of Medical Primatology	1972-2016	44	2047	0.24% (n=5)	20% (n=1)
Journal of the American Veterinary Medical Assoc *(surgery only)*	1975-2016	41	4489	2.94% (n=132)	53.03% (n=70)
Veterinary Record *(surgery only)*	1945-2016	71	2426	2.56% (n=62)	56.45%(n=35)
Total abstracts read for screening			**20466**	**3.07% (n=628)**	**40.3% (n=293)**

Table 2: Published surgical complications reported by study size

Study type	Complications	95% CI	St Error	Studies	Individual cases
All abstracts	5.67%	(5.12-6.24%)	0.28	n=635	n=6582
All primary surgery abstracts	5.98%	(5.23-6.83%)	0.41	n=264	n=3377
Single case reports (all)	25.33%	(21.21-29.94%)	2.23	n=379	n=379
Single case reports (Primarily surgery)	22.29%	(16.49-29.42%)	3.32	n=157	n=157
Small case series <9 (all)	13.78%	(10.98-17.15%)	1.57	n=115	n=479
Small case series <9 (Primarily surgery)	10.33%	(6.71-15.56%)	2.24	n=44	n=184
Studies >10 cases (all)	4.17%	(3.63-4.78%)	0.29	n=99	n=4726
Studies >10 cases (Primarily surgery)	4.85%	(4.14-5.68%)	0.39	n=66	n=3009
Level 3 OEBM evidence > 10 cases, comparative	7.82%	(5.95-10.21%)	1.08	n=21	n=614

Table 3: Published surgical complications reported by primary journal article focus

Primary article focus	Complications	95% CI	St Error	Studies	Individual cases
Primary surgery	5.98%	(5.23-6.83%)	0.41	n= 264	n=3377
Primarily oncology/pathology	19.87%	(14.37-26.82%)	3.19	n= 64	n=156
Primarily anaesthesia	1.27%	(0.64-2.48%)	0.45	n= 25	n=623

Table 4: Published surgical complications by taxonomic group

Primary article focus	Complications	95% CI	St Error	Studies	Individual cases
Mammals	4.67%	(3.4-6.36%)	0.75	n=112	n=793
Primates	1.86%	(0.9-3.78%)	0.7	n=21	n=377
Carnivores	4.30%	(2.2-8.26%)	1.49	n=45	n=186
Birds	3.71%	(2.96-4.63)	0.42	n=74	n=1996
Reptiles	7.66%	(5.66-10.3%)	1.18	n=60	n=509

Table 5: Published surgical complication rates by discipline (not mutually exclusive)

Surgical discipline	Complications	95% CI	St Error	Studies	Individual cases
Soft tissue surgery	5.57%	(4.97-6.24%)	0.32	n=459	n=5118
Reproductive surgery	1.17%	(0.8-1.71%)	0.23	n=86	n=2226
Oncological surgery	19.87%	(14.37-26.82%)	3.19	n= 64	n=156
Orthopaedic surgery	15.80%	(12.76-19.41%)	1.7	n=124	n=462
Neurological surgery	21.43%	(10.21-39.54%)	7.75	n=17	n=28
Opthalmic surgery	20.25%	(12.87-30.4%)	4.52	n=38	n=79
Surgical novelty	2.21%	(1.6-3.04%)	0.36	n=121	n=1629

<u>3.2. Study 2:</u> *Complications of open versus minimally invasive surgery in wildlife: A systematic review and indirect comparison meta-analysis*

Complications of open versus minimally invasive surgery in wildlife: A systematic review and indirect comparison meta analysis

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ABSTRACT

A systematic literature review was performed, with indirect comparison meta analysis of studies in wildlife surgery, evaluating complications between different taxa undergoing open surgery or minimally invasive surgery (MIS) of the abdomen or coelomic cavity. PRISMA guidelines for systematic reviews and the Cochrane manual were used for guidance. Databases searched were MEDLINE, CAB Abstracts, Scopus, and Zoological Record. Only two publications directly compared MIS and open surgery, and the meta analysis results, while appearing to favour MIS, were not statistically significant. 243 individual studies met the search criteria for open or MIS surgery of the abdomen or coelomic cavity in wildlife species, of which only 50 studies included 10 or more individuals. Individual patients and reported complications were summated from all studies, according to taxa, to calculate total published complication rates. Across all wildlife species a 6.54% absolute risk reduction (95% confidence interval [CI] of the difference 5.08-8.14%, SE 0.78%, $p<0.001$) was evident in publications of MIS surgery compared to open abdominal or coelomic surgery. There was a statistically significant lower complication rate across all analysed taxa (mammals, birds, reptiles, fish), with the greatest difference of 17.61% (95% CI of the difference 12.21-23.82%, SE 2.94%, $p<0.001$) between reptiles undergoing open versus MIS coelomic cavity surgery. Available published data appears overall to demonstrate MIS has statistically significant superior outcomes in comparison to open abdominal and coelomic cavity surgery in wildlife. However, the evidence is at high risk of bias, with the only two direct comparison studies failing to demonstrate a statistically significant difference. Studies examined for the two types of surgery were not directly comparable in taxa, surgical procedure, or pathology. There appeared to be a high likelihood of publication bias and outcome bias, and the conclusions must be interpreted with caution.

Keywords: *wildlife; surgery; systematic review; zoo; endoscopy; minimally invasive*

INTRODUCTION

Minimally invasive surgical (MIS) techniques are commonly performed in humans, with many procedures regarded as the gold standard in developed countries (van Dijk and others 2014; Küper and others 2014; Antoniou and others 2015; Coccolini and others 2015a; Mandrioli and others 2016). There have been systematic reviews and meta analysis in human surgery, demonstrating advantages such as lower complication rates and better outcomes in laparoscopic versus open surgery for common procedures such as cholecystectomy (Laurence and others 2012; Cheng and others 2012; de Goede and others 2013; Coccolini and others 2015b; Sedaghat and others 2017), and appendectomy (Meynaud-Kraemer and others 1999; Garbutt and others 1999; Temple and others 1999; Aziz and others 2006; Markides and others 2010; Ciarrocchi and Amicucci 2014), as well as for other surgical procedures such as hernia repair, adhesiolysis, and oncology staging and resections (Sajid and others 2009, 2016; Zullo and others 2012; Li and others 2012, 2014; Ha and others 2016; Xiong and others 2017).

MIS in domestic companion animals has also been demonstrated to have patient benefits over open surgery in several studies (Sánchez-Margallo and others 2017; Culp and others 2009; Shariati and others 2014; Mayhew and others 2014; Gauthier and others 2015), although at present no systematic review or meta analysis has been performed (Katic and Dupré 2016). Domestic animals have further functioned as important models for human laparoscopic surgical research and human surgeon training (Usón Gargallo and others 2006; Sanchez-Margallo and others 2011; Yiannakopoulou and others 2013; Sánchez-Margallo and others 2014, 2017; Beyer-Berjot and others 2014; Díaz-Güemes and others 2015; Tapia-Araya and others 2016; Correa-Martín and others 2016).

Some studies, case reports and case series on MIS in captive or free ranging wildlife species have been published, but currently evidence is limited by the inclusion of small numbers of animals, disparate taxonomic groups and species, differing anatomy, pathological processes, and surgical procedures, and studies frequently have no comparative aspect, and may be published in a variety of difference journals, as the impact factor of zoo and wildlife focused journals is relatively low (Hernandez-Divers and others 2009; Stetter 2010; Pizzi and others 2011; Steeil and others 2012; Marais and others 2013; Campbell-Palmer and others 2015; Pizzi 2015; Divers 2015).

Wildlife veterinarians may be working in developing countries, and outside of academia, and access to full text articles from a wide variety of different journals, many of which are behind a pay-wall, may not be practical or affordable. Without a specific database search, wildlife veterinarians may simply be unaware of developments in the field of MIS as it applies to the wildlife species they treat. Even when an electronic internet database is used to search the peer-reviewed published literature for evidence upon which to base clinical decisions, it has been demonstrated through PubMed user log analysis that the majority of researchers predominately only read titles and abstracts, rather than consulting full papers (Islamaj Dogan and others 2009).

Opinionated (non-systematic) reviews and book chapters are at present likely an important source of information in wildlife MIS for wildlife veterinarians (Stetter 2010; Divers 2010a,b,c, 2015; Innis 2010; Pizzi 2012, 2015; Chai 2015; Desmarchelier and Ferrell 2015; Proença and Divers 2015). Systematic reviews, in contrast, provide a structured summary of the results of trials that have been carried out on any particular subject (Altman 2015). If the data from multiple trials are sufficiently homogenous, a meta-analysis can then be performed to calculate pooled effect estimates. (Haidich 2010; Garas and others 2012) However traditional meta-analysis involves groups of trials that compare the same two interventions directly (head to head), and if this type of data is not available indirect comparison may be required (Hoaglin and others 2011; Kiefer and others 2015).

This study aims to evaluate the current published peer-reviewed literature comparing complication rates between MIS and open surgical procedures in captive and free ranging wildlife species.

MATERIALS AND METHODS

A search of the published peer-reviewed veterinary literature was performed using MEDLINE, CAB Abstracts, Scopus, Zoological Record, as shown to have comprehensive coverage of veterinary journals (Grindlay and others 2012). Search terms used (MEDLINE) were:

((((((((((((((zoo[Title/Abstract]) OR wildlife[Title/Abstract]) OR wild[Title/Abstract]) OR zoological[Title/Abstract]) OR exotic[Title/Abstract]) OR exotic animal[Title/Abstract]) OR primate[Title/Abstract]) OR avian[Title/Abstract]) OR bird[Title/Abstract]) OR reptile[Title/Abstract]) OR reptilian[Title/Abstract])) OR herpetolog*[Title/Abstract])) AND (((((((((((((((surgery[Title/Abstract]) OR surgical[Title/Abstract]) OR operation[Title/Abstract]) OR operativ*[Title/Abstract]) OR biops*[Title/Abstract]) OR incision*[Title/Abstract]) OR incise*[Title/Abstract]) OR excision*[Title/Abstract]) OR excise*[Title/Abstract]) OR resect*[Title/Abstract]) OR sutur*[Title/Abstract]) OR endoscop*[Title/Abstract]) OR laparoscop*[Title/Abstract]) OR minimally invasive[Title/Abstract]) OR MIS[Title/Abstract]).

In additional, all journal article titles and abstracts available online as of the 31 December 2016 from the main journals covering the field of zoo and wildlife medicine and surgery were read for any reference or relevance to open or MIS abdominal or coelomic cavity surgery (see table 1). In two journals, Journal of the American Veterinary Medical Association (JAVMA), and the Veterinary Record, due to the high number of articles with frequent publication, abstracts read for screening were limited to those with the surgery specific half of the keywords, as listed above.

All article titles and abstracts were entered in to an Excel 2007 (Microsoft) sheet and duplicates removed. Duplication was checked by two authors.

Studies were evaluated for inclusion using a modified Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart (Moher and others 2009; Beller and others 2013), (see figure 1). Abstracts involving small exotic pet rodents, rabbits, ferrets, pot belly pigs as well as those involving farmed South American camelids, water buffalo and deer, where the procedure was not of likely relevance to captive or free ranging wild animals were excluded. Opinionated reviews (non-systematic), letters, non peer-reviewed contributions, and expert opinions were excluded, as level 5 evidence on the Oxford scale of evidence based medicine (Howick and others 2011a,b). Studies where no abdominal or coelomic surgery was performed, as well as post-mortem studies, were excluded. Studies where no accurate indication of animal numbers, or reasonable reporting of complication and outcome numbers were included, were also omitted.

For the purpose of this study surgical complications were defined as ‘Any deviation from the normal postoperative course (Clavien and others 1992). Classification was adopted from Clavien and others (1992) and Dindo and others (2004), but to include peri-operative complications, and adverse surgical outcomes. Surgical outcome was defined as the result of the surgical intervention. The outcome was deemed as favourable if (1) The aim of the surgical procedure was attained, (2) The patient returned to similar or improved functionality as before the surgery, with no adverse effect on the quality of life, and (3) The patient survived for at least a period of 6months after the procedure, without any major complications arising from the surgery; or the patient died/ was euthanized during the 6 months’ post-operative period for reasons unrelated to the surgical procedures. Surgical outcome was considered as adverse if (1) The patient died or was euthanized peri-operatively or postoperatively because of major surgical or anaesthetic complications, or (2) the surgical procedure was unable to fulfil its original aim, or (3) the quality of life of the patient was affected negatively, or (4) surgical intervention was found to be unnecessary, or (5) any major complications arising due to the surgical procedure, such as, repeated surgical interventions because of the failure of the previous surgery.

Statistical analysis was performed with Minitab 17 (Minitab Inc.), Confidence Interval Analysis 2.2 (University of Southampton), and RevMan Review Manager 5.3 (The Cochrane Collaboration). Data was examined for normality using the Anderson-Darling Normality test. Summation of all complications (including adverse outcomes) reported and all patient numbers in the abstracts were calculated to yield a publication complication rate. 95% Confidence intervals were calculated for all proportions (rates), medians, summations, and their differences to facilitate clinical decision making as recommended by the International Committee of Medical Journal Editors (ICMJE 1988) and others (Altman 1998, 2005, 2015; Greenland and others 2016). Power calculations were performed to estimate adequate sample sizes need to detect with 95% confidence a 50% difference in relative risk reduction of a baseline complication rate of 10% in open surgery to a 5% complication rate in MIS.

RESULTS

After removal of duplication and exclusion after screening for relevance and eligibility, a total of 243 articles were included for analysis (see figure 1 - flow chart). The data was non-parametric, as was anticipated. Power calculation at a 95% confidence level to detect a 50% relative risk reduction from a baseline of 10% complications in open surgery to 5% complications in MIS yielded a desired sample size of 719 for each group, indicating the total was adequately powered to eliminate a type II error for this anticipated difference, with individual patients from all open surgery studies totally 1498, and patients from MIS studies totalling 2447. However further subdivisions of the data would result in underpowered comparisons.

The majority of published open surgery studies, 66% were single individual case reports (95% CI 58.62-72.8%, SE 3.65%, n=111), whereas only 41.33% of published MIS reports were single case reports (95% CI 30.88-52.63%, SE 5.69%, n=31), a statistically significant difference of 24.74% (95% CI of the difference in proportions 11.2-37.17%, SE 6.76%).

Similarly only 15.48% of published open surgery studies contained 10 or more patients (95% CI 10.79-21.71%, SE 2.79, n=26), while 45.33% of MIS studies contained 10 or more patients (95% CI 34.57-56.55%, SE 5.75, n=34), a statistically significant difference of 29.86% (95% CI 17.42-42.02%, SE 6.39, Z=4.67, p<0.001).

Of the open surgical studies, only 8.93% (95% CI 5.49-14.21%, SE 2.2, n=15) contained 10 or more patients and were primarily surgery focused, and only 2.98% (95% CI 1.28-6.78%, SE 1.31, n=5) had higher than level 4 evidence on the Oxford scale of evidence based medicine (Howick and others 2011a,b). Of the MIS wildlife studies 42.67% (95% CI 32.1-53.95%, SE 5.71, n=32) included 10 or more patients and were primarily surgery focused, a statistically significant difference of 33.74% (95% CI of the difference 21.93-45.53%, SE 6.12). In MIS studies 14.67% (95% CI 8.39-24.38%, SE 4.09, n=11) had higher than level 4 evidence on the Oxford scale of evidence based medicine, although the difference from open surgery was not significant statistically.

Only two publications directly compared MIS and open surgery. Boone and others (2008) performed a randomised controlled trial comparing open coeliotomy and MIS liver biopsies in channel catfish (*Ictalurus punctatus*), with 10 fish in either group, and compared to a control group of 10 fish. 30% (n=3/10) of the coeliotomy fish experienced severe wound dehiscence, which did not occur in the MIS operated fish; an absolute risk reduction of 30% (95% CI of the difference -37.6% to 60.32%, SE 14.49, p=0.34), which was not statistically significant. Steeil and others (2012) performed a comparison of laparoscopic ovariectomy performed in seven tigers with the use of a vessel-sealing device and a three-port technique, to a retrospective group assembled from a medical record search that underwent traditional ovariohysterectomy. They found differences in mean surgical time and combined incision length, but no clinically important complications were observed in either group. A forest plot and analysis of the combined results are given in figure 2. The results, while appearing to favour MIS, were not statistically significant.

Median complication rate for all MIS studies was 0% (95% CI 0-0%) and all open studies was also 0% (95% CI 0-0%), with the 95% CI of the difference in medians 0-0%.

Individual patients and reported complications for all 243 studies were summated according to taxonomic group (table 2), to calculate total published complication rate in taxa and in open surgery versus MIS. Calculated differences between open surgery and MIS for the total and individual taxa are given in table 3. Differences were statistically significant in all taxa examined (mammals, birds, reptiles, fish), and overall. A forest plot was performed on the data (figure 3), with the risk ratio for all taxa individually and combined favouring MIS as having a lower risk of complications or adverse outcomes.

