

A SYSTEMATIC REVIEW OF THE LITERATURE RELATING TO CAPTIVE GREAT APE MORBIDITY AND MORTALITY

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Abstract: Wild bonobos (*Pan paniscus*), chimpanzees (*Pan troglodytes*), Western gorillas (*Gorilla gorilla*), and orangutans (*Pongo pygmaeus*, *Pongo abelii*) are threatened with extinction. In order to help maintain a self-sustaining zoo population, clinicians require a sound understanding of the diseases with which they might be presented. To provide an up-to-date perspective on great ape morbidity and mortality, a systematic review of the zoological and veterinary literature of great apes from 1990 to 2014 was conducted. This is the first review of the great ape literature published since 1990 and the first-ever systematic literature review of great ape morbidity and mortality. The following databases were searched for relevant articles: CAB Abstracts, Web of Science Core Collection, BIOSIS Citation Index, BIOSIS Previews, Current Contents Connect, Data Citation Index, Derwent Innovations Index, MEDLINE, SciELO Citation Index, and Zoological Record. A total of 189 articles reporting on the causes of morbidity and mortality among captive great apes were selected and divided into comparative morbidity–mortality studies and case reports–series or single-disease prevalence studies. The content and main findings of the morbidity–mortality studies were reviewed and the main limitations identified. The case reports–case series and single-disease prevalence studies were categorized and coded according to taxa, etiology, and body system. Subsequent analysis allowed the amount of literature coverage afforded to each category to be calculated and the main diseases and disorders reported within the literature to be identified. This review concludes that reports of idiopathic and infectious diseases along with disorders of the cardiovascular, respiratory, and gastrointestinal body systems were particularly prominent within the great ape literature during 1990–2014. However, recent and accurate prevalence figures are lacking and there are flaws in those reviews that do exist. There is therefore a critical need for a robust, widespread, and more up-to-date review of mortality among captive great apes.

Keywords: Bonobo, chimpanzee, gorilla, mortality review, orangutan, zoologic.

INTRODUCTION

As a result of the growing threats posed by the pet and bush-meat trades, habitat destruction and disease, wild populations of all great apes (bonobos, chimpanzees, gorillas, and orangutans) are rapidly diminishing.³⁶ Therefore great apes housed in zoos serve not only as ambassadors for their species in helping to raise funds and public awareness of conservation issues but as a potential source for repopulation, thereby providing insurance against extinction. Due to their endangered status, the international trade of all ape species is prohibited although movements between zoos is permitted for breeding purposes.²⁹ The zoo population must therefore be self-sustaining and the management of the breeding

programs is guided within Europe by the Great Ape Taxonomic Advisory Group (TAG) under the European Association of Zoos and Aquaria. The success of the program relies on the occurrence of successful births, the rearing of animals to sexual maturity, the maintenance of a population of healthy adults of sound reproductive status and the genetic management of the population to maintain genetic diversity and health.⁹⁰ Any disease threat to captive great apes is therefore of great concern not only for the individual or zoologic collection affected, but more widely, for the future breeding and conservation of these species.

Historically, infectious diseases and disorders of the gastrointestinal and respiratory systems have been consistently identified as the most significant causes of morbidity and mortality among captive great apes.^{9,32,112} However, as a consequence of advances in animal husbandry and veterinary care, patterns of disease are continually changing. Janssen and Bush⁵⁹ published an overview of a number of diseases that had been reported to affect orangutans, gorillas,

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and chimpanzees during the 1980s. One of their conclusions was that age-related conditions such as gonadal neoplasia and cardiovascular disease dominated the literature at this time. There are, however, two potential criticisms of this review. Firstly, with the exception of the aforementioned statement about cardiovascular and neoplastic disorders, there was little attempt to quantify the relative importance of each condition. Also, given that the paper was a narrative review with no methodology provided, it is difficult to confirm the completeness of the information presented.

To the authors' knowledge, there have been no reviews of the veterinary literature of great apes published since 1990. With a view to expanding upon the work of Janssen and Bush,⁵⁸ a systematic review of the zoologic and veterinary literature of great apes from 1990 to 2014 was conducted. The aims of the study were as follows: 1) to identify and critique papers that report upon the comparative prevalence of various diseases and disorders (morbidity and mortality reviews) within the captive great ape population and 2) to calculate the amount of literature coverage afforded to each of the various causes of great ape morbidity or mortality in the zoologic and veterinary literature between 1990 and 2014 by taxa, etiology, and body system affected.

METHODS

Methodology for literature search

The methodology for this systematic literature review followed published guidelines.^{21,100}

Eligibility criteria

The research question was defined as the following: "What are the main causes of morbidity and mortality among great apes kept in captivity?" The inclusion criteria were set to include papers that reported upon specific, naturally occurring diseases or disorders of clinical relevance among captive bonobos, chimpanzees, gorillas, and orangutans.

Information sources

Databases were selected based upon their reputation, relevance, and reported coverage of the literature.⁴⁵ CAB Abstracts is reported to be the database that provides the widest coverage of veterinary journals and was selected for this reason. Also selected for their breadth of coverage were databases available through the Web of Knowledge interface covering a wide range of topic areas: Web

of Science Core Collection, BIOSIS Citation Index, BIOSIS Previews, Current Contents Connect, Data Citation Index, Derwent Innovations Index, MEDLINE, and SciELO Citation Index. Zoological Record was searched due to its coverage of zoology-specific journals not indexed elsewhere.

Search

Alternative search terms and synonyms for each of the key words within the research question were used. The search was limited to include only those papers in English and those published since 1990. The papers obtained from all three databases were merged and duplicates removed.

Article selection and sorting

Papers were screened for relevance and the final list of relevant publications was exported to an Excel spreadsheet.⁸⁴ The content of each was reviewed and the papers classified as either 1) comparative morbidity-mortality studies or 2) case reports-series and papers reporting upon the prevalence of single diseases.

Data collection and processing

The morbidity-mortality studies were reviewed and the following data extracted from each: author, date of publication, period of study, type of study (retrospective-prospective, interventional-observational, multi-single center, longitudinal or cross-sectional), details relating to the study population (taxa, number of subjects, age, sex), and the main causes of morbidity-mortality identified. The reviews were assessed for risk of bias and the main limitations of each identified.

The contents of the case reports-case series and single-disease frequency studies were reviewed and each article categorized and coded according to 1) the taxa under study, 2) the etiology of the primary condition being reported, and 3) the body system affected. Etiologic categories were adapted from the DAMNITV classification system as used by Rizzo et al.¹⁰⁶ and on categories used by Mesle.⁸³ Body system categories were adapted from those used by Robinson et al.¹⁰⁷ Descriptive statistics were carried out and the amount of literature coverage afforded to each of the categories was calculated. The main diseases and disorders reported within the literature were also identified.

RESULTS AND DISCUSSION

The initial search yielded 1,146 results and following relevance screening, 189 full-text arti-