A similar analysis combining individual patients and reported complications, but only for studies that included 10 or more individuals was performed (table 4), to again calculate total published complication rate in taxa and in open surgery versus MIS. Calculated differences between open surgery and MIS for the total and individual taxa are given in table 5. Differences were statistically significant in the individual taxa examined, and overall, with the exception of mammals, where open surgery had a 0.11% lower complications and adverse outcomes rate (95% CI -2.19 to 1.46%, SE 0.8, p=0.887), although this was not statistically significant. A forest plot performed on the data (figure 4), with the risk ratio for all taxa individually and combined, demonstrated similar findings, favouring MIS as having a lower risk of complications or adverse outcomes in all taxonomic groups and combined, with the exception of mammals, where there was no statistically significant difference.

The forest plot was repeated excluding a single potential outlier MIS study (Marais and others 2013) (figure 5), and did not fundamentally alter the findings. The difference between complications and adverse outcomes in mammals was still not statistically significant despite appearing to favour MIS with a difference of 1.18% lower complications(absolute risk reduction) (95% CI of the difference -0.39 to 2.54%, SE 0.48, p=0.07). Heterogeneity was acceptable in the forest plot of all combined studies (figure 2), with I^2=43%.

The largest difference in outcomes was for reptiles, with a highly statistically significant difference in combined complications rates (absolute risk reduction) between open surgery and MIS of 17.61% (95%CI of the difference in proportions

12.21-23.82%, SE 2.94, p<0.001), favouring MIS, and this difference appeared even greater when only considering studies including 10 or more animals (20.76% absolute risk reduction, 95% CI 14.52-28.28%, SE 3.5, p<0.001)

DISCUSSION

As with any systematic review and meta analysis the results are dependent on the quality of evidence available to the reviewers (Garbutt and others 1999; Temple and others 1999; Bailey and others 2004; Slim 2005; Chalmers 2007; Walter and others 2007; Mittal and Perakath 2010; Haidich 2010; Kanaan and others 2011; Hoaglin and others 2011; Ayeni and others 2012; Garas and others 2012; Stewart and others 2015; Coccolini and others 2015b). The low number of studies actually comparing open and MIS abdominal or coelomic surgery limited the application of classic meta analysis and forest plot depictions. An indirect comparison was hence performed (Hoaglin and others 2011), but it is acknowledged that this has notable limitations. Included study design and generated evidence levels varied from individual case reports through to small randomised controlled trials. Different studies had different primary objectives, which were not always of a primary surgical focus, such as anaesthesia, assessment of diagnostic biopsy quality, and diagnostic sensitivity and specificity for specific pathology. These studies may have under reported complications, as these were not the primary focus of those publications. There was also inclusion of widely differing species and taxa, not directly comparable between the two surgery types, as well as varying and quiet different open and minimally surgery procedures. Studies varied from elective procedures on healthy animals, such as sterilisation, to diagnostic or operative procedures in ill animals with varying pathology and severity.

The small study sizes and small overall total patient numbers precluded any meaningful further subdivisions in order to try to better match animal patients according to species (or other more closely related taxonomic groups, than the categories presented in the results), procedure, study type (retrospective case series versus cohort studies), and the like, as indicated by the pre-study power calculations. Small sample sizes had a high likely hood of making type II statistical errors (failing to detect or demonstrate a true difference statistically) (Bailey and others 2004; Ayeni and others 2012), and risked leading to erroneous conclusions from the statistical analysis of this systematic review, and hence this was not pursued. Simply limiting mammalian publications to those only containing 10 or more individual patients, resulted in failure to detect a statistically significant difference.

While limiting included studies to those with 10 or more animals appeared to result in smaller differences in complication rates between open and MIS surgery in taxonomic groups (with the exception of reptiles), the difference in results between all studies (table 3), and only those containing 10 or more animals (table 5) was not statistically significant, for all taxonomic groups and total combined taxa. This is evident from the tables, which demonstrate widely overlapping 95% confidence intervals.

Failure to demonstrate a statistically significant difference in complication rates for mammalian publications containing 10 or more animals was further investigated. The effect appeared to be due to a combination of small group sample size, underpowered according to power calculations , and the inclusion of a single outlier study (Marais and others 2013), which reported results of 45 laparoscopic vasectomies in wild African elephants. A seperate publication including 14 of these elephants had previously be excluded in screening (Rubio-Martínez and others 2014). This surgery had a notably higher complication rate than other included mammal MIS studies with 10 or more animals. While open abdominal surgery elephants may, or may not, have markedly higher complication rates, this number of elephants was not matched at all in the mammal open surgery studies with 10 or more patients, introducing a potential source of bias. However repeating analysis and the forest plot with this study excluded, while appearing to then favour MIS, still failed to demonstrate a statistically significant difference in complication rate in mammals undergoing open or MIS abdominal surgery in publications with 10 or more individuals included (figure 5).

More of the included MIS publications had better design, being prospective cohort studies, with a primary surgical outcome focus, while in contrast open surgery studies were more often not primarily focused on the surgical outcomes, and included more pathology focused cases, while more MIS publications were elective surgery, such as sterilisation, on clinically healthy animals. This again was a potential source of bias, with the populations not directly comparable or suitable for matching. These factors do make this systematic review and meta analysis at high risk of bias (Burton and Clarke 2006; Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Haidich 2010; Higgins and Green 2011).

CONCLUSION

Available published data appears overall to demonstrate minimally invasive surgery has statistically significant superior outcomes in comparison to open abdominal and coelomic cavity surgery in wildlife. However, the evidence was at high risk of bias, with the only two direct comparison studies failing to demonstrate a statistically significant difference. There appeared to be a high likelihood of positive publication bias and positive outcome bias, and the conclusions should be interpreted with caution.

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Figure 1: Modified PRISMA flowchart of systematic review of wildlife open and minimally invasive surgery outcomes (Modified from Moher et al, 2009)

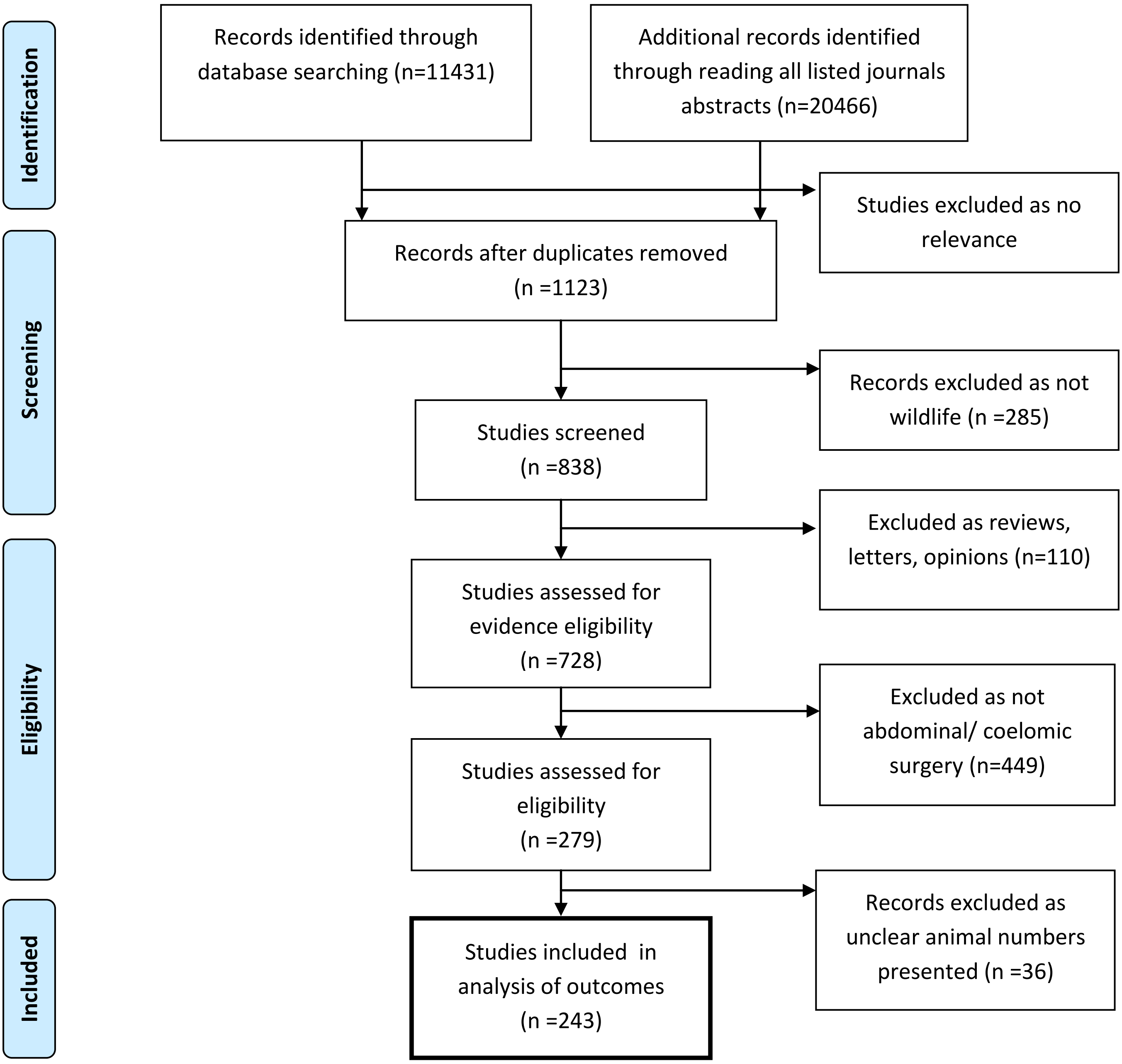

Figure 2: Forest plot of the two wildlife surgery publications with direct comparison of open and MIS abdominal or coelomic surgery

	Endosurgery		Open surgery			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Boone 2008	0	10	3	10	100.0%	0.14 [0.01, 2.45]
Steeil 2012	0	7	0	7		Not estimable
Total (95% CI)		**17**		**17**	**100.0%**	**0.14 [0.01, 2.45]**
Total events	0		3			

Heterogeneity: Not applicable

Test for overall effect: Z = 1.34 (P = 0.18)

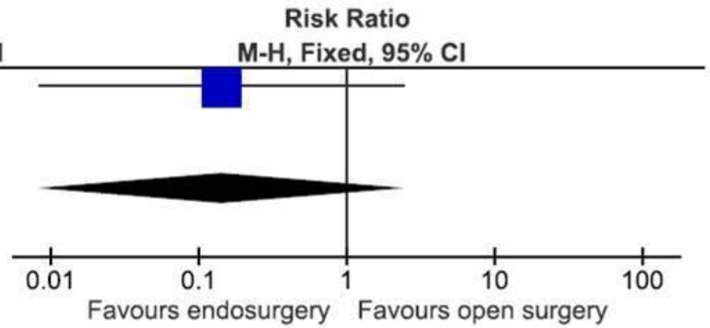

Figure 3: Forest plot of combined individual patients in all studies, and all complications reported, according to taxonomic group in an indirect comparison of open and MIS surgery in wildlife

	MI wildlife surgery		Open wildlife surgery			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Birds	33	1555	42	500	42.3%	0.2526 [0.1620, 0.3941]
Fish	3	213	12	170	8.9%	0.1995 [0.0572, 0.6957]
Mammals	7	360	36	633	17.4%	0.3419 [0.1537, 0.7603]
Reptiles	6	319	38	195	31.4%	0.0965 [0.0416, 0.2241]
Total (95% CI)		**2447**		**1498**	**100.0%**	**0.2144 [0.1526, 0.3012]**
Total events	49		128			

Heterogeneity: $Chi^2 = 5.29$, $df = 3$ ($P = 0.15$); $I^2 = 43\%$

Test for overall effect: $Z = 8.88$ ($P < 0.00001$)

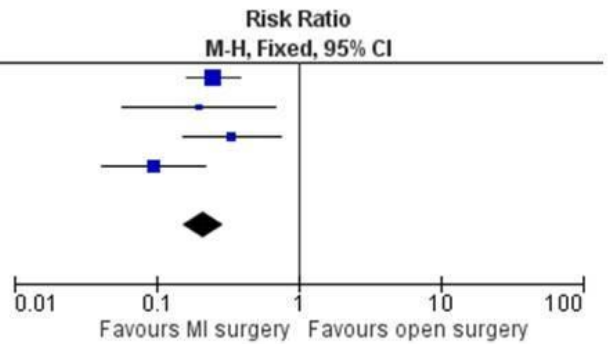

Figure 4: Forest plot of combined individual patients only in studies containing 10 or more animals, and all complications reported, according to taxonomic group in an indirect comparison of open and MIS surgery in wildlife

Study or Subgroup	MIS Events	MIS Total	Open surgery Events	Open surgery Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Birds (10+)	26	1532	32	450	47.1%	0.24 [0.14, 0.40]
Fish (10+)	3	213	9	158	9.8%	0.25 [0.07, 0.90]
Mammals (10+)	4	310	6	510	4.3%	1.10 [0.31, 3.86]
Reptiles (10+)	2	297	30	140	38.8%	0.03 [0.01, 0.13]
Total (95% CI)		**2352**		**1258**	**100.0%**	**0.20 [0.13, 0.29]**
Total events	35		77			

Heterogeneity: Chi² = 14.31, df = 3 (P = 0.003); I² = 79%

Test for overall effect: Z = 8.13 (P < 0.00001)

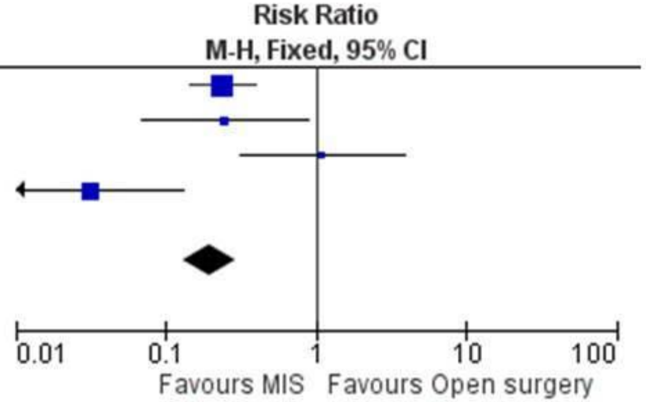

Figure 5: Forest plot of combined individual patients only in studies containing 10 or more animals, and all complications reported, according to taxonomic group in an indirect comparison of open and MIS surgery in wildlife, but excluding an outlier mammal MIS study (Marais and other, 2013)

Study or Subgroup	MIS Events	MIS Total	Open surgery Events	Open surgery Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Birds (10+)	26	1532	32	450	47.1%	0.24 [0.14, 0.40]
Fish (10+)	3	213	9	158	9.8%	0.25 [0.07, 0.90]
Mammals (10+)	0	265	6	510	4.2%	0.15 [0.01, 2.61]
Reptiles (10+)	2	297	30	140	38.8%	0.03 [0.01, 0.13]
Total (95% CI)		**2307**		**1258**	**100.0%**	**0.16 [0.10, 0.24]**
Total events	31		77			

Heterogeneity: Chi² = 8.15, df = 3 (P = 0.04); I² = 63%

Test for overall effect: Z = 8.41 (P < 0.00001)

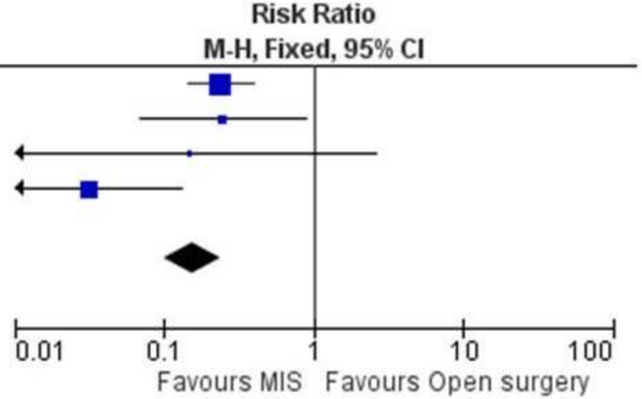

Table 1: Journal abstract screened by reading for surgery. * *Due to the high number of articles, abstracts read for screening were limited to those with surgery specific search words*

Journal	**Dates**	**Journal years**	**Total journal abstracts screened**	**All wildlife surgery papers**	**Open surgery & MIS papers included in final review**
Journal of Zoo & Wildlife Medicine	1997-2016	19	2100	11.9% (n=250)	4.38% (n=92)
Journal of Avian Medicine & Surgery	2007-2016	9	386	21.24% (n=82)	3.37% (n=13)
Journal of Wildlife Diseases	1975-2016	41	5004	0.88% (n=44)	0.28% (n=14)
Journal of Herpetological Medicine & Surgery	2009-2016	5	102	22.55% (n=23)	14.71% (n=15)
Veterinary Surgery	1987-2016	29	2856	0.56% (n=16)	0.25% (n=7)
Journal of Exotic Pet Medicine	2006-2016	10	395	1.77% (n=7)	0.76% (n=3)
Vet Clinics of North America - Exotic Animal Practice	2001-2016	15	661	0.76% (n=5)	0.15% (n=1)
Journal of Medical Primatology	1972-2016	44	2047	0.34% (n=7)	0.34% (n=7)
Journal of the American Veterinary Medical Association*	1975-2016	41	4489	2.94% (n=132)	1.14% (n=51)
Veterinary Record*	1945-2016	71	2426	2.56% (n=62)	0.95% (n=23)
Total abstracts included from read abstracts			**20466**	**3.07% (n=628)**	**1.1% (n=226)**