FIGURES

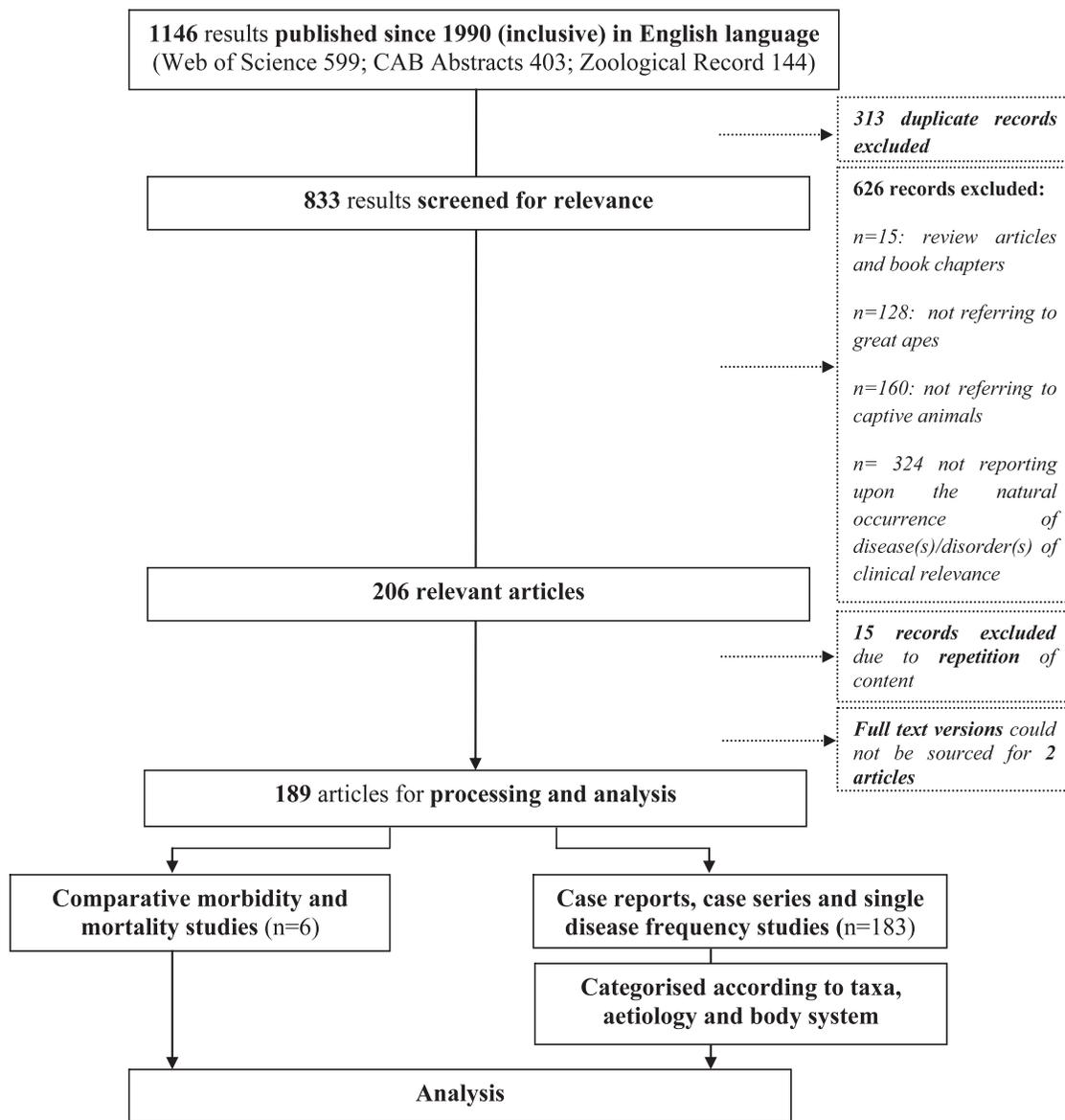


Figure 1. Flow chart showing sequential steps involved in reference selection and exclusion process based on the PRISMA checklist and flow diagram.

cles remained (Fig. 1). The literature search revealed a variety of reference types: journal articles, conference proceedings, meeting papers, and correspondence pieces. A total of 183 (97%) of the articles were classified as case reports, case series, and single-disease frequency studies. The remaining six papers were morbidity and mortality studies, which reported upon the comparative frequency of occurrence of various diseases and disorders within a population.

Case reports, case series, and single-disease frequency studies

The absolute number and percentage of papers identified for each taxon are displayed in Table 1. Chimpanzees (40%) and gorillas (35%) received greater literature coverage than orangutans (19%) and especially bonobos (2%). This distribution may be related to the relative numbers of each species kept in captivity and due to the involve-

Table 1. Amount of literature coverage afforded to each taxa, displayed as absolute number and percentage of total ($n = 1,831$), ordered alphabetically.

Taxa	Absolute number	% of total
Bonobos	4	2%
Chimpanzees	73	40%
Gorillas	64	35%
Orangutans	35	19%
All four taxa	2	1%
Two or three taxa	5	3%

ment of chimpanzees in biomedical and behavioral research.

Etiology: A total of 174 (95%) of the 183 papers could be categorized according to the etiology of the primary condition being reported (Table 2). The three etiologies that received most literature coverage were infectious (39%), idiopathic (17%), and neoplastic (9%) disorders.

Infectious diseases, especially of the gastrointestinal and upper respiratory tracts, were reported more commonly in the literature from 1990 to 2014 than disorders of any other etiology. This is despite the fact that infection has been stated elsewhere as becoming less important over recent years.¹³⁰ The papers that reported upon infectious disease were further categorized by causal agent (Table 3). Bacterial infection was often reported in association with disorders of the gastrointestinal system such as enteritis, colitis, and the clinical presentation of diarrhea. Reported pathogenic agents include *Salmonella* spp., *Escherichia coli* and *Campylobacter* spp.^{10,95,97} The most commonly cited gastrointestinal disorder of bacterial etiology was shigellosis, which was also implicated in cases of reactive arthritis.^{5,102,133} Bacterial

Table 2. Amount of literature coverage afforded to each etiology, displayed as absolute number and percentage of total ($n = 174$), ordered alphabetically.

Etiologic category	Absolute number	% of total
Behavioral/psychological	8	5%
Congenital/hereditary	6	3%
Degenerative	11	6%
Husbandry related	9	5%
Idiopathic	30	17%
Immune mediated	5	3%
Infectious	62	36%
Metabolic	6	3%
Miscellaneous	4	2%
Neoplastic	15	9%
Trauma-accidental death	7	4%
Vascular	11	6%

Table 3. Infectious disease, broken down by pathogenic agent, displayed as percentage of total ($n = 62$), ordered alphabetically.