Table 2: Complication rates (summated) reported in open and minimally invasive surgery in all studies

Study type	Complications	95% CI	St Error	Studies	Individual cases
Mammals open surgery	5.69%	(4.14-7.77%)	0.92	69	633
Mammals MIS	1.94%	(0.95-3.96%)	0.73	29	360
Birds open surgery	8.40%	(6.27-11.16%)	1.24	31	500
Birds MIS	2.12%	(1.52-2.97%)	0.37	20	1555
Reptile open surgery	19.49%	(14.54-25.61%)	2.84	44	195
Reptiles MIS	1.88%	(0.86-4.04%)	0.76	21	319
Fish open surgery	7.06%	(4.08-11.93%)	1.96	13	170
Fish MIS	1.41%	(0.48-4.06%)	0.81	5	213
All species open surgery	8.54%	(7.23-10.07%)	0.72	168	1498
All species MIS	2.00%	(1.52-2.64%)	0.28	75	2447

Table 3: Difference (absolute risk reduction) in complication rates (summated) reported between open surgery and MIS in all studies

Absolute Risk Reduction (ARR)	Complication ARR	95% CI of the difference	St Error	Studies	Individual cases	Z	p-value
Mammals	3.74%	(1.2-6.06%)	1.17	98	993	3.19	p<0.005
Birds	6.28%	(3.99-9.1%)	1.29	51	2055	4.85	p<0.001
Reptiles	17.61%	(12.21-23.82%)	2.94	65	514	6	p<0.001
Fish	5.65%	(1.67-10.61%)	2.12	18	383	2.66	p<0.01
All species	6.54%	(5.08-8.14%)	0.78	243	3945	8.43	p<0.001

Table 4: Complication rates (summated) reported in open surgery and MIS in all studies including 10 or more animals

Study type	Complications	95% CI	St Error	Studies	Individual cases
Mammals >10 open surgery	1.18%	(0.54-2.54%)	0.48	10	510
Mammals >10 MIS	1.29%	(0.5-3.27%)	0.64	9	310
Birds >10 open surgery	7.11%	(5.08-9.87%)	1.21	7	450
Birds >10 MIS	1.70%	(1.16-2.48%)	0.33	9	1532
Reptile >10 open surgery	21.43%	(15.44-28.94%)	3.47	6	140
Reptiles >10 MIS	0.67%	(0.184-2.42%)	0.47	11	297
Fish >10 open surgery	5.70%	(3.03-10.47%)	1.84	2	158
Fish >10 MIS	1.41%	(0.48-4.06%)	0.81	5	213
All species >10 open surgery	6.12%	(4.93-7.58%)	6.76	26	1258
All species >10 MIS	1.49%	(1.07-2.06%)	0.25	34	2352

Table 5: Difference (absolute risk reduction) in complication rates (summated) reported between open surgery and MIS in studies including 10 or more animals **not statistically significant*

Absolute Risk Reduction (ARR)	Complication ARR	95% CI of the difference	St Error	Studies	Individual cases	Z	p-value
Mammals >10	-0.11%	***(-2.19-1.46%)****	0.8	19	820	0.14	***p=0.887***
Birds >10	5.41%	(3.24-8.22%)	1.26	16	1982	4.31	p<0.001
Reptiles >10	20.76%	(14.52-28.28%)	3.5	17	437	5.93	p<0.001
Fish >10	4.29%	(0.53-9.15%)	2.01	7	371	2.13	p<0.05
All species>10	4.63%	(3.31-6.15%)	0.72	60	3610	6.43	p<0.001

<u>**3.3. Study 3:**</u> *Captive wildlife surgery complication rates in zoological collections in the United Kingdom over a 25 years period*

Captive wildlife surgery complication rates in zoological collections in the United Kingdom over a 25 years period

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ABSTRACT

A pilot study was performed to assess the baseline number of all wildlife surgery patients in zoological collections affected by post-operative complications. Surgical records for a 25 year period ending in 2014, were reviewed from four zoological collections in the UK. A total of 1633 zoo surgical procedures were found. Across all wildlife species and surgical procedure types 22.84% (95% CI20.87-24.94%, SE 1.04%, n=1633) of wildlife surgical patients in the zoological collections in this study suffered from a surgical complication. 12.31% (10.8-13.99%, SE 0.81%) of wildlife surgical patients were affected by major or life threatening complications. Birds and reptiles had a statistically significant higher absolute risk of major complications compared to mammals of 9.38% (95% CI 5.32-13.91%, SE 2.19%). 56.81% of wildlife orthopaedic surgery patients across all species were found to have suffered from a post-operative complication, an absolute risk increase of 35.85% (95% CI of 25.14-45.98%, SE 5.42%, p<0.001) in comparison to soft tissue surgical procedures, and a major complication rate of 35.96%, and absolute risk increase of 24.44% (95% CI 14.98-34.97%, SE 5.19%, p<0.001). Wildlife surgery complication rates published in the peer-reviewed literature are notably lower than encountered in this study, at 5.67%, a relative risk 3.42 (95% CI 2.99-3.91%, p,0.0001). This likely indicates a positive publication bias in the literature that need consideration by zoo and wildlife veterinarians when making clinical decisions, as actual outcomes are likely to be poorer than reported in the literature at present.

Keywords: *wildlife; surgery; zoo; endoscopy; minimally invasive; laparoscopy*

INTRODUCTION

In critically endangered species, successful veterinary treatment of even a single individual may impact the species chance of survival by maintaining a minimal viable genetic population (Shaffer, 1981). Surgical interventions in captive wildlife species may play a role in the conservation of endangered wildlife species, as part of captive maintained breeding programs. Optimum treatment in wildlife, as in human and domestic animal veterinary medicine, should ideally be evidence based (Cockcroft & Holmes, 2008; Huntley, Dean, Massey, & Brennan, 2016).

While evidence based medicine is well established in the human medical field, and increasingly recognised to be important in veterinary medicine, (Charalambous, Shivapour, Brodbelt, & Volk, 2016; Evans, Gordon-Evans, & Conzemius, 2008; Langerhuus & Miles, 2017; Munsterman, Kottwitz, & Reid Hanson, 2016; Schmidt et al., 2013, 2016) it is still under developed in the field of wildlife surgery, with a sparse current evidence base that is highly fragmented due to the wide variety of wildlife taxonomic groups and species, differing pathophysiology, and environments (Pizzi, 2015).

Systematic reviews and metanalysis of randomised controlled trials are the desirable level of evidence, but the majority of wildlife medicine literature is a variety of lower level evidence according to classifications in use by the Oxford Centre for Evidence-Based Medicine (OCEBM) Levels of Evidence (Howick et al., 2011a, 2011b). Zoo and wildlife veterinarians may also experience a low case load of a specific condition in a species or taxonomic group, especially if rare or endangered, leading to limited experience upon which to base decisions.

The quality of the published wildlife surgery literature remains unquantified with the possibility of bias, an important problem in all research (Cooper, Khan, & Clark, 2015; Kanaan et al., 2011; O'Neil et al., 2014; Pannucci & Wilkins, 2010; Pitak-Arnnop et al., 2010). Biased literature can lead to sub-optimal decision making, and poorer than expected outcomes, with increased complications, adverse outcomes, and mortalities (Pannucci & Wilkins, 2010; Pitak-Arnnop et al., 2010).
Positive publication bias, where cases or studies with positive or flattering results are more likely to be submitted or accepted for publication, and outcome reporting bias, where some outcomes are reported preferentially, depending on the results, are a particular concern in individual case reports and small case series, such as the majority of wildlife surgery publications, but can affect all study types.

This pilot study aimed to assess the baseline number of all wildlife surgery patients affected by post-operative complications, irrespective of surgical procedure.

MATERIALS AND METHODS

Surgical records for a 25 year period ending in 2014, were reviewed from four zoological collections in the UK, Bristol Zoo Gardens, Royal Zoological Society of Scotland (RZSS), Zoological Society of London (ZSL) and Longleat Safari Park. Data was collected through searching records on Zoological Information Management System (ZIMS) (Species 360, Bloomington, Minnesota), and other electronic and written veterinary records. Search terms used for screening electronic records in ZIMS were: surgery; surger*; surgical*; operation; operativ*; biops*; incision*; incise*; excision*; excise* resect*; sutur*; laparotom*; coeliotom*; endoscop*; laparoscop*; coelioscop*; minimally invasive; keyhole; MIS.

For the purpose of this study surgical complications were defined as ‘Any deviation from the normal postoperative course (Clavien, Sanabria, & Strasberg, 1992). Classification was adopted from Clavien and others (1992) and Dindo and others (2004), but to include peri-operative complications, and adverse surgical outcomes. Minor complications were defined as those not requiring surgical interventions, which were managed therapeutically or resolved without treatment, for example, post-operative seroma formation or minor superficial wound dehiscence. Major complications were defined as: those complications requiring repeated surgical interventions to correct (example, wound dehiscence requiring re-suturing under anaesthesia); prolonged post-operative anorexia; adverse effect on functionality of the animal post-operatively; post-operative death; euthanasia on the ground of the complications or their severity; or notable post-operative welfare concerns arising from the surgical intervention.

Statistical analysis was performed with Minitab 17 (Minitab Inc., Pennsylvania) and Confidence Interval Analysis 2.2 (University of Southampton, Southampton). 95% Confidence intervals were calculated for all proportions (rates) and results to facilitate clinical decision making as recommended by the International Committee of Medical Journal Editors (ICMJE 1988) and others (D G Altman, 1998; Douglas G Altman, 2005, 2015; Greenland et al., 2016).

Power calculations were performed to estimate adequate sample sizes need to detect with 95% confidence a 50% difference in relative risk increase of a baseline orthopaedic complication rate of 20%, compared to a soft tissue complication rate of 10%.

RESULTS

Across all wildlife species and surgical procedure types 22.84% (95% CI20.87-24.94%, SE 1.04%, n=1633) of wildlife surgical patients in the zoological collections in this study suffered from a surgical complication (table 1), and 12.31% (10.8-13.99%, SE 0.81%) of wildlife surgical patients were affected by major or life threatening complications (table 2). The overall proportion of animals suffering a complication was similar between mammals, birds, and reptiles, as well as the two mammalian orders primates and carnivores. While birds appeared to have a slightly higher proportion of the surgical population affected, this difference was not demonstrated as significant statistically.

Birds and reptiles had a statistically significant higher absolute risk of major complications compared to mammals of 9.38% (95% CI 5.32-13.91%, SE 2.19%) (table 2). Mustelids had the highest number of individuals affected by surgical complications. More than half of all mustelids that underwent surgery (95% CI 31.71-72.67%, SE 11.45%, n=19) were affected by a complication, a statistically significant increase over the total carnivore order results (table 3). Other apparent differences in major complication rates and individual affected between taxonomic groups in the orders primates and carnivores were not statistically different (table3 and table 4).

The power calculation performed to estimate adequate sample sizes need to detect with 95% confidence a 50% difference in relative risk increase of a baseline orthopaedic complication rate of 20%, to a soft tissue complication rate of 10%, yielded a required sample size of 329 in each group . This sample size was not met, as the total orthopaedic surgery group was only 89 individuals. However 56.81% of wildlife orthopaedic surgery patients across all species were found to have suffered from a post-operative complication, an absolute risk increase of 35.85% (95% CI of 25.14-45.98%, SE 5.42%, p<0.001) in comparison to soft tissue surgical procedures, and a major complication rate of 35.96%, and absolute risk increase of 24.44% (95% CI 14.98-34.97%, SE 5.19%, p<0.001) (table 5).

Wildlife surgery complication rates published in the peer-reviewed literature are notably lower than encountered in this study, at 5.67% (Pizzi and others, unpublished data), a relative risk 3.42 (95% CI 2.99-3.91%, p,0.0001).

DISCUSSION

The findings of this pilot study are limited, only reflect the complication rates and individual animals affected by surgical complications in zoological collections. They do not include: perioperative deaths and adverse outcomes; where surgery was not successful in resolution of the original complaint or indication for surgery; cases where animals were later euthanased due to the fact that surgery did not solve or ameliorate their clinical problem; or cases where complications progressed to result in the animals death or necessitated euthanasia .

Yet, there is a notable difference in complication rates reported in the current body of peer-reviewed literature on wildlife surgery, and the reality found in this retrospective study across a complete captive wildlife population. There was more than threefold increase in animals affected by complication in the study population, than in the complete published wildlife surgery literature (relative risk 3.42%). These findings are highly suspect for a notable positive publication bias in the literature. This needs to be given important consideration by zoo and wildlife veterinarians when making clinical decisions, as actual outcomes are likely to be poorer than reported in the literature at present, and patients may be at risk of harm from currently unrealistic wildlife surgery outcome expectations

Despite a much higher number of wildlife patients affected by complications than reported in the literature (22.84%), it is also important to consider, that the majority of procedures, particularly in primates, were very minor surgical procedures, such as simple suturing of a minor bite wound or skin laceration. Orthopaedic complication rates were highly statistically significantly higher across all species than for soft tissue surgery, and other complex soft tissue surgical procedure may similarly have higher complication rates. It is important to highlight that in this pilot study the comparison between orthopaedic and soft tissue surgical complications was not adjusted to take into account the complexity of the procedure performed, but many of the soft tissue surgical interventions being minor surgery.

The high number of complications seen in this study in mustelids could be due to the relatively small sample size of this taxonomic group, but may also be due to otters having a high rate of post-operative complications if they were returned to their social group and had access to water. While this is not ideal post-operative management in most species, keeping these animals separated from the group and water for prolonged periods, risks social group disruption, and increased fighting, with its own risks and even mortalities.

It is interesting to note that birds and reptiles had a statistically significant higher absolute risk of major complications compared to mammals, and the factors contributing to this warrant further elucidation.

CONCLUSION

Wildlife surgery complication rates published in the peer-reviewed literature are notably lower than encountered in this study, likely indicating positive publication bias in the literature that need careful consideration when assessing the benefits of wildlife surgical intervention, as actual outcomes are likely to be poorer than reported in the literature at present.

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Table 1: Individual animals affected by post-operative complications

Taxonomic group	Individuals affected by complications	95% CI of the difference	St Error	
All species	22.84%	(20.87-24.94%)	1.04%	n=1633
Mammals	21.79%	(19.59-24.17%)	1.17%	n=1248
Birds	28.15%	(23.12-33.79%)	2.74%	n=270
Reptiles	21.74%	(15.18-30.12%)	3.85%	n=115

Table 2: Major complication rates between taxonomic routes in zoological collections

Taxonomic group	Major complications	95% CI of the difference	St Error	
All species	12.31%	(10.8-13.99%)	0.81%	n=1633
Mammals	10.10%	(8.55-11.89%)	0.85%	n=1248
Birds	19.63%	(15.33-24.78%)	2.42%	n=270
Reptiles	19.13%	(12.99-27.27%)	3.67%	n=115

Table 3: Individual mammals affected by post-operative complications

Taxonomic group	Individuals affected by complications	95% CI of the difference	St Error	
Carnivores	22.93%	(17.05-30.11%)	3.36%	n=157
Felines	15.94%	(9.14-26.33%)	4.41%	n=69
Canine	15.79%	(5.52-37.57%)	8.37%	n=19
Mustelids	52.63%	(31.71-72.67%)	11.45%	n=19
Primates	21.12%	(17.59-25.16%)	1.93%	n=445
Callitrichids	35.19%	(23.82-48.52%)	6.50%	n=54
Great apes	25.68%	(17.1-36.65%)	5.08%	n=74
Lemurs	18.64%	(12.65-26.62%)	3.59%	n=118
Macaques	24.24%	(12.83-41.02%)	7.46%	n=33

Table 4: Major complication rates in mammals in zoological collections

Taxonomic group	Major complications	95% CI of the difference	St Error	
Carnivores	13.38%	(8.92-19.58%)	2.72%	n=157
Felines	5.80%	(2.28-13.98%)	2.81%	n=69
Canine	10.53%	(2.94-31.39%)	7.04%	n=19
Mustelids	36.84%	(19.15-58.96%)	11.07%	n=19
Primates	8.99%	(6.67-12.01%)	1.36%	n=445
Callitrichids	22.22%	(13.2-34.94%)	5.66%	n=54
Great apes	14.86%	(8.51-24.69%)	4.14%	n=74
Lemurs	4.24%	(1.82-9.54%)	1.87%	n=118

Macaques	12.12%	(4.82-27.33%)	5.65%	n=33

Table 5: Difference in post-operative complications between orthopaedic and soft tissue surgery in captive wildlife in zoological collection. * *denotes results that are not statistically significant*

Taxonomic group	Orthopaedic surgery	Soft tissue surgery	Difference (Absolute Risk increase)	95% CI of the difference	St Error
All animals					
Major	35.96%	11.52%	24.44%	(14.98-34.97%)	5.19%
Minor	22.47%	11.19%	11.28%	(3.53-21.16%)	4.54%
Total individuals affect	56.18%	20.34%	35.84%	(25.14-45.98%)	5.42%
Mammals					
Major	30.30%	9.00%	21.30%	(8.12-38.46%)	8.08%
Minor	18.18%	13.67%	*4.52%**	(-5.51-20.92%)	6.86%
Total individuals affect	42.42%	20.67%	21.76%	(6.19-38.80)	8.76%
Primates					
Major	30.43%	7.82%	22.61%	(7.49-43.16%)	9.68%
Minor	13.04%	15.40%	*-2.36%**	(-11.66-16.98%)	7.24%
Total individuals affect	34.78%	20.38%	*14.40%**	(-2.09-35.04%)	10.12%
Carnivores					
Major	30.43%	12.75%	*17.68%**	(-2.44-50.53%)	15.48%
Minor	13.04%	8.72%	*4.32%**	(-6.69-46.61%)	15.55%
Total individuals affect	34.78%	21.48%	*13.31%**	(-0.87-57.59%)	17.99%
Birds					
Major	41.86%	15.42%	26.44%	(11.97-41.82%)	7.90%
Minor	25.58%	5.29%	20.30%	(25.58-35.12%)	6.82%
Total individuals affect	67.44%	20.70%	46.74%	(30.75-59.71%)	7.64%
Reptiles					
Major	30.77%	17.65%	*13.12%**	(-6.88-40.69%)	13.35%
Minor	23.08%	9.80%	*13.27%**	(-3.32-40.81%)	12.05%
Total individuals affect	53.85%	17.65%	36.20%	(10.06-59.97%)	14.33%

<u>3.4. Study 4:</u> *Comparison of outcomes and complications between open and minimally invasive surgery in zoological collections*

Comparison of outcomes and complications between open and minimally invasive surgery in zoological collections

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ABSTRACT

Surgical records for a 25 year period ending in 2014, were reviewed from four zoological collections in the UK. Out of a total of 1633 zoo surgical procedures 361 animals underwent an abdominal or coelomic cavity surgical procedure, either via open surgery or minimally invasive surgery (MIS). Across all species, open surgery carried a major complication rate of 26.35%, while MIS only carried a major complication rate of 5.16%, with an absolute risk reduction of 21.19% (95% Confidence Interval [CI] of 13.69-29.14%, SE 3.93%, n=361). The relative risk of an individual mammal suffering a post-operative complication due to open abdominal surgery was 21.14 times higher than for MIS (95% CI 2.91-153.33, p<0.005, n=205), and the absolute risk reduction in major complications was greatest in birds at 33.84% (95% CI of 17.97-50.38%, SE 8.59%, n=151), followed by primates at 32.14% (95% CI of 15.03-45.18%, SE 6.24%, n=81). Primates also had the smallest number needed to treat, to benefit from MIS over open surgery, this being 2.36 animals (95% CI of 1.6-4.5, p<0.05). Kaplan-Meier survival curves demonstrated a significant difference in post-operative survival between MIS and open surgery in mammals. These improved outcomes are broadly in line with the published zoo and wildlife surgical peer-reviewed literature. Published complication rates are however notable lower, likely indicating a high degree of positive publication bias in journals. The learning curve associated with MIS, combined with low surgical case load, wide variety in species, anatomy, and different operative procedures, are however notable hurdles to zoological collections developing in-house MIS capacity. MIS appears to result in statistically significant improvements in surgical outcome and complication rates in wild animals held in zoological collections.

Keywords: *wildlife; surgery; zoo; endoscopy; minimally invasive; laparoscopy*

INTRODUCTION

Minimally invasive surgery (MIS)IS has been performed in non-domestic animals and captive wildlife species for over 50 years, with studies in a variety of non-human primates performed in the 1960's and early 1970's (Balin and others 1966; Dierschke and Clark 1976; Graham 1976; Mahone and Dukelow 1978; Harrison 1980). Endoscopic sexing of birds was developed in the 1970's (Bush and others 1978a; Harrison 1978; Bush 1980), with the late 1970's also seeing laparoscopic surgical examination for reproductive studies in a variety of captive wildlife species, such as large felids, bears, deer, and reptiles (Bush and others 1978b, 1980; Wildt and others 1978). The first veterinary multiple authored book on "Animal laparoscopy" was published in 1980, and included chapters on zoo and exotic animal species, as well as birds and reptiles (Harrison and Wildt 1980). This was all the more remarkable, considering procedures were still largely done by eye while holding the endoscope, and that at this stage laparoscopy was still very much on the fringe in human surgery. Despite the first laparoscopic examination in a live patient being a demonstration in a dog in 1901 by Georg Kelling (Spaner and Warnock 1997;

Vecchio and others 2000), before Hans Christian Jacobaeus performed the first human laparoscopic examinations in 1910 (Hatzinger and others 2006), it was only after the first video assisted laparoscopic cholecystectomy was performed in 1987 by Phillipe Mouret (Polychronidis and others 2017; Spaner and Warnock 1997; Vecchio and others 2000; Blum and Adams 2011), that laparoscopic surgery entered the mainstream medical profession. Uptake progressed so rapidly, that by only 6 years later in 1993, the National Institutes of Health (NIH) held a consensus conference that declared laparoscopic cholecystectomy the treatment of choice for uncomplicated gallstones (Neugebauer and others 1995; Lhermette and Sobel 2008). MIS is now regarded as the gold standard for many human surgical procedures (Sica and Biancone 2013; Ruffolo and others 2013; van Dijk and others 2014; Küper and others 2014; Antoniou and others 2015; Coccolini and others 2015; Mandrioli and others 2016)

As in human surgery, veterinary MIS techniques in domestic animals have also been demonstrated to hold benefits for veterinary patients, such as reduced post-operative pain and morbidity, reduced wound infection or dehiscence, shorter post-operative recovery to function, shorter hospitalisation periods, and reduced post-operative care requirements, while yielding adequate diagnostic biopsy samples (Devitt and others 2005; Walmsley 2007; Culp and others 2009; Parkinson 2012; Mayhew and others 2012; Shariati and others 2014; Case and others 2015; Gauthier and others 2015; Collins and others 2016; McDevitt and others 2016), although findings between different studies can be inconsistent (Mayhew 2014).

MIS appears to hold potential benefits to captive or free free-ranging wildlife patients, just as in domestic animals. MIS carries the potential advantage of good visualisation and magnification, especially useful in anatomic locations that are difficult to visualise in open surgery (Freeman 1999; Rijkenhuizen and others 2008; Pizzi and others 2010; Mayhew 2014), offering the potential for achieving safe, atraumatic and physiological surgery.

However the current evidence base is still limited, and there is a paucity of detailed studies addressing safety, techniques, and specific applications relevant to wildlife veterinary patients (Divers et al, 2010; Hernandez-Divers et al, 2005; Hernandez-

Divers et al,2009; Maclean et al, 2006; Pizzi et al, 2010; Pizzi et al, 2011; Pizzi et al, 2012). Reporting of clinical outcomes and complication rates, with comparisons between MIS and traditional open surgery, is still sparse in the wildlife surgical published literature (Boone and others 2008; Pizzi 2012b, 2015; Steeil and others 2012).

While MIS techniques potentially hold even greater advantages in the veterinary treatment of captive and free ranging wildlife species, their application also faces specific challenges not encountered in either human surgery, or domestic animal surgery. In these veterinary patients post-operative care and monitoring is difficult, and it may not be possible to restrict post-operative activity at all (Cook 1999; Pizzi 2012a, 2015; Llano Sanchez and others 2016). Intelligent dextrous animals such primates and bears can remove sutures, and open and interfere with wounds. (Graham 1976; Pizzi and others 2011a; Pizzi 2015; Llano Sanchez and others 2016). Small MIS wounds help reduce the risks of wound contamination and infection both intra operatively- and post-operatively, especially when operating under less than ideal conditions such as in animal enclosures, outdoors, or in makeshift theatres in the field (Pizzi and others 2011a,b; Campbell-Palmer and others 2015; Llano Sanchez and others 2016). In sociable species, such as many primates, separation from the group for any length of time can adversely affect social group stability and behaviour, and result in fighting and serious injury or death, on reintroduction of the operated individual. Individual primates undergoing MIS procedures may be more rapidly returned to their normal outdoor enclosures and groups, resulting in minimal social disruption of the group (Pizzi 2012c). Aquatic species undergoing MIS may need to be allowed an early post-operative return to water and swimming, so small water proof wounds are required (Campbell-Palmer and others 2015).

Optimum treatment in wildlife, as in human and domestic animal veterinary medicine, should ideally be evidence based (Cockcroft and Holmes 2008; Huntley and others 2016), and wildlife MIS could benefit from a non-selective large scale study to supplement the existing evidence base and help inform future clinical decisions. This study aims to elucidate if there is a difference in surgical outcomes and complications between MIS and open surgery across wildlife species, by examining all cases in a large population of captive wildlife held in different collections, and over a long time frame.

MATERIALS AND METHODS

Surgical records for a 25 year period ending in 2014, were reviewed from four zoological collections in the UK, Bristol Zoo Gardens, Royal Zoological Society of Scotland (RZSS), Zoological Society of London (ZSL) and Longleat Safari Park. Data was collected through searching records on Zoological Information Management System (ZIMS) (Species 360, Bloomington, Minnesota), and other electronic and written veterinary records. Search terms used for screening electronic records in ZIMS were: surgery; surger*; surgical*; operation; operativ*; biops*; incision*; incise*; excision*; excise* resect*; sutur*; laparotom*; coeliotom*; endoscop*; laparoscop*; coelioscop*; minimally invasive; keyhole; MIS.

For the purpose of this study surgical complications were defined as ‘Any deviation from the normal postoperative course’ (Clavien and others 1992). Classification was adopted from (Clavien and others 1992; Dindo and others 2004), but to include peri-operative complications, and adverse surgical outcomes. Minor complications were defined as those not requiring surgical interventions, which were managed therapeutically or resolved without treatment, for example, post-operative seroma formation or minor superficial wound dehiscence. Major complications were defined as: those complications requiring repeated surgical interventions to correct (example, wound dehiscence requiring re-suturing under anaesthesia); prolonged post-operative anorexia; adverse effect on functionality of the animal post-operatively; post-operative death; euthanasia on the ground of the complications or their severity; or notable post-operative welfare concerns arising from the surgical intervention.

Surgical outcome was defined as the result of the surgical intervention. The outcome was deemed as favourable if (1) The aim of the surgical procedure was attained, (2) The patient returned to similar or improved functionality as before the surgery, with no adverse effect on the quality of life, and (3) The patient survived for at least a period of 6months after the procedure, without any major complications arising from the surgery; or the patient died/ was euthanized during the 6 months’ post-operative period for reasons unrelated to the surgical procedures. Surgical outcome was considered as adverse if (1) The patient died or was euthanized peri-operatively or postoperatively because of major surgical or anaesthetic complications, or (2) the surgical procedure was unable to fulfil its original aim, or (3) the quality of life of the patient was affected negatively, or (4) surgical intervention was found to be unnecessary, or (5) any major complications arising due to the surgical procedure, such as, repeated surgical interventions because of the failure of the previous surgery.

Statistical analysis was performed with Minitab 17 (Minitab Inc., Pennsylvania), Confidence Interval Analysis 2.2 (University of Southampton, Southampton), SQL Server (Microsoft, Washington) and R version 3.2.2. 95% Confidence intervals were calculated for all proportions (rates) and results to facilitate clinical decision making as recommended by the International Committee of Medical Journal Editors (Editors 1988) and others (Altman 1998, 2005, 2015; Greenland and others 2016).

RESULTS

Out of a total of 1633 surgical procedures, 361 animals underwent an abdominal or coelomic cavity surgical procedure during the period studied in the four zoological collections; either via open surgery or MIS. A total of 37 different veterinarians were involved with the care, including surgery, of the animals in the four collections during the study period. The major and minor complication rates, as well as the proportion of operated individuals affected by complications in the UK zoological collections over the study period are given in table 1. Overall (all vertebrate species) open surgery carried a major complication rate of 26.35%, while MIS only carried a major complication rate of 5.16%, with a highly statistically significant absolute risk reduction of 21.19% (95% CI of 13.69-29.14%, SE 3.93%, n=361).

Relative risk of an individual mammal suffering a post-operative complication due to open abdominal surgery was 21.14 times higher than for MIS (95% CI 2.91-153.33, $p<0.005$, n=205), as demonstrated in table 2. Absolute risk reduction in major complications was greatest in birds at 33.84% (95% CI of 17.97-50.38%, SE 8.59%, n=151). This was closely followed by primates at 32,14% (95% CI of 15.03-45.18%, SE 6.24%, n=81), where relative risk posed by open abdominal surgery was 16.88 times higher than for MIS (95% CI 1.06-269.47, Z 1.99, $p<0.05$), as demonstrated in table 2. Primates also had the small number needed to treat, to benefit from MIS over open surgery, this being 2.36 animals (95% CI of 1.6-4.5, p<0.05), in terms of numbers of individual animals affected by complications (table 3).

Of all mammal reproductive abdominal surgery performed in the zoological collections, such as simple sterilisation, 69.77% (95% CI 59.39-78.46%, SE 4.95%) were performed as open abdominal surgery, while across all species 72.73% (95% CI 62.62-80.93%, SE 4.75%) of reproductive surgery was performed as open surgery. Of all simply diagnostic abdominal surgery performed in mammals 60% (95% CI 44.6-73.65%, SE 7.75) was performed as open abdominal surgery. In contrast, in birds 96.03% (95% CI 91.6-98.17%, SE 1.59%) of diagnostic coelomic surgery was performed by MIS (endoscopy or coelioscopy). Birds had the largest proportion of all coelomic procedures performed by MIS at 76.16% (95% CI 68.77-82.25%, SE 3.47%). Of operative abdominal and coelomic procedures performed, 80.77% (95% CI 72.15-87.19%, SE 3.86%) of all species surgery was performed as open surgery, and 87.04% (95% CI 75.58-93.58%, SE 4.57%) of all operative mammalian abdominal surgery was performed by open surgery.

Kaplan-Meier survival curves demonstrated a significant difference in post-operative short and long term survival between MIS and open surgery in Mammals, as well as in the initial post-operative period in primates (figures 1-4), although no statistically significant difference could be demonstrated in the survival of all species overall, or for birds.

DISCUSSION

Across species overall, as well as in mammals, birds and primates, there was a clearly demonstrable statistical difference (absolute risk reduction) in major complication rate, and individual animals affected by a post-operative complications (figure 1). While there was a statistically significant difference in post-operative survival, particularly in the first 30 days after surgery in mammals and primates, the difference in post-operative survival between open surgery and MIS could not be demonstrated statistically in birds.

This finding in birds could be at least partly due to a type II statistical error (failure to detect a true difference), as 76.16% of all avian coelomic surgery was via MIS endoscopy, resulting in relatively few open coelomic avian surgical procedures for accurate comparison. Of the avian open coelomic surgical procedures, the majority were enterotomies and gastrotomies for foreign body obstructions in penguins, which is high risk surgery in birds, as noted by numerous authors (Coles 1985; Honnas and others 1993; Harrison and Lightfoot 2006; Gaydos and others 2011), and the Kaplan-Meier survival curves do appear to differ, but fail to demonstrate a statistically significant difference at the 95% confidence level.

The complication rate calculated by summation of all reported complications in the peer-reviewed zoo and wildlife surgery literature, across all species and surgical procedures was only 5.98% (95% CI 5.23-6.83%, SE 0.41, n=3377), while the complication rate for primates reported in the literature was even lower, at 1.86% (95% CI of 0.9-3.78%, SE 0.7, n=377) (Pizzi et al, unpublished data). In a systematic review and indirect comparison meta analysis of open versus MIS in zoo and wildlife surgery publications (Pizzi et al, unpublished data), a total complication rate of only 8.54% (7.23-10.07%, SE 0.72, n=1498) was calculated for open surgery, with a 6.54% absolute risk reduction (95% confidence interval of the difference 5.08-8.14%, SE 0.78, $p<0.001$) in complications evident in publications of MIS surgery. The complication rates demonstrated in this study are notably higher, despite the large number of veterinarians and different collections encompassed. Most notable is the discrepancy in primates, between the published literature which has extremely low reported post-operative complication rates, and this study which found primates had a very high post-operative complication rate in open surgery.

This appears to demonstrate a likely and notable positive publication and positive outcome bias in the peer reviewed wildlife surgical literature. This needs to be carefully considered and accounted for by zoo and wildlife veterinarians when attempting to make evidence based surgical decisions. Reliance on the published literature may well result in unrealistically optimistic expectations and higher than anticipated complication rates and adverse outcomes. Biased low published complication rates and positive outcomes risks resulting in animals being harmed through unjustified surgical interventions, where the actual risks of harm outweighs the potential benefit, but this is not accurately reflected in the published literature.

One potential and important source of bias in this study, if that the majority of mammalian MIS in these zoological collections was performed by a single veterinarian, while open abdominal surgery was performed by a large number of different veterinarians. This could have resulted in better or worse complication rates than could be expected by a general population of zoo and wildlife veterinary surgeons, and hence have influenced the absolute and relative risk reduction calculations (tables 1 and 2), and calculation of the numbers needed to treat (benefit) (table 3). In contrast MIS procedures in birds were performed by a large number of different veterinarians. The higher complication rates observed in birds undergoing MIS than in mammals, as well as the fact the veterinarian performing the majority of mammalian MIS procedures has post-graduate qualifications in both surgery and zoological medicine, hint that the true risk reduction in mammals could possibly be lower when MIS procedures are performed by a general zoo veterinarian population.