Pathogenic agent	% of total
Bacterial	45%
Fungal	5%
Mixed	8%
Undetermined	6%
Viral	15%

infections were also commonly implicated in respiratory disorders, which were particularly frequently reported in orangutans.^{17,73,123,137} *Balantidium coli* and *Balamuthia mandrillaris* were the most frequently cited parasitic infections. Viral diseases reported, amongst others, included cases of fatal viral myocarditis^{61,88,93,136} and also herpesvirus infection.^{66,108} Respiratory syncytial virus (RSV), often in association with concurrent *Streptococcus pneumoniae* infection, was reported to cause severe, often fatal, bronchopneumonia.^{27,126,129} Fungal infections including coccidioidomycosis^{49,52} and a suspected case of dermatophilosis¹⁴ were also reported. Human-to-great ape zoonotic disease transmission reported in the literature included cases of respiratory disease due to RSV, *Streptococcus pneumoniae*, and whooping cough, and cases of coxsackie B3 virus, *Entamoeba histolytica*, and varicella virus infection.^{30,46,79,93,126,129}

The majority of those articles classified as being on the topic of idiopathic disorders were reporting on the occurrence of cardiovascular disease. Reports identified suggest that disorders of the cardiovascular system are associated with high rates of mortality in at least three (chimpanzees, gorillas, and orangutans) of the four great ape taxa. However, there is very little evidence presented in the literature about the epidemiology, diagnosis, and treatment of great ape cardiovascular disease, suggesting that current understanding remains poor and that there is a critical need for further research in this area. Other reported idiopathic conditions were varied, and included epilepsy, appendicitis, hyperthyroidism, and diverticulitis.^{33,42,80,91}

The female reproductive tract^{30,54,116,124} and gastrointestinal system were the body systems most commonly reported to be affected by neoplastic disorders^{26,111} (Table 4).

Body system: A total of 177 (97%) of the 183 papers could be classified according to a single body-system category. The body systems most commonly reported on were cardiovascular

Table 4. Neoplastic disorders reported in the literature with references (ref.), by taxa, listed alphabetically.

Taxa	Condition	Ref.
Chimpanzee	Gastrointestinal stromal tumor	110
	Gingival mass	109
	Hepatocellular carcinoma and myelolipoma	99
	Maxillary sarcoma	41
	Nevus lipomatosus cutaneus superficialis	67
	Renal carcinoma	44
	Uterine leiomyoma	116
Gorilla	Acute lymphocytic leukemia	7
	Choriocarcinoma	30
	Inoperable obstetric cancer	54
	Intracranial tumor gorilla (possible lymphoma)	82
	Leydigocytoma and a large cell lung carcinoma	96
	Metastatic pancreatic islet cell carcinoma	26
	Primary hyperparathyroidism (presumed adenoma)	53
	Prolactin secreting pituitary adenoma	25
	Squamous cell carcinoma of the skin	40
	Uterine adenocarcinoma and squamous cell carcinoma of vagina, cervix, and uterus	124
Orangutan	Malignant gastric rhabdoid tumor	111

(18%), generalized–multi-system (18%), gastrointestinal (12%), and respiratory (11%).

Cardiovascular: Idiopathic myocardial fibrosis (often referred to as fibrosing cardiomyopathy) was reported among gorillas, chimpanzees, and orangutans and was associated with sudden death, peri-anesthetic death, congestive heart failure, and cerebrovascular infarction.^{26,70,85,90,113} Other cardiomyopathies reported include dilated cardiomyopathy^{118,119} and arrhythmogenic right-ventricular cardiomyopathy.¹²⁷ Several reports of aortic aneurysm or dissection in male gorillas^{3,64} and cardiac arrhythmias, particularly among male chimpanzees, also featured.^{34,69,120} Hypertension was reported to affect gorillas and chimpanzees and has been shown to correlate with age and obesity and to increase mortality risk.^{36,37,85} Other reports included congenital heart disease,^{43,128} fatal myocarditis,^{88,93,103,136} a case of coronary artery disease in a gorilla,¹¹⁴ and three cases of cerebrovascular accident (stroke) in female chimpanzees.⁶⁰

Generalized–multi-system: This category consisted largely of infectious disorders. Noninfectious conditions in this category included cases of idiopathic hypocalcaemia, Reyes-like syndrome, systemic anaphylaxis, protein deficiency, clinically significant chromosomal abnormalities, and intra-abdominal abscesses or cysts.^{12,15,24,48,72,86,89,92} Obesity (with or without concurrent metabolic syndrome) was also categorized as a generalized condition.^{74,94,122,131}