There is a well reported learning curve to MIS (Jung and others 2016; Terzi and others 2016), with even the relatively simple procedure of laparoscopic ovariectomy in canines, a single species, requiring an initial 80 cases to acquire competency (Pope and Knowles 2014). This is similar to the number of cases required in human surgery for various more complex procedures as well (Toledano Trincado and others 2014; Park and others 2015; Tan and others 2015; Tsai and others 2016; Jung and others 2016; Terzi and others 2016). From the low number of overall abdominal procedures encountered in this study, over a long time period, combined with the high number of different individual veterinarians involved in the zoological collections in the study, it seems unlikely for the majority of full time zoo veterinarians to experience a sufficient caseload to become safe and competent with MIS techniques, particularly in mammals, where multiple port techniques are needed.

Acquisition of safety and competency in MIS techniques in zoo mammals is likely to be further hampered by the large variety in species and difference in anatomy, as well as importantly, the differences in pathology and hence different surgical procedures and intervention indications encountered. These factors may potentially even impact veterinarians competent and experienced with domestic animal MIS, those dealing with a high volume exotic pet caseload, or even human surgeons, dealing with these unfamiliar surgical situations.

Coelioscopy in birds is possibly a simpler procedure than MIS in mammals, with this usually performed via a single puncture, not requiring insufflation, and most commonly employed in a diagnostic capacity for visualisation and organ biopsy (Lumeij and others 1985; Chavez and Echols 2007; Blanco and others 2009; Divers 2010a,a,b, 2015; Desmarchelier and Ferrell 2015). There has been no published evaluation of the learning curve in avian coelioscopy, but the higher complication rates encountered in this study in birds compared to mammals, combined with the low case volume, indicate that even for this simpler technique there is possibly a learning curve threshold that is not been reached, or insufficient case volume presenting for maintenance of skills, by some of the veterinarians in zoos performing these interventions, likely again due to low case volume. Low surgical case volume appears an overall hurdle to improving surgical outcomes in zoo animal surgery, and not only in developing inhouse MIS capacity.

Another source of potential bias is that the complication rates and outcomes reported here are compared indirectly. Due to the small surgical case numbers, it was not possible to directly compare the same procedures in the same species between MIS and open surgery, which would have led to more robust results.

An important consideration, not apparent from the data captured in this study, is that not all procedures can be performed by MIS methods, no matter what equipment is available or relevant surgeon experience. Some procedures, such as caesarean section, have to be performed via open surgery. Even in human surgery some procedures have failed to demonstrate any advantage when performed MISly over standard open abdominal surgery (Lei and others 2017; Wu and others 2017; Xie and others 2017).

Current evidence appears to demonstrate that when a MIS approach to a surgical procedure in a wild animal held in a zoological collection is possible, this carries a lower risk of complications and better outcome than if performed by open surgery.

CONCLUSION

Minimally invasive surgery appears to result in significant improvements in surgical outcome and complication rates in captive wildlife kept in zoological collections, in comparison to open abdominal and coelomic surgery. While improved outcomes are broadly in line with the published zoo and wildlife surgical peer-reviewed literature, published complication rates are notable lower. This indicates likely positive publication bias in journals, which needs careful consideration when wildlife veterinarians predict likely surgical outcomes and formulate risk-benefit wildlife surgical decisions.

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<u>Table 1:</u> Comparison of the differences in major and minor complication rates, as well as proportion of operated individuals affected by complications between open surgery and MIS in 7 UK zoological collections over 25 years. *Differences that are not statistically significant are marked with an asterisk*.*

Taxonomic group	**Surgery type**		**Absolute Risk Reduction**	**95% CI of Absolute Risk Reduction**	**St Error**	
	Open	**MIS**				
All Animals						
Major complications	26.35%	5.16%	21.19%	(13.69-29.14%)	3.93%	n=361
Minor complications	11.49%	6.1%	*5.38%**	(-4.5-12.01%)	3.09%	n=361
Individuals affected	35.81%	15.02%	20.79%	(11.72-29.81%)	4.764%	n=361
Mammals						
Major complications	22.02%	1.04%	20.98%	(12.79-29.68%)	4.10%	n=205
Minor complications	11.93%	3.13%	8.80%	(1.36-16.5%)	3.58%	n=205
Individuals affected	30.28%	4.17%	26.11%	(16.2-35.63%)	4.85%	n=205
Primates						
Major complications	32.14%	0.00%	32.14%	(15.03-45.18%)	6.24%	n=81
Minor complications	21.43%	4.00%	*17.43%**	(-0.4-30.25%)	6.74%	n=81
Individuals affected	46.43%	4.00%	42.43%	(22.54-55.71%)	7.73%	n=81
Birds						
Major complications	41.67%	7.83%	33.84%	(17.97-50.38%)	8.59%	n=151
Minor complications	13.89%	8.7%	*5.19%**	(-5.01-20.47%)	6.33%	n=151
Individuals affected	55.56%	23.48%	*32.08%*	(13.97-48.46%)	9.18%	n=151

<u>Table 2</u>: Relative risk of developing a major complication associated with open surgery in comparison to minimally invasive surgery

	Relative Risk of Open Surgery	95% Confidence Interval	Z Statistic	p-value	
All Species	5.10	2.7-9.63	5.03	<0.0001	n=361
Mammals	21.14	2.91-153.33	3.018	0.0025	n=205
Primates	16.88	1.06-269.47	1.99	0.0456	n=81
Birds	5.32	2.55-11.12	4.45	<0.0001	n=151

Table 3: Number of individual animals needed to treat to benefit from reduction in complications by performance of minimally invasive surgery in comparison to open surgery

	Number Needed to Benefit	95% Confidence Interval	p-value	
All Species	4.81	3.4-8.23	<0.0001	n=361
Mammals	3.83	2.78-6.18	0.0001	n=205
Primates	2.36	1.6-4.5	0.013	n=81
Birds	3.12	2.06-6.44	0.0001	n=151

Figure 1: Kaplan-Meier survival curve for all mammals, comparing post-operative survival (days) after open (top) versus MIS surgery (bottom) with 95% confidence intervals indicated

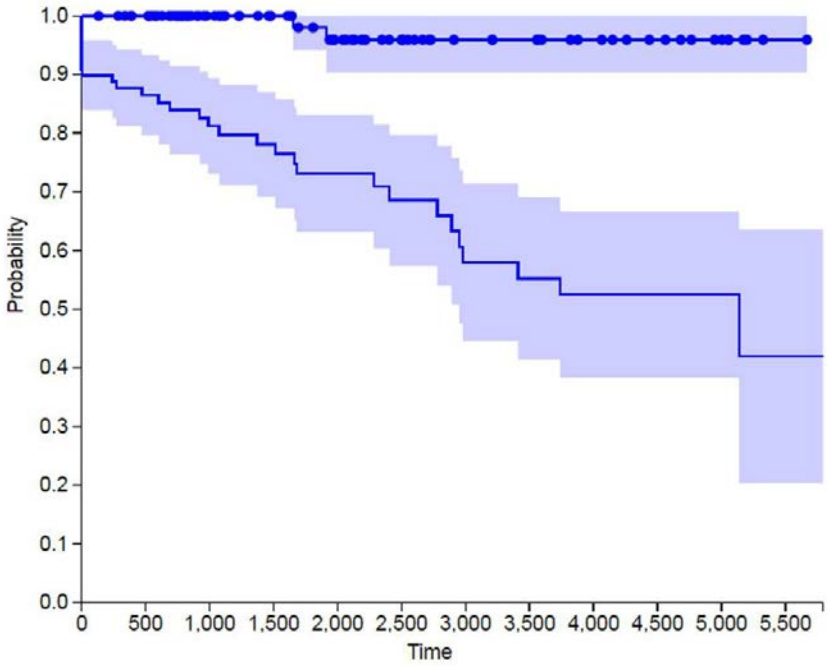


Figure 2: Kaplan-Meier survival curve for all mammals, comparing the first 30 days post-operative survival (days) after open (top) versus MIS surgery (bottom) with 95% confidence intervals indicated

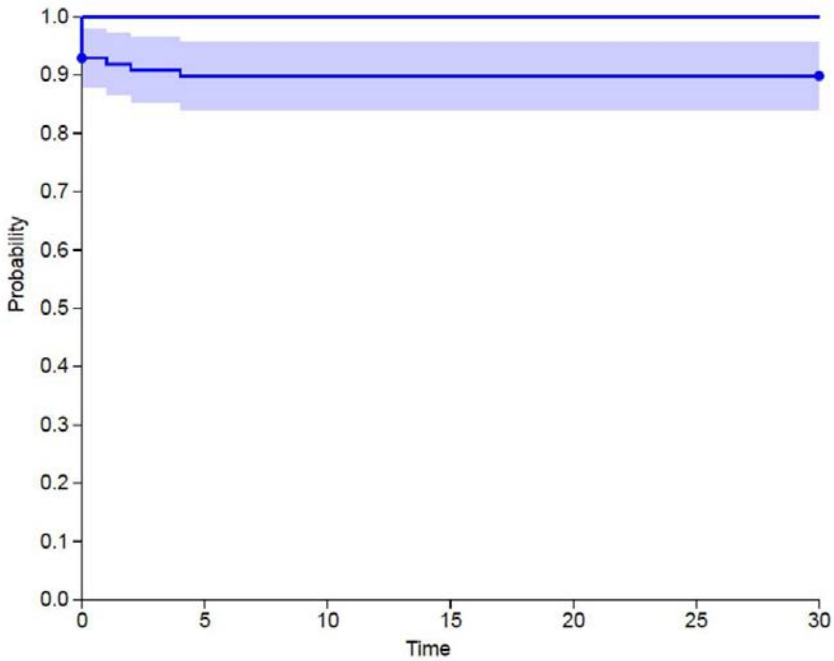


Figure 3: Kaplan-Meier survival curve for primates, comparing post-operative survival (days) after open (top) versus MIS surgery (bottom) with 95% confidence intervals indicated

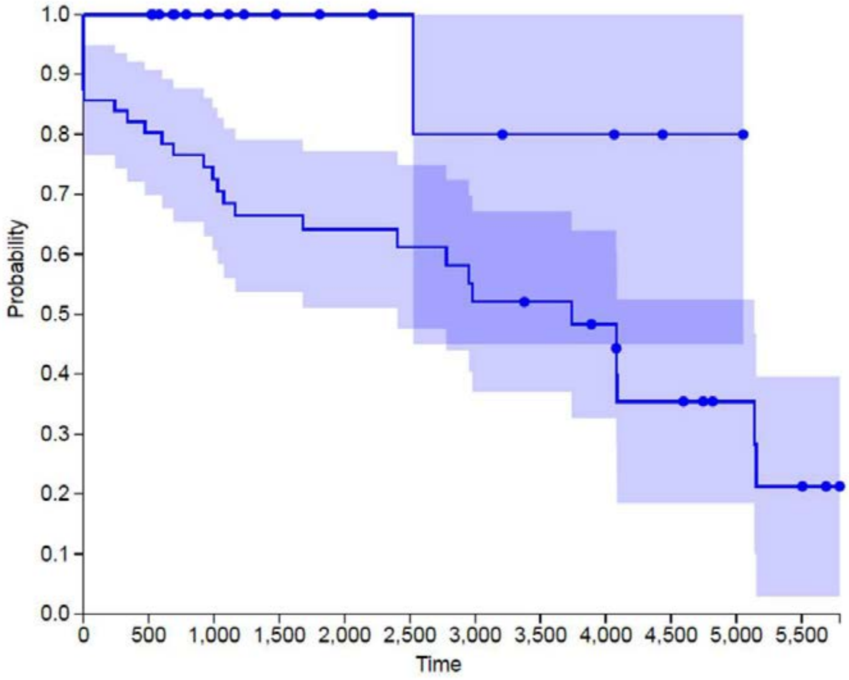


Figure 4: Kaplan-Meier survival curve for primates, comparing the first 30 days post-operative survival (days) after open (top) versus MIS surgery (bottom) with 95% confidence intervals indicated

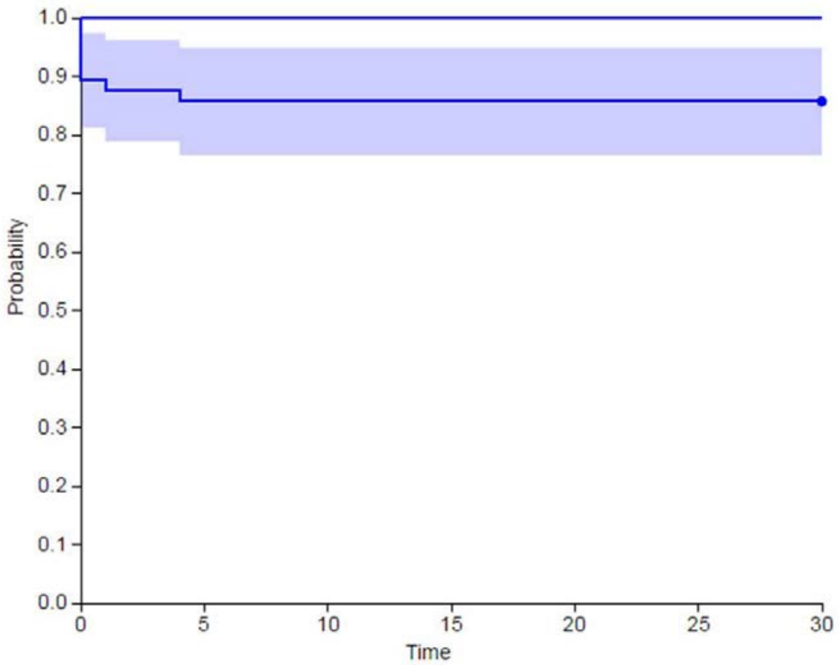


Figure 5: Kaplan-Meier survival curve for birds, comparing post-operative survival (days) after open versus MIS surgery with 95% confidence intervals indicated

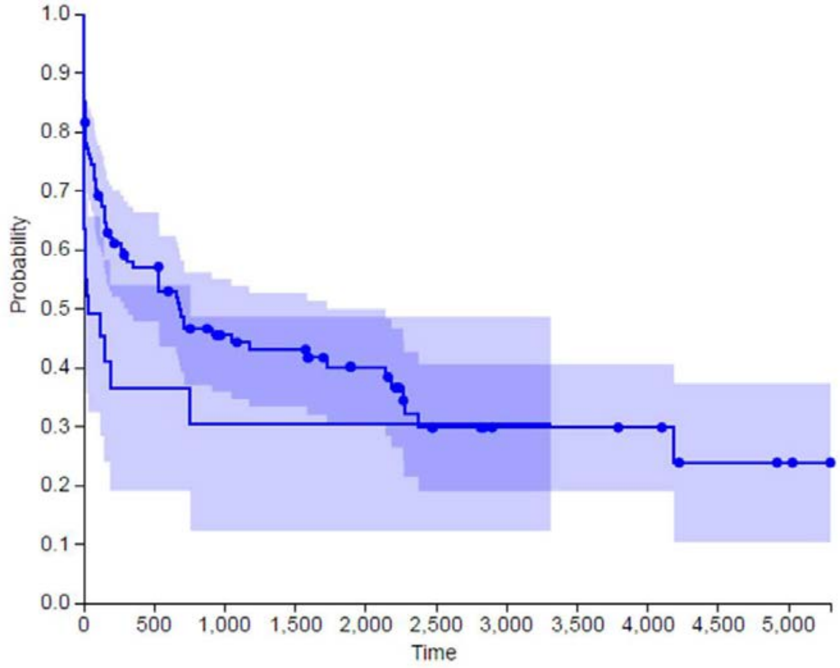


Figure 6: Kaplan-Meier survival curve for birds, comparing the first 30 days post-operative survival (days) after open versus MIS surgery with 95% confidence intervals indicated

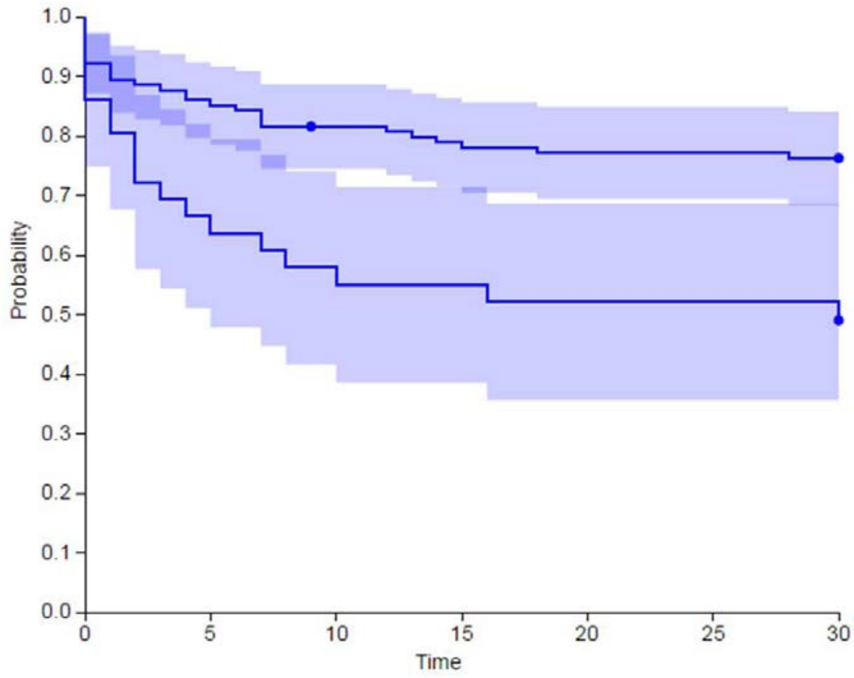


Figure 7: Kaplan-Meier survival curve for all animal species, comparing post-operative survival (days) after open versus MIS surgery with 95% confidence intervals indicated