Gastrointestinal: Most reported gastrointestinal diseases were infection-associated. The most

commonly reported presenting sign was diarrhea, which was occasionally hemorrhagic,^{57,71,95,97} but lethargy, inappetence, anorexia, tenesmus, rectal prolapse, and abdominal pain also featured.^{33,91} Three cases of neoplasia of the gastrointestinal system (Table 5) and one case of paralytic ileus in an orangutan, which occurred secondary to severe depression, were also reported.¹²¹

Respiratory: Air sacculitis was the most frequently discussed respiratory disorder, especially in orangutans.^{17,73,105,137,138} RSV, with or without concurrent *Streptococcus pneumoniae* infection, was also identified as a common cause of fatal disease.^{27,126,129} Other infectious agents reported included *Bordetella pertussis*,⁴⁶ *Streptococcus anginosus*,⁵⁵ *Mycobacterium kansasii*,⁴ and *Mycobacterium tuberculosis*.^{115,117} Noninfectious disorders included allergic respiratory disease and anesthetic complications.^{35,63,65} Clinical signs included nasal discharge, coughing, tachypnea, dyspnea, and, less commonly, facial swelling, exophthalmos, and cyanosis.

Musculoskeletal: The majority of musculoskeletal disorders reported were degenerative in origin.^{1,19,132,134} Rickets was reported in a gorilla, an orangutan, and a group of chimpanzees.^{8,22,62}

Neurologic: Four great apes (one orangutan; three gorillas) displayed nonspecific clinical signs progressing to ataxia, disorientation, and death caused by the amoeba species *Ballamuthia mandrillaris*.^{18,78,104} Encephalopathy was also the cause of death in a case of septicemia due to *Aeromonas hydrophilia* infection in a gorilla.⁴⁷ Noninfectious

Table 5. Amount of literature coverage afforded to each body system, displayed as absolute number and percentage of total ($n = 177$), ordered alphabetically.

Body system category	Absolute number	% of total
Behavioral	10	6%
Cardiovascular	31	18%
Dental	3	2%
Endocrine	8	5%
Gastrointestinal	21	12%
Generalized–multi-system	31	18%
Hepatobiliary	1	<1%
Hematopoietic–lymphatic	1	<1%
Musculoskeletal	14	8%
Neurological	12	7%
Ophthalmic	6	3%
Renal	2	1%
Reproductive	9	5%
Respiratory	20	11%
Skin–integumentary	6	3%
Urinary (lower)	2	1%

neurologic conditions reported include inflammatory polyradiculoneuropathy, cerebral calcinosis, vascular mineralization, and acute transverse myelitis in chimpanzees;^{2,28,87,139} intracranial mass, hydrocephalus, and age-related pallido-nigral degeneration in gorillas;^{77,82} demyelinating polyneuropathy in an orangutan;³¹ and epilepsy in bonobos.⁴²

Behavioral: One observational study of zoo-housed chimpanzees concluded that abnormal behavior is endemic in the population.¹¹ The paper reported that all 40 animals displayed at least two abnormal behaviors, including coprophagy, stereotypic grooming, genital touching, rocking, regurgitation, hair plucking, and self-injury. Regurgitation–reingestion syndrome was also reported in gorillas,^{51,75} chimpanzees,¹²⁵ and orangutans.²⁰ Self-injurious behavior was identified in a gorilla,³⁸ a chimpanzee,¹³ and a bonobo.¹⁰¹ Mood and anxiety disorders were also described in chimpanzees.^{16,39}

Other body systems: Disorders of the integument, reproductive and genitourinary tracts, and endocrine, hepatobiliary, and hematopoietic-lymphatic systems as well as ophthalmic and dental conditions each constituted five percent or less of the articles identified

Whilst these figures relating to the frequency of reporting are informative, it must be remembered that amount of literature coverage a disorder receives might be influenced by a number of factors; for example, the veterinary knowledge

and diagnostic capabilities available at the time, the level of allocated funding, the specific clinical and academic interests of the author, or simply the author's perceived importance of the condition. Perhaps almost ironically, an author's perception of a condition's importance can in turn be influenced by the amount of literature coverage it receives. Case reports are an invaluable resource but they give very little perspective on the significance of a condition at a population level. An appreciation of this latter point requires in depth epidemiologic study and the calculation of comparative prevalence of various diseases and disorders. This was the purpose of just six of the records identified by the literature search (Table 6).

Comparative morbidity and mortality studies

Six (3%) of the 189 papers identified consisted of reviews of the various causes of morbidity and mortality among captive chimpanzees, gorillas, and orangutans. The main findings of each are summarized in Table 6.

Three of the six prevalence reviews were single-center studies.^{68,90,94} The three remaining studies reviewed morbidity and mortality across more than one institution.^{50,81,130} This allowed for a larger number of animals to be studied, arguably deeming the findings more representative of the wider population. Five of the six were retrospective reviews,^{50,81,90,130} involving the use of routine information that had been collected for another purpose. The researchers therefore had very little control over the accuracy and completeness of the dataset, which might negatively impact upon the reliability of the findings. In contrast, the screening of 16 geriatric female chimpanzees for the presence of chronic and age-related disease⁹⁴ was a prospective study and therefore had the advantage that data collection methods were specifically designed for a purpose. The results of this study might therefore be considered more reliable, although the potential for observer bias (bias introduced due to the investigator's prior knowledge of the hypothesis under investigation of the individual's exposure or disease status)⁶ remains. All six studies reported the frequency of occurrence of various conditions but were only able to speculate about underlying causes and risk factors.

Inclusion criteria were not always stated, making it difficult to ascertain the degree of selection bias present. In two of the multi-center studies,^{50,81} the investigators were reliant on various institutions submitting data to the study.

Table 6. Summary of key components of the six morbidity–mortality reviews identified by the literature search.

Author and year	Period of study	Study type	Study population	Main causes of morbidity–mortality
Meehan and Lowenstine 1994 ⁸¹	1980–1994	Retrospective, observational, longitudinal, multi-center (unknown no.); review of postmortem records	Gorillas ($n = 74$); all ages, genders; Species Survival Plan population	Infants: trauma (60%) Adults (<30 yr): gastrointestinal (36%), cardiovascular (32%) Elderly (>30 yr): cardiovascular (53%)
Varki et al. 2009 ¹³⁰	1966–1991 1992–2008	Retrospective, observational, longitudinal, multi-center (2); review of postmortem records	Chimpanzees ($n = 58$); adult (>10 yr); Yerkes National Primate Research Center; Primate Foundation of Arizona	1966–1991: enterocolitis (16%), heart disease (11%), meningitis (11%), pneumonia (5%), renal disease (5%), trauma (3%), miscellaneous (50%) 1992–2008: heart disease (36%), renal disease (16%), trauma (12%), miscellaneous (36%)
Nunamaker et al. 2012 ⁹⁴	2009	Prospective, observational, cross-sectional single center; incidence of disease at routine health assessment	Chimpanzees ($n = 16$); aged >35 yr; females; Alamogordo Primate Facility	Cardiovascular disease (81%), metabolic syndrome (44%), renal disease (31%)
Munson and Montali 1990 ⁹⁰	Unknown	Retrospective, observational, longitudinal, single center; review of pathology and medical records	Gorillas, orangutans and chimpanzees ($n =$ unknown); National Zoological Park, Washington, D.C.	Orangutans: myocardial fibrosis, gastrointestinal disease, perinatal infections Gorillas: arthritis, gastrointestinal disease, infertility, Chimpanzee: myocardial fibrosis
Lammey et al. 2008 ⁶⁸	2001–2006	Retrospective, observational, longitudinal, single center; review of postmortem records	Chimpanzees ($n = 36$); aged 10–40 yr; Alamogordo Primate Facility	Sudden cardiac death (36%), renal failure (25%), trauma and septicemia (each 23%), anesthetic complications and neoplasia (each 15%)
Hewitt 2005 ⁵⁰	1896–2005	Retrospective, observational, longitudinal, multi-center (9); review of postmortem records	Gorillas ($n = 109$); all ages; United Kingdom and Ireland populations (various zoological collections)	Respiratory (27%), multi-system (26%), gastrointestinal (15%) (cardiovascular disease: <9%)

This self-selection process has the potential to introduce bias but in retrospective studies that involve voluntary participation, it is largely unavoidable.

In five of the six studies^{50,68,81,90,130} the data collected consisted of medical records or pathology reports written by various clinicians and pathologists at the time of an animal's illness or

death. In one study,⁵⁰ reported morbidity and mortality events date as far back as 1896, when veterinary diagnostic capabilities were limited.

In view of the small sample sizes, the time span, and the single-center focus of the studies, they may not be representative on a wider population level, and they may not provide an accurate and up-to-date representation of the current situation.

Limitations of this systematic literature review

The validity of the conclusions depends heavily on the reliability of the initial literature search. Every effort was made to make the search as exhaustive as possible through the use of synonyms and Medical Subject Headings (MeSH) terms. The search strategy used within this review returned a total of 1,146 initial results, which were considered to constitute a representative proportion of the literature body as a whole. Less than one-third ($n = 313$) of the 1,146 results were duplicates, suggesting that there is a relatively low degree of overlap of coverage by the databases accessed. Some relevant papers were not identified by the literature search;^{23,76,98} this might have been due to words (for example, “captive” or “zoo”) not being included in the key words provided by authors, or at the point of database indexing. This highlights the importance of the application of accurate and representative key words by journal authors and editors in order to facilitate such search and review processes. These omissions might, however, simply reflect the inherent limitations of any literature search, and the difficulties associated with striking the balance between maximizing sensitivity whilst retaining specificity.