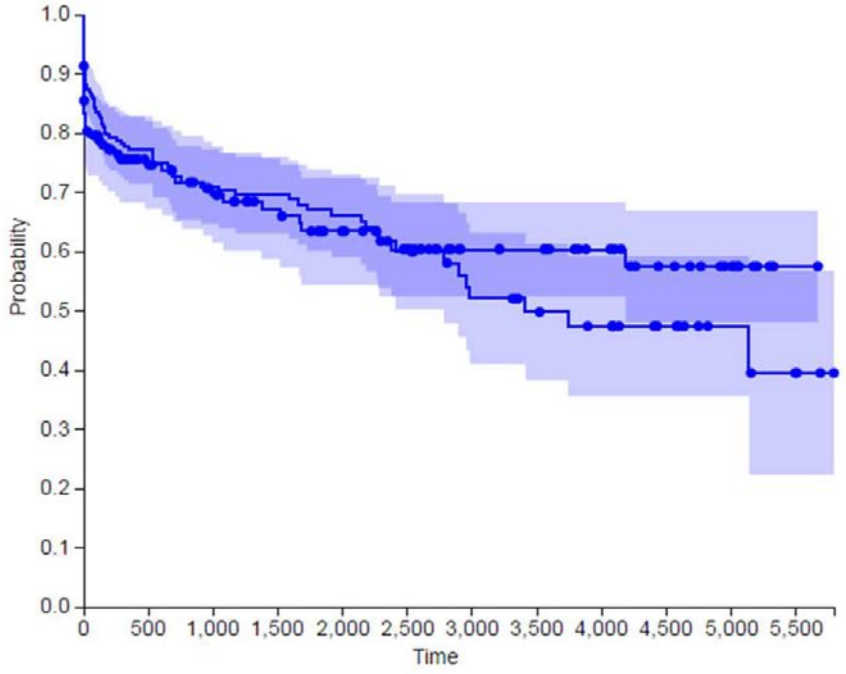
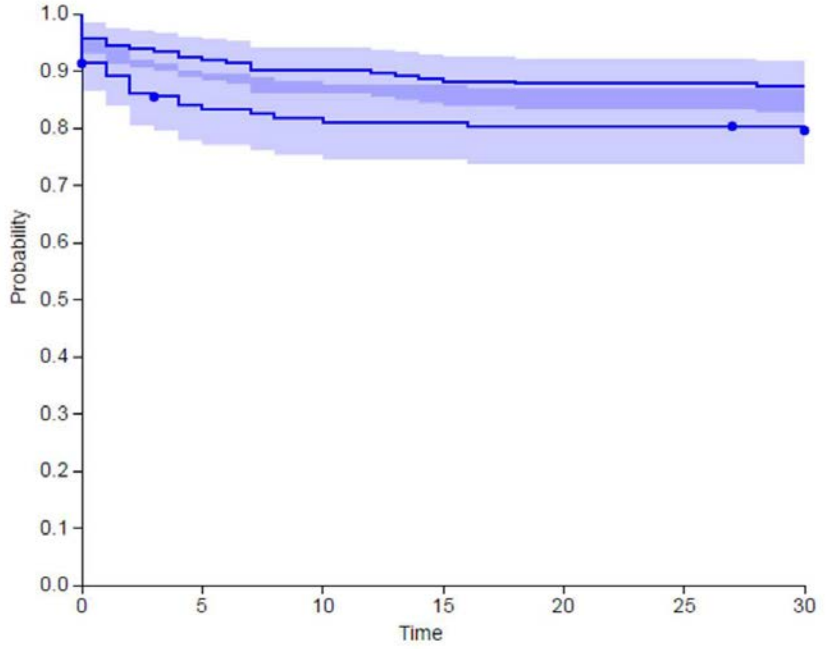


Figure 8: Kaplan-Meier survival curve for all animal species, comparing the first 30 days post-operative survival (days) after open versus MIS surgery with 95% confidence intervals indicated



3.5. Study 5: *Preclinical veterinary students manifest a illusory superiority bias when self-evaluating surgical aptitude and future surgical skill, and do not innately perceive the value of clinical audit*

Preclinical vet students manifest a illusory superiority bias when self-evaluating surgical aptitude and future surgical skill, and do not innately perceive the value of clinical audit

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ABSTRACT

Heuristics may result in systematic errors, or cognitive biases, making irrational poor clinical decisions and surgical errors occur, even when good evidence is available. Veterinary students in preclinical years from the established veterinary schools in the United Kingdom were surveyed. 38.91% (95% confidence interval [CI] 32.17-46.1%, SE 3.58%, n=189) of students self-evaluated their surgical aptitude as above average, while only 8.65% (95% CI 5.39-13.59%, SE 2.07%) self-evaluated as below average. When self-predicting their surgical skills 5 years after graduation in comparison to their peers 57.14% (95%CI 50.01-63.99%, SE 3.6%) believed they would be above average, while only 3.7% (95% CI 1.81-7.45%, SE 1.37%) believed they would be below average There was no statistically significant difference between male and female students, or universities. When asked to rank which of 6 options would most improve their personal surgical outcomes once qualified veterinary surgeons, only 3.17% (95% CI 1.46-6.75%, SE 1.28, n=189) ranked clinical auditing as being the most important method, and only 25.93% (95% CI 20.2-

32.61%, SE 3.19) listed auditing as one of their first 3 of the 6 choices. Pre-clinical veterinary students in the United Kingdom appear to have an illusory superiority bias, or suffer from the "above-average effect" when self-evaluating their surgical aptitude and future surgical performance, despite little experience of actually performing surgery, an apparent demonstration of the Dunning-Kruger effect. Despite media coverage and professional bodies highlighting the value of clinical auditing, pre-clinical veterinary students to not appear to have an innate appreciation or understanding of its value in improving surgical skills and performance.

***Keywords*:** *superiority bias, cognitive bias, heuristics, Dunning-Kruger effect, audit, veterinary*

INTRODUCTION

Heuristics are simple mental rules used to make decisions and judgements efficiently (Newell and others 1957; Simon and Newell 1958; Simon 1977). These mental "shortcuts" function by focusing on one, or limited, aspects of a complex problem, and ignoring other aspects. While heuristics commonly govern automatic and intuitive judgments and decisions, they can also be used as mental strategies when presented with limited information. Some heuristics are believed to have had evolutionary advantages, in adaptations where speed may be more important than accuracy, or be the results of neural processing limitations, limited capacity for processing information, or from "bounded rationality" where there is a lack of appropriate mental mechanisms (Simon 1972; Kahneman 2003).

Heuristics may result in systematic errors, or cognitive biases, making judgements and decisions that are irrational. Numerous different types of cognitive biases have been reported (Kahneman and Tversky 1996; Kahneman 2003; Sunstein and others 2003). While their impact has been particularly well highlighted in fields such as behavioural economics (Tversky and Kahneman 1975; Griffin and Tversky 1992; Kahneman and Tversky 1996; Kahneman 2003), research has also demonstrated their influence in poor clinical decision making in human medicine and surgical errors, even in situations where a good scientific evidence base is available upon which to make decisions (Bernstein and Khu 2009; Mittal and Perakath 2010a,b; MacDermid and others 2017).

Illusory superiority bias, also referred to as superiority bias, or the "above-average effect" (Hoorens 1993; Odean 1998; Alicke and Govorun 2005; Krizan and Suls 2008; Beer and Hughes 2010; Brown 2012) manifests itself in multiple professions, despite their data based evidence or professional knowledge base, including academia (Cross 1977; Zuckerman and Jost 2001), law (Neale and Bazerman 1985), financial services (Odean 1998), and human medicine (Tan 2011; Jager and others 2014). In one university survey, 68% of academics rated themselves as in the top 25%, and more than 90% rated themselves as above average (Cross 1977). One of the best known illustrations of superiority bias was the finding that 93% of American drivers rate themselves as better than the median (Svenson 1981). The findings were later repeated (McCormick and others 1986) in a similar study that found 80% of drivers rated themselves as being above average.

A further bias relevant to inexperienced medical and veterinary clinicians, or those in training, is the Dunning-Kruger effect (Kruger and Dunning 1999), a cognitive bias encountered when unskilled or incompetent individuals mistakenly asses their ability as much higher than is accurate. This bias is encountered either with simpler tasks, or where success is common, or people feel competent (Simons 2013; Pennycook and others 2017). This makes it of special significance for surgery performed or seen by trainees or inexperienced surgeons, where in some fields of simple routine surgery, adverse outcomes or complication rates may be low (Tan 2011; Abdullah 2014).

Cognitive biases, including illusory superiority bias and the Dunning-Kruger effect, are well recognised as being problematic in multiple facets of medical and veterinary medicine (van den Berge and Mamede 2013; Msaouel and others 2014; Park and others 2014; Fargen and Friedman 2014), and training of medical student to recognise and avoid cognitive biases has been highlighted as important in reducing errors in clinical decision making (Hershberger and others 1995; Stiegler and others 2012; Msaouel and others 2014), while supervising medical students has been found to be helpful in preventing senior clinicians committing cognitive bias errors, and considering alternative treatment options (Roswarski and Murray 2006).

Clinical auditing of surgical outcomes and using this to feedback into and improve an individual surgeon or surgical teams outcomes is part of good governance, and one means of countering some effects of clinical cognitive bias. The National Institute for Health and Clinical Excellence defines clinical audit as: "*a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change. Aspects of the structure, processes, and outcomes of care are selected and systematically evaluated against explicit criteria. Where indicated, changes are implemented at an individual, team, or service level and further monitoring is used to confirm improvement in healthcare delivery*." (National Institute for Clinical Excellence 2012), and the Royal College of Veterinary Surgeons (RCVS) code for professional conduct states that "*Clinical governance is a continuing process of reflection, analysis and improvement in professional practice for the benefit of the animal patient and the client owner.... Audit the results of clinical procedures of interest to the practice team and use the results to improve patient care....*." (RCVS 2017).

Only by measuring surgical outcomes and complications can a surgeon judge their improvement, if any, over time. This may help highlight and mitigate against some of the cognitive biases that medical and veterinary clinicians are prone to. Clinical auditing may be regarded as a virtuous upward spiral of appraisal and improvement (Viner 2005, 2006).

There has been widespread media coverage in the United Kingdom of the importance and value of clinical auditing of surgical outcomes, after events such as a scandal involving unacceptably high paediatric cardiac surgery mortality rates in individual hospitals in the 1990's (Smith 1998). However, despite increased public awareness of the need for clinical audit, it is unclear if veterinarians and veterinary students actually understand the value and implications of clinical auditing in improving an individual surgeons outcomes and reducing complication rates.

This pilot study attempts to evaluate if pre-clinical veterinary surgeons have an innate perception of the value of auditing in improving surgical outcomes, and whether these students further suffer from cognitive biases that could adversely affect surgical performance in their future career if uncorrected.

MATERIALS AND METHODS

200 veterinary students in preclinical years of their studies (years 1-3) were asked to complete a questionnaire. Female and male students were sampled from the fully established veterinary schools in England and Scotland (London, Cambridge, Liverpool, Nottingham, Edinburgh, and Glasgow). The University of Surrey was excluded, as it has not completed developing its veterinary curricululm, or graduated any veterinary surgeons by the time of this study.

Questions were posed as part of a general survey of veterinary interests, and were anonymous, but recorded gender, age, university, and year of veterinary studies. The three questions are given in figure 1. Questionnaires were completed at the end of lecture periods on an unrelated field (native wildlife rehabilitation medicine in the United Kingdom, or general zoo health management).

Questionnaires were paper based, and data was entered in to Excel 2007 (Microsoft, Washington). Statistical analysis was performed with Minitab 17 (Minitab Inc., Pennsylvania) and Confidence Interval Analysis 2.2 (University of Southampton, Southampton). 95% Confidence intervals were calculated for all proportions (rates) and results to facilitate clinical decision making as recommended by the International Committee of Medical Journal Editors (Editors 1988) and others (Altman 1998, 2005, 2015; Greenland and others 2016).

RESULTS

Of the 200 students completing questionnaires, 189 completed these specific questions and ranked at least one or more of the 6 options for improving surgical results.

38.91% (95% confidence interval [CI] 32.17-46.1%, SE 3.58%) of students self-evaluated their surgical aptitude as above average, while only 8.65% (95% CI 5.39-13.59%, SE 2.07%) self-evaluated their existing surgical aptitude as below average (figure 2). There was no statistically significant difference between male and female students, or between different universities.). Anderson-Darling normality test confirmed a normal distribution (A^2 13.32, $p<0.005$).

When self-predicting their surgical skills 5 years after graduation in comparison to their peers 57.14% (95%CI 50.01-63.99%, SE 3.6%) believes they would be above average, while only 3.7% (95% CI 1.81-7.45%, SE 1.37%) believed they would be below average (figure 3). Again, there was no statistically significant difference between male and female students, or between different universities, and Anderson-Darling test confirmed a normal distribution (A^2 8.99, $p<0.005$).

The improved change (absolute effect) in self-predicted future surgical competency was calculated between these figures. 43.24% (95% CI 36.31-50.45%, SE 3.64) self-predicted an improvement in ranked surgical competency compared to their peers, while the same amount (43.24%, 95% CI 36.31-50.45%, SE 3.64) self-predicted no change (absolute effect) from their initial surgical aptitude, while only 13.51% (95% CI 9.32-19.19%, SE 2.51) self-predicted their surgical skills to deteriorate over the 5 years after graduation.

When pre-clinical veterinary students ranked the options as to what they thought would most improve their surgical results once they qualified as a veterinary surgeon, only 3.17% (95% CI 1.46-6.75%, SE 1.28, n=189) ranked auditing of outcomes as being the most important method of improving one's own surgical outcomes, despite this clearly being the only way of actually achieving this outcome as stated in the question. Only 25.93% (95% CI 20.2-32.61%, SE 3.19, n=189) of respondents listed auditing as one of their first 3 of the 6 choices (figure 3). The ranking mode value was 4, as was the median value (figure 4). Anderson-Darling normality test confirmed a normal distribution (A^2 5.1, $p<0.005$).

DISCUSSION

From this pilot study's results, pre-clinical veterinary students appear to demonstrate an innate and notable lack of understanding of clinical auditing, and possibly fail to appreciate the value of auditing in improving their own surgical skills and performance, despite media and professional bodies highlighting the fact. This is particularly surprising considering the fact that this cohort of students would have been exposed to media reports of medical scandal and the recent high profile requirement for human surgical speciality units to audit their outcomes and make the results publically available before reaching university (BBC NEWS 2017; Smith 1998).

Veterinary students believed mentoring by a more experience surgeon was most likely to improve their personal surgical outcomes, followed by practical workshops, and then continuing professional education (CPD) lectures provided by specialists. While clinical auditing was only ranked fourth by the students, interestingly, this was before reading books and journal articles, or online surgery videos. This point is worthy of consideration by both the modern online continuing education providers, as well as traditional peer-reviewed journal and veterinary book publishers, if they are to keep their CPD offerings relevant in this age of expanding information sources and social media. Social media and new technologies have already impacted CPD in the medical field, lowering costs, and increasing convenience (Curran and others 2016; MacWalter and others 2016; Ibrahim and others 2016; Wu and others 2016; Maloney and others 2017) but this small pilot study hints that it cannot be assumed that the same models will be as appealing or relevant to new veterinary practitioners.

Interestingly, there was no difference between the genders in either their self-evaluation of their surgical aptitude or of their future surgical skills. This is despite the facts that while veterinary medicine in many developed countries has become increasingly feminised (Koolmees 2000; Corbett 2007; Kinnison and May 2013; Allen 2016), there still appears to be gender bias towards men in many human and veterinary surgical disciplines (Pitak-Arnnop and others 2010; Cochran and others 2013; Phillips and others 2016), most marked in fields such as orthopaedic surgery (O'Connor 2016), due to factors such as harassment and gender discrimination, with the different genders having also been shown to have different surgical learning and training preferences (Burgos and Josephson 2014). Gender has also been shown to play a role in veterinary surgeons career ambitions and chosen field of work (Kinnison and May 2013).

The failure to demonstrate a statistically significant difference between the genders in their self-evaluation of their surgical aptitude or of their future surgical skills in this study could however also be due to a type II statistical error from a small sample size, with the study being underpowered to detect a small but real difference.

The results of this pilot study appear to demonstrate some potentially detrimental inherent cognitive biases evident in veterinary pre-clinical students. These findings warrant further elucidation, and highlight a likely need to specifically teach awareness of cognitive bias in the clinical years of the veterinary curriculum in the United Kingdom, and strategies to mitigate its impact, as has been done in human medicine (Hershberger and others 1995; Stiegler and others 2012; Msaouel and others 2014).

Cognitive biases can potentially lead to a host of veterinary surgical errors. The Dunning-Kruger effect may lead veterinary surgeons to have the erroneous belief that they are able to perform procedures that are beyond their competence, or that a specific operation is indicated when it is not, or that the outcome is likely to be more favourable than the evidence indicates. Illusory superiority bias may lead veterinary surgeons to have unrealistically optimistic expectations for the surgical outcome of a specific surgical case, despite their knowledge of published evidence to the contrary. Ultimately these have the biases have the potential to result in patient harm.