For case report–case series or single diseases, category definitions were described and closely adhered to but some degree of subjectivity and ambiguity was still encountered. An example of this is regurgitation–reingestion, categorized in this review as a behavioral disorder. However, since diet and environmental conditions have been suggested as underlying causes, it might have been categorized as husbandry-related, illustrating how easily categorization can influence results.

Differences in the approach to categorization might also have been responsible for the variation in findings between the two gorilla comparative mortality studies identified by the search: Meehan and Lowenstine⁸¹ found that cardiovascular disease was responsible for 32% of adult and 41% of aged gorilla deaths. However, Hewitt⁵⁰ identified it as the cause of death in less than 9% of the

animals. If this discrepancy were genuine, it might suggest that there are differences in the cardiac risk factors (such as genetics, diet, husbandry) to which the North American and United Kingdom–Irish populations are exposed. Upon closer examination, however, a number of animals included in the latter study were diagnosed as having cardiovascular and another concurrent disease on postmortem examination. These deaths were categorized as being multi-system in origin, which might have led to underrepresentation of the importance of cardiovascular disease as a cause of mortality within this population.

Categorization according to etiology does not account for disorders or events that occur due to a more complicated, multi-factorial pathophysiology. Examples of such are anesthesia-related complications and infection-associated disorders. In the latter case, the pathogen may not be the primary or sole cause; the infection might be a complicating factor in another disease process or may be occurring secondarily to underlying reasons such as immunosuppression, poor husbandry, or environmental conditions. In human medicine, many of the issues highlighted here are overcome by the implementation of the International Classification of Diseases system.¹³⁵ This might in fact be a more appropriate categorization model for morbidity and mortality reviews in veterinary medicine to utilize in the future.

CONCLUSIONS

This is the first review of the great ape literature published since 1990 and the first-ever systematic literature review of great ape morbidity and mortality. The review highlights cardiovascular disease, multi-system disorders, and infectious diseases as areas of current topical interest within the current great ape literature. It identifies cardiovascular and other chronic or age-related diseases to be of particular importance, especially in light of the increasing longevity of great apes housed in modern zoos.

The review concludes, however, that there is a critical need for a robust, widespread and more up-to-date review of mortality among captive great apes. The aims of such a review would be to identify the main causes of morbidity and mortality for each age group and species. Any retrospective review performed should focus upon a relatively recent time period in order to produce findings that provide an accurate and reliable representation of the current situation. Prospectively, data collection methods should provide the opportunity for more an in-depth

study of subpopulations, such as specific age groups (e.g., infant or geriatric animals), between which patterns of disease and mortality are likely to differ. In particular, in-depth study of the risk factors associated with the development of diseases of significance would be especially interesting, as would comparison of mortality between captive and wild great apes. The findings of such a study would be informative, not only for the practicing clinician, but also in providing a focus for further investigation and research to help improve captive great ape health and welfare. Working closely with the Great Ape TAG, studbook coordinators, and vet advisors would facilitate data collection and maximize the potential benefits of such a study.

Acknowledgments: Thanks go to supervisors and colleagues at the named institutions for their ongoing support and assistance.