Without consideration of innate cognitive bias, or the appreciation of the role of clinical audit, veterinary surgery risks resembling “a chance to cut is a chance to cure,” rather than “primum non nocere” (First do no harm) (Gillon 1985; Gjurić 1989; Body and Foex 2009). Auditing surgical outcomes is vital to improving surgical skills and reducing complications, as well as to improving future surgical decisions.

CONCLUSION

Pre-clinical veterinary students in the United Kingdom appear to have an illusory superiority bias when self-evaluating their surgical aptitude and future surgical performance, despite little experience of actually performing surgery, an apparent demonstration of the Dunning-Kruger effect. Students also do not appear to have an innate appreciation or understanding of the value of clinical auditing in improving surgical skills and performance, despite media and professional bodies highlighting the fact. Teaching awareness of cognitive bias in clinical decision making, and the value of clinical auditing in the undergraduate veterinary curriculum appears warranted.

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Figure 1: Survey questions put to pre-clinical veterinary students

Question 1:

What do you think will most help you improve your surgical results once you are a qualified vet? *(1 most import, 6 least important)*

- CPD lectures by recognised specialists
- Participating in practical surgery workshops
- Being taught by a more experienced surgeon
- Doing an audit of your own cases
- Reading veterinary books and articles
- Watching online videos

Question 2:

One a scale of 0 to 10 (5 is average; 3 is below average, 7 is above average, etc):

Do you think you are of average (5), or higher or lower surgical aptitude than the rest of your veterinary class?

0 1 2 3 4 5 6 7 8 9 10

Do you think you once you *have been qualified for 5 years* you will be average (5), or higher or lower in your surgical skills than other vets your age?

0 1 2 3 4 5 6 7 8 9 10

Figure 2: Distribution of veterinary pre-clinical students self-evaluation of their own surgical aptitude in comparison to their peers

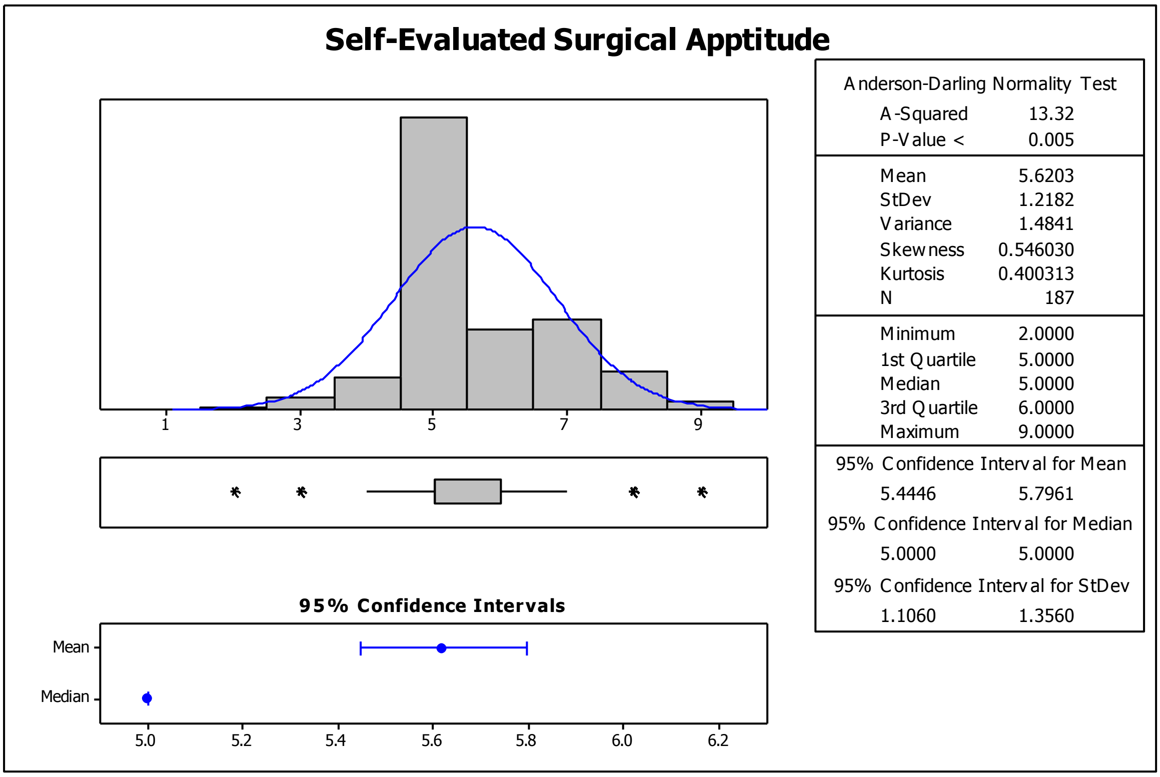


Figure 3: Distribution of veterinary pre-clinical students self-prediction of their own surgical skill in comparison to their peers

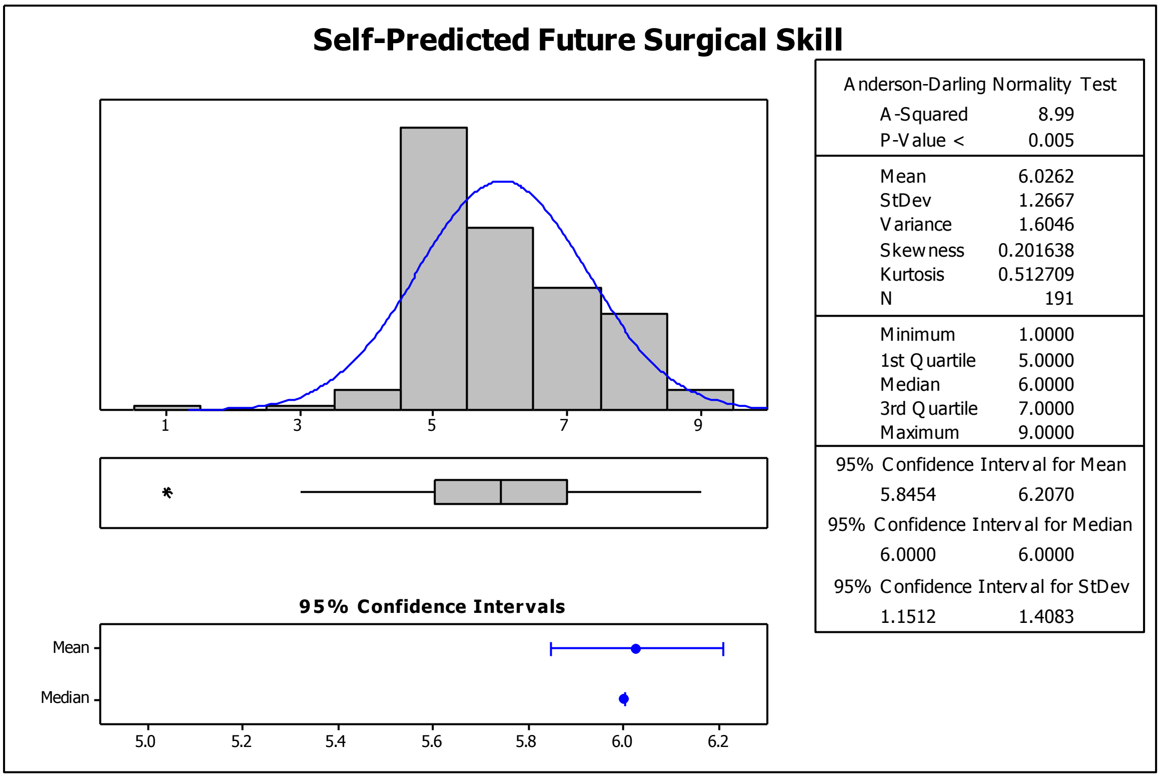


Figure 4: Veterinary pre-clinical students ranking of the question: *What do you think will most help you improve your surgical results once you are a qualified vet?*

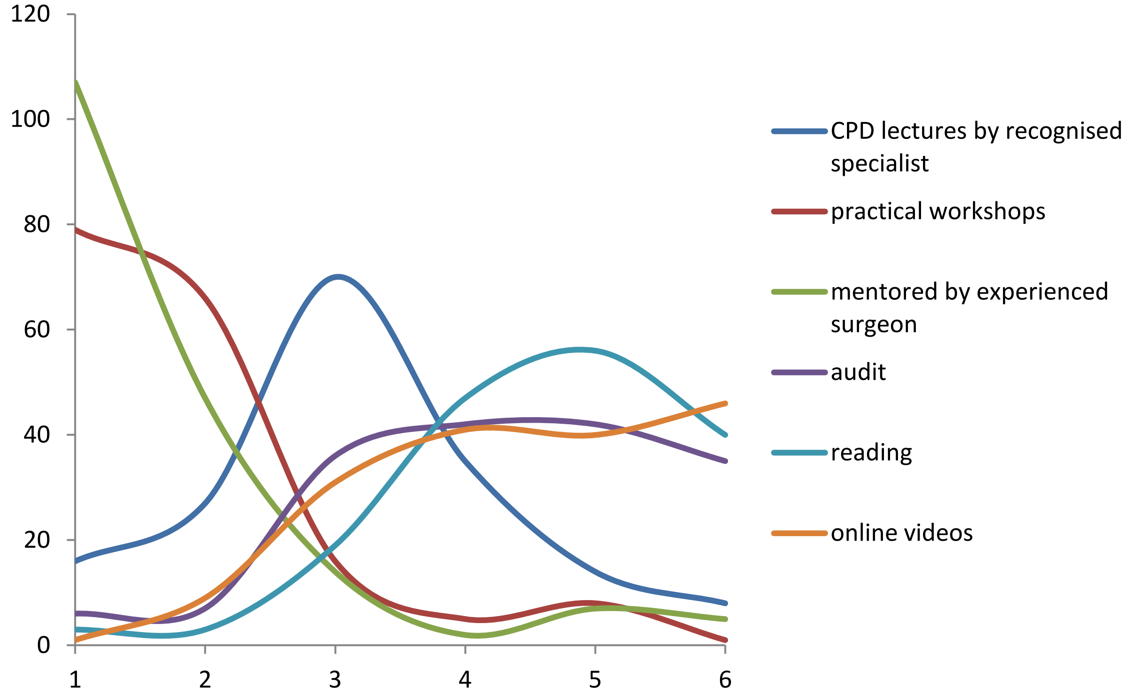
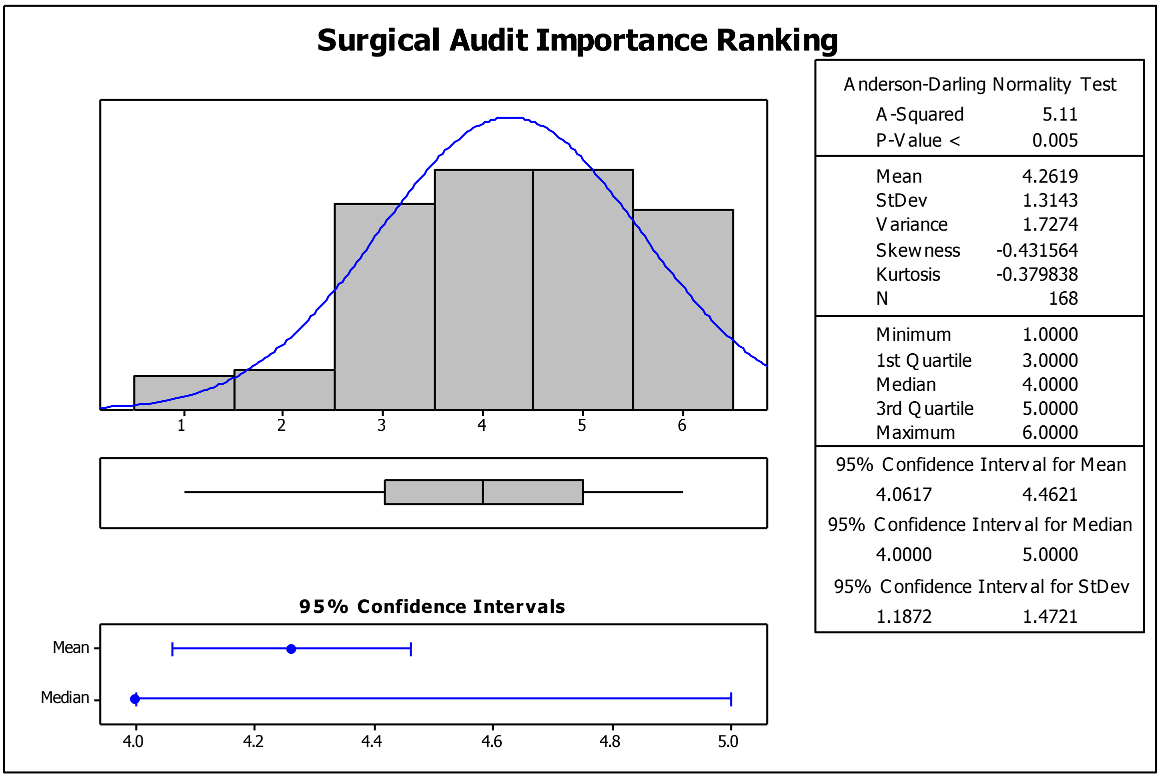


Figure 5: Distribution of veterinary pre-clinical students ranking of clinical audit to the question of: *What do you think will most help you improve your surgical results once you are a qualified vet? (1 most import, 6 least important).*



4. DISCUSSION

Expert opinion holds that minimally invasive surgery (MIS) is beneficial in wildlife species, but until now there has been little synthesis of current published data, nor any large scale broad studies across taxonomic groups attempting to validate or quantify this benefit. These studies have attempted to go some way towards addressing this, but there were some unexpected results

While the majority of wildlife surgical publications are single case reports, or small case series without any comparative aspect, overall these appear to suffer less from positive publication and outcome bias than larger studies in relation to reporting complications. This was an outcome that was not anticipated before this thesis was undertaken. It may naturally be assumed that larger studies would result in more robust evidence. Larger studies may contain more data, information, and complexity, all factors competing for inclusion in the limited word count of an abstract, as well as the article itself. Further, many publications with data of wildlife surgical relevance or interest may not be primarily focused on the surgical aspects, but rather on anaesthesia, pathology, or other aspects. Surgical complications and outcomes may hence not be judged to be important, considering the focus of a study, hence their being under reported or omitted completely.

Prior to these studies there was little synthesis of data upon which to estimate any baseline complication rates or outcomes. The establishment of some baseline complication rate data in these studies will be of benefit to wildlife surgery investigators going forward, allowing a basis for power calculations and the determination of adequate sample size or case load in order not to perform future comparative wildlife surgical studies at risk of a type II statistical error (Chang and others 2013; Greenland and others 2016). However, this may be somewhat limited by the conflicting complication rates found by the primary research data, which was notably higher than the overall complication rates reported in the literature, either in the majority of individual studies, or when the complication rates were calculated by summation of all individuals included across studies.

Wildlife veterinarians using published peer-reviewed literature, and in particular abstracts as a basis for clinical decision should be cautious as to expected outcomes, complication rates, and adverse effects. It should be anticipated that these may be notably higher than reported in journal abstracts. Reviewers should further ensure that authors adequately report complications and adverse surgical outcomes in publication abstracts.

It was interesting that rather than the valuable charismatic and endangered species, such as primates, large felids, and mega-vertebrates having the best level of evidence to their surgery, it was instead birds with the most level 3 evidence studies (Howick and others 2011a,b), and in particular, pigeons. This was likely because they are well suited to experimental studies, inexpensive, and easy to house, with findings likely of relevance to other bird species, whether in zoological collections, or kept as companion animals or for breeding.

As with any systematic review and meta analysis, results are dependent on the quality of evidence available to the reviewers (Garbutt and others 1999; Temple and others 1999; Bailey and others 2004; Slim 2005; Chalmers 2007; Walter and others 2007; Mittal and Perakath 2010; Haidich 2010; Kanaan and others 2011; Hoaglin and others 2011; Ayeni and others 2012; Garas and others 2012; Stewart and others 2015; Coccolini and others 2015). The low number of studies actually comparing open and MIS abdominal or coelomic surgery limited the application of classic meta analysis and forest plot depictions. An indirect comparison was hence performed (Hoaglin and others 2011), but it is acknowledged that this has notable limitations, and suffers a high risk of bias.

Published wildlife surgery study designs and generated evidence levels varied from individual case reports through to small randomised controlled trials. Different studies had different primary objectives, which were not always of a primary surgical focus, such as anaesthesia, assessment of diagnostic biopsy quality, or diagnostic sensitivity and specificity for specific pathology. These studies may have under reported complications, as these were not the primary focus of those publications. There was also inclusion of widely differing species, and taxonomic groups were not equally represented either in the literature, or in the research study. Furthermore case load between MIS and open surgery covered varying procedures, again not directly comparable. Studies varied from elective procedures on healthy animals, such as sterilisation, to diagnostic or operative procedures in ill animals with varying pathology and severity. The small study sizes and small overall total patient numbers precluded any meaningful attempts at further subdivisions in order to try to better match animal patients according to species (or other more closely related taxonomic groups, than the categories presented in the results), procedure, study type (retrospective case series versus cohort studies), and the like, as indicated by the pre-study power calculations. Small sample sizes had a high likelihood of leading to type II statistical errors (failing to detect or demonstrate a true difference statistically) (Bailey and others 2004; Ayeni and others 2012), and risked leading to erroneous conclusions from the statistical analysis of these studies, and hence were not pursued further than presented here. Simply limiting mammalian publications to those only containing 10 or more individual patients, resulted in failure to detect a statistically significant difference. Only including studies with 10 or more animals appeared to result in smaller differences in complication rates between open and MIS surgery in taxonomic groups (with the exception of reptiles). The difference in results between all studies, and only those containing 10 or more animals was not however statistically significant.

Failure to demonstrate a statistically significant difference in complication rates for mammalian publications containing 10 or more animals appeared to be due to a combination of being underpowered according to power calculations because of small group sample sizes, and the inclusion of a single outlier study (Marais and others 2013), which reported results of 45 laparoscopic vasectomies in wild African elephants. A separate publication including 14 of these elephants had previously be excluded in screening (Rubio-Martínez and others 2014). These surgeries had a notably higher complication rate than other included mammal MIS studies with 10 or more animals. While open abdominal surgery in elephants is likely to have markedly higher complication rates, this number of elephants was not matched at all in the mammal open surgery studies with 10 or more patients, introducing another potential source of bias. However repeating analysis and the forest plot with this study excluded, while appearing to then favour MIS, still failed to demonstrate a statistically significant difference in complication rate in mammals undergoing open or MIS abdominal surgery in publications with 10 or more individuals included.

More of the included MIS publications had better design, being prospective cohort studies, with a primary surgical outcome focus. In contrast, open surgery studies were more often not primarily focused on the surgical outcomes, and included more pathology focused cases, while more MIS publications were elective surgery, such as sterilisation, on clinically healthy animals. This again was a potential source of bias, with the populations not directly comparable or suitable for matching. These factors do make the systematic review and meta analysis at high risk of bias (Burton and Clarke 2006; Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Haidich 2010; Higgins and Green 2011).

Sharma (2016) found an overall surgical complication rate (including adverse outcomes) of 31.6% (95% CI 26.33-37.38%, SE 2.83, n=269) for birds and 40% (95% CI 31.51-49.14%, SE 4.57, n=115) for reptiles, from a comprehensive review of all surgical procedures performed at major zoological collections in the United Kingdom over a 25 year period. In contrast, these studies found a statistically significant lower reported rate of complications in the published literature for birds of only 3.71%, a difference between Sharma (2016) and the literature summed complication rate of 27.89% (95% CI of the difference in proportions 22.55-33.72%, SE 2.87, $p<0.001$). In reptiles this study found a statistically significant lower reported rate of complications in the published literature of only 7.66%, a difference of 32.34% (95% CI of the difference in proportions 23.45-41.69%, SE 4.71, $p<0.001$) from Sharma (2016). Sharma (2016) found complex orthopaedic procedures (fracture repairs) (OR 7.69, 95%CI 1.40 to 42.01, p-value 0.019) were the major risk factors for an adverse outcomes in birds. While the published avian orthopaedic complication rate was higher than other avian surgical procedures, these are still notably lower than the general avian surgery complication rate found by Sharma (2016).

It hence appears likely that the published peer-reviewed wildlife surgery literature is notably biased. Positive publication bias (Pannucci and Wilkins 2010; Kanaan and others 2011; Richards and Burrett 2013) is likely influencing the literature overall, although it would be expected to particularly affect single case reports and small series. Positive publication bias is the publication or non-publication of research findings, depending on the nature and direction of results (Lacchetti and others 2002; Chalmers 2007; Pitak-Arnnop and others 2010; Richards and Burrett 2013). With limited time and resources, clinicians are likely favouring writing and submitting cases and series with positive outcomes, and less complications and adverse effects. Positive outcome cases and case series, may be simpler to write. Review may also have some influence on positive publication bias, with rebuttal and revisions being easier to achieve with straight forward cases without complications or adverse outcomes (Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Kanaan and others 2011; O'Neil and others 2014; Cooper and others 2015).

Larger studies should be better powered statistically to detect and determine outcomes and complications accurately, although almost no studies included in this study mentioned power calculations in their abstract, similarly a notable problem in the human surgical literature (Dimick and others 2001; Bailey and others 2004; Walter and others 2007; Pitak-Arnnop and others 2010; Pannucci and Wilkins 2010; Ayeni and others 2012; Greenland and others 2016). Interestingly, in this systematic review of abstracts, larger studies with more than 10 animals reported far fewer complications and adverse outcomes than the single case reports. It seems less likely this is due to positive publication bias, and it may be likely that the majority of this is due to outcome reporting bias. Outcome reporting bias is the selective reporting of some outcomes but not others, depending on the nature and direction of the results (Moher and others 2009; Pannucci and Wilkins 2010; Kanaan and others 2011). Larger studies may contain more data, information, and complexity competing within the limited word count of the abstract for inclusion. It appears that complications are likely under reported in abstracts, although the full papers, or ideally the original data, would need to be analysed and compared to confirm or refute this possibility.

There is a risk of readers assuming that larger studies would have more robust evidence, and believing in a false low complication rate gleaned from the abstract. This could adversely impact surgical decision making, with wildlife veterinarians and conservation managers having unrealistically optimistic expectations regarding surgical interventions, and resulting in poorer than expected outcomes, with increased complications, adverse outcomes, and mortalities. In publications that have a primary focus other than surgery, such as anaesthesia, surgical complications and outcomes may not be judged to be the focus of the study, or of importance to the anaesthesia aspects, hence their omission from abstracts. It is also possible that different submitting authors felt it necessary to put as positive a description on published cases or studies as possible for reasons of professional reputation, or even commercial or clinical competitiveness. This possibility appeared to be apparent in the large number of publications that were evaluated to be showcasing surgical novelty. These studies also had a particularly low rate of reported complications and adverse outcomes in comparison to primary surgical publications.

Journal abstracts are possibly the most important part of a published peer-reviewed study, with readers relying on the information provided in an abstract when deciding whether to read the full text of an article (Islamaj Dogan and others 2009). Due to time pressures veterinarians may only read abstracts when searching for information on a specific case (Bigna and others 2016). Many wildlife veterinarians work outside academic institutions, in developing countries, where access to full text articles is not possible, and may only have access to abstracts to inform their clinical decision making. It is essential that reviewers and journal editors ensure abstracts accurately and adequately detail surgical complications and adverse outcomes in the field of wildlife surgery.

Across species overall, as well as in mammals, birds and primates, there was a clearly demonstrable statistical difference (absolute risk reduction) in major complication rate, and individual animals affected by a post-operative complications, between MIS and open surgery. While there was a statistically significant difference in post-operative survival, particularly in the first 30 days after surgery in mammals and primates, the difference in post-operative survival between open surgery and MIS could not be demonstrated statistically in birds.

This finding in birds could be at least partly due to a type II statistical error (failure to detect a true difference), as 76.16% of all avian coelomic surgery was via MIS endoscopy, resulting in relatively few open coelomic avian surgical procedures for accurate comparison. Of the avian open coelomic surgical procedures, the majority were enterotomies and gastrotomies for foreign body obstructions in penguins, which is high risk surgery in birds, as noted by numerous authors (Coles 1985; Honnas and others 1993; Harrison and Lightfoot 2006; Gaydos and others 2011), and the Kaplan-Meier survival curves do appear to differ, but fail to demonstrate a statistically significant difference at the 95% confidence level.

The complication rate calculated by summation of all reported complications in the peer-reviewed zoo and wildlife surgery literature, across all species and surgical procedures was only 5.98% (95% CI 5.23-6.83%, SE 0.41, n=3377), while the complication rate for primates reported in the literature was even lower, at 1.86% (95% CI of 0.9-3.78%, SE 0.7, n=377). In the systematic review and indirect comparison meta analysis of open versus MIS in zoo and wildlife surgery publications, a total complication rate of only 8.54% (7.23-10.07%, SE 0.72, n=1498) was calculated for open surgery, with a 6.54% absolute risk reduction (95% confidence interval of the difference 5.08-8.14%, SE 0.78, $p<0.001$) in complications evident in publications of MIS surgery. The complication rates demonstrated in this study are notably higher, despite the large number of veterinarians and different collections encompassed. Most notable is the discrepancy in primates, between the published literature which has extremely low reported post-operative complication rates, and this study which found primates had a very high post-operative complication rate in open surgery. A possible source of potential bias is that the complication rates and outcomes reported here are compared indirectly. Due to the small surgical case numbers, it was not possible to directly compare the same procedures in the same species between MIS and open surgery, which would have led to more robust results.

This appears to demonstrate a likely and notable positive publication and positive outcome bias in the peer reviewed wildlife surgical literature. This needs to be carefully considered and accounted for by zoo and wildlife veterinarians when attempting to make evidence based surgical decisions. Reliance on the published literature may well result in unrealistically optimistic expectations and higher than anticipated complication rates and adverse outcomes. Biased low published complication rates and positive outcomes risks resulting in animals being harmed through unjustified surgical interventions, where the actual risks of harm outweighs the potential benefit, but this is not accurately reflected in the published literature.

One potential and important source of bias in this study, if that the majority of mammalian MIS in these zoological collections was performed by a single veterinarian, while open abdominal surgery was performed by a large number of different veterinarians. This could have resulted in better or worse complication rates than could be expected by a general population of zoo and wildlife veterinary surgeons, and hence have influenced the absolute and relative risk reduction calculations, and calculation of the numbers needed to treat (benefit). In contrast MIS procedures in birds were performed by a large number of different veterinarians. The higher complication rates observed in birds undergoing MIS than in mammals, as well as the fact the veterinarian performing the majority of mammalian MIS procedures has post-graduate qualifications in both surgery and zoological medicine, hint that the true risk reduction in mammals could possibly be lower when MIS procedures are performed by a general zoo veterinarian population.

There is a well reported learning curve to MIS (Jung and others 2016; Terzi and others 2016), with even the relatively simple procedure of laparoscopic ovariectomy in canines, a single species, requiring an initial 80 cases to acquire competency (Pope and Knowles 2014). This is similar to the number of cases required in human surgery for various more complex procedures as well (Toledano Trincado and others 2014; Park and others 2015; Tan and others 2015; Tsai and others 2016; Jung and others 2016; Terzi and others 2016). From the low number of overall abdominal procedures encountered in this study, over a long time period, combined with the high number of different individual veterinarians involved in the zoological collections in the study, it seems unlikely for the majority of full time zoo veterinarians to experience a sufficient caseload to become safe and competent with MIS techniques, particularly in mammals, where multiple port techniques are needed.

Acquisition of safety and competency in MIS techniques in zoo mammals is likely to be further hampered by the large variety in species and difference in anatomy, as well as importantly, the differences in pathology and hence different surgical procedures and intervention indications encountered. These factors may potentially even impact veterinarians competent and experienced with domestic animal MIS, those dealing with a high volume exotic pet caseload, or even human surgeons, dealing with these unfamiliar surgical situations.

Coelioscopy in birds is possibly a simpler procedure than MIS in mammals, with this usually performed via a single puncture, not requiring insufflation, and most commonly employed in a diagnostic capacity for visualisation and organ biopsy (Lumeij and others 1985; Chavez and Echols 2007; Blanco and others 2009; Divers 2010a,a,b, 2015; Desmarchelier and Ferrell 2015). There has been no published evaluation of the learning curve in avian coelioscopy, but the higher complication rates encountered in this study in birds compared to mammals, combined with the low case volume, indicate that even for this simpler technique there is possibly a learning curve threshold that is not been reached, or insufficient case volume presenting for maintenance of skills, by some of the veterinarians in zoos performing these interventions, likely again due to low case volume. Low surgical case volume appears an overall hurdle to improving surgical outcomes in zoo animal surgery, and not only in developing inhouse MIS capacity.

An important consideration, not apparent from the data captured in this study, is that not all procedures can be performed by MIS methods, no matter what equipment is available or relevant surgeon experience. Some procedures, such as caesarean section, have to be performed via open surgery. Even in human surgery some procedures have failed to demonstrate any advantage when performed by MIS over standard open abdominal surgery (Lei and others 2017; Wu and others 2017; Xie and others 2017).

Current evidence appears to demonstrate that when a MIS approach to a surgical procedure in a wild animal held in a zoological collection is possible, this carries a lower risk of complications and better outcome than if performed by open surgery.

Pre-clinical veterinary students were used as a model for studying innate cognitive biases in veterinary surgeons that may have an adverse affect on their surgical decision making. Students appear to completely lack any inherent understanding or appreciation of clinical auditing in surgery. They did not appear to understand that measuring one's own surgical outcomes and complications, and acting on this information was the only way of measurably improve one’s surgical outcome results. This was particularly surprising considering the fact that this cohort of students would have been exposed to repeated media reports of medical scandals involving poor surgical outcomes and high infant operative mortalities, and the recent requirement for human surgical speciality units to audit their outcomes and make the results publically available in the United Kingdom, which was extensively covered and discussed by the main stream media, before they had even reaching university (BBC NEWS 2017; Smith 1998).

Students appeared to irrationally confuse acquiring more technical skills with a likely improvement in surgical outcomes, ranking mentoring by a more experience surgeon as the most likely way to improve their personal surgical outcomes. This was followed by practical workshops, and then continuing professional education (CPD) lectures provided by specialists. Clinical auditing was only ranked fourth by the students, but interestingly, this was before reading books and journal articles, arguably the next most important resources for improving an individual veterinarian’s surgical outcomes, by rationally providing a peer-reviewed literature evidence base, upon which to make clinical decisions (Slim 2005; Mittal and Perakath 2010; Zani-Ruttenstock and others 2015).

Unexpectedly, in this time of pervasive social media, online videos were ranked last of the methods. While social media and new technologies have changed traditional CPD in the medical field by lowering costs and increasing convenience (Curran and others 2016; MacWalter and others 2016; Ibrahim and others 2016; Wu and others 2016; Maloney and others 2017) this did not appear to be valued as a resource for improving surgical outcomes and skills by the veterinary students. This warrants further elucidation, at a time when many universities are increasingly moving towards self-directed electronic media based learning.

While it appears interesting that there was no difference between the genders in their self-evaluation of their surgical aptitude and future surgical competency, this may have simply been a type II statistical error due to small sample size, and the study being underpowered to detect a small but real difference (Chang and others 2013), as changes in the gender balance in the veterinary profession are well recognised (Koolmees 2000; Corbett 2007; Kinnison and May 2013; Allen 2016). However there still appears to be male gender bias in many human and veterinary surgical disciplines and training programs (Pitak-Arnnop and others 2010; Cochran and others 2013; Phillips and others 2016), especially noted in fields such as orthopaedic surgery (O'Connor 2016). The different genders having also been shown to require different surgical learning and have different training preferences (Burgos and Josephson 2014). Gender has also been shown to play a role in veterinary surgeons career ambitions and chosen field of work (Kinnison and May 2013).

The results of the students' irrational self-evaluation of their surgical aptitude, despite never having performed surgery, and their self-evaluation of their likely future surgical competence appear to reveal innate cognitive biases that could potentially lead to veterinary surgical errors. Illusory superiority bias may lead veterinary surgeons to have unrealistically optimistic expectations for the surgical outcome of a specific surgical case, despite their knowledge of published evidence to the contrary. The Dunning-Kruger effect may lead veterinary surgeons to have the erroneous belief that they are able to perform procedures that are beyond their competence, or that a specific operation is indicated when it is not, or that the outcome is likely to be more favourable than the evidence indicates. Ultimately these biases have the potential to result in real patient harm.

These cognitive biases warrant further elucidation, and highlight the likely requirement to teach awareness of cognitive bias in the clinical years of the veterinary curriculum in the United Kingdom, and strategies to mitigate their impact, as has been done in human medicine (Hershberger and others 1995; Stiegler and others 2012; Msaouel and others 2014).

5. CONCLUSIONS

1. The available published peer-reviewed evidence base appears to demonstrate that minimally invasive surgery (MIS) carries a lower risk of post-operative complications than open abdominal or coelomic surgery in wildlife species.

2. The results of MIS and open surgery performed in four UK zoological collections over a 25 year period, show a notable absolute risk reduction in major complications when MIS was performed rather than open surgery in mammals and birds, as well as across species.

3. Post-operative survival was also demonstrated to be better in mammals, and particularly primates undergoing MIS compared to open abdominal surgery.

4. Abdominal and coelomic surgical case volume was found to be low in zoological collections, and likely insufficient to overcome the expected initial learning curve needed to develop safe and effective MIS expertise and capacity in these zoos by its self.

5. Surgical complication rates encountered were significantly higher than those presented in the current published literature, indicating likely positive publication and positive outcome bias.

6. Published wildlife surgical outcomes appear overly optimistic, and need to be extrapolated to actual clinical wildlife situations with caution.

7. Untrained veterinary surgeons demonstrate an illusory superiority bias when estimating their surgical aptitude and future surgical performance.

8. Untrained veterinary surgeons fail to have an innate grasp of the necessity of clinical audit in improving an individual veterinary surgeons surgical

outcomes. Combined with current apparent publication bias, this risks leading to poorer than anticipated wildlife surgical outcomes.

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