LITERATURE CITED

1. Aldridge VJ. A search for probable cause: self-wounding in a zoo chimpanzee (*Pan troglodytes*). *Am J Primatol.* 2005;66(Suppl. 1):82 (Meeting Abstr.).
2. Alford PL, Satterfield WC. Paralytic illness resembling inflammatory polyradiculoneuropathy in a chimpanzee. *J Am Vet Med Assoc.* 1995;207(1):83–85.
3. Allchurch AF. Sudden death and cardiovascular disease in the lowland gorilla. *Dodo.* 1993;29:172–178.
4. Alvarado T. Atypical mycobacterial pneumonia in a western lowland gorilla caused by *Mycobacterium kansasii*. In: AAZPA Regional Conf Proc; 1992. p. 629–632.
5. Banish LD, Bush M, Montali RJ, Sac D. Shigellosis in a zoological collection of primates. *J Zoo Wildl Med.* 1990;21:302–309.
6. Barratt H, Kirwan M. Biases: bias in epidemiological studies [Internet]. Health Knowledge. 2009 [cited 2015 Jul 15]. Available from: <http://www.healthknowledge.org.uk/public-health-textbook/research-methods/1a-epidemiology/biases>
7. Barrie MT, Backeus KA, Grunow J, Nitschke R. Acute lymphocytic leukemia in a six-month-old western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med* [Internet]. 1999;30:268–272. Available from: <Go to ISI>://000081607900011
8. Bellisari A, Duren DL, Sherwood RJ, Barrie M. A captive infant female gorilla with vitamin D and calcium deficiency: preliminary description. *Am J Phys Anthropol.* 2004;S38:61.
9. Benirschke K, Adams FD. Gorilla diseases and causes of death. *J Reprod Fertil Suppl.* 1980;Suppl 28:139–148.
10. Beutin L, Knollmann-Schanbacher G, Rietschel W, Seeger H. Animal reservoirs of *Escherichia coli* O157:[H7]. *Vet Rec.* 1996;139(3):70–71.
11. Birkett LP, Newton-Fisher NE. How abnormal is the behaviour of captive, zoo-living chimpanzees? *PLoS One.* 2011;6(6):e20101.
12. Blampied N le Q, De K, Fullerton D, Coleman P, Purcell-Jones G, Carroll B. Surgical removal of an abdominal cyst from a Bornean orang-utan *Pongo pygmaeus pygmaeus*. *Dodo.* 1992;28:165–169.
13. Bourgeois SR, Vazquez M, Brasky K. Combination therapy reduces self-injurious behavior in a chimpanzee (*Pan troglodytes troglodytes*): a case report. *J Appl Anim Welf Sci.* 2007;10(2):123–140.
14. Brack M, Hochleithner C, Hochleithner M, Zenker W. Suspected dermatophilosis in an adult orangutan (*Pongo pygmaeus pygmaeus*). *J Zoo Wildl Med.* 1997;28:336–341.
15. Bradford CM, Tupa L, Wiese D, Hurley TJ, Zimmerman R. Unusual Turner syndrome mosaic with a triple x cell line (47,X/49,XXX) in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 2013;44:1055–1058.
16. Bradshaw GA, Capaldo T, Lindner L, Grow G. Building an inner sanctuary: complex PTSD in chimpanzees. *J Trauma Dissociation.* 2008;9:9–34.
17. Cambre RC, Edwards JE, Wilson HL, Todd JK, Strain JD, Hendee RW, Jaskunas JM, Knox RF, Chang JHT. Maxillary and ethmoid sinusitis with orbital and intracranial extension in an infant orangutan (*Pongo pygmaeus*). *J Zoo Wildl Med.* 1995;26:144–151.
18. Canfield PJ, Vogelnest L, Cunningham MI, Visvesvara GS. Amoebic meningoencephalitis caused by *Balamuthia mandrillaris* in an orangutan. *Aust Vet J.* 1997;75(2):97–100.
19. Carter ML. Skeletal and dental pathology of wild and captive chimpanzees Clinical and evolutionary implications. *Am J Phys Anthropol.* 1992;90(S16):67–68.
20. Cassella CM, Mills A, Lukas KE. Prevalence of regurgitation and reingestion in orangutans housed in North American zoos and an examination of factors influencing its occurrence in a single group of Bornean orangutans. *Zoo Biol.* 2012;31(5):609–620.
21. Centre for Reviews and Dissemination. Systematic reviews: CRD's guidance for undertaking reviews in health care. York (United Kingdom) CRD, University of York; 2009. Chapter 1, p. 6–14.
22. Chai N, Bomsel MC, Berthier JL. A case of osteodystrophy in an orang-utan. In: *Erkrankungen der Zootiere: Verhandlungsbericht des 41 Internationalen Symposiums über die Erkrankungen der Zoo- und Wildtiere*; 2003. p. 81–86.
23. Chai N, Hazan T, Wedlarski R, Rigoulet J. Treatment of a retroperitoneal abscess by omentalization in an orangutan (*Pongo pygmaeus pygmaeus*). *J Zoo Wildl Med.* 2009;40:350–353.
24. Chatfield J, Stones G, Jalil T. Severe idiopathic hypocalcemia in a juvenile western lowland gorilla, *Gorilla gorilla gorilla*. *J Zoo Wildl Med.* 2012;43:171–173.

25. Chatfield J, Zhang L, Ramey J, Bowsher T, Loskutoff N, O'Neill K. Resolution of a hyperprolactinemia in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 2006;37:565–566.
26. Chiu E, Bodley K. A psychogeriatrician's home visit to the zoo: a case report. *Int Psychogeriatrics.* 2010;22:671–673.
27. Clarke CJ, Watt NJ, Meredith A, McIntyre N, Burns SM. Respiratory syncytial virus-associated bronchopneumonia in a young chimpanzee. *J Comp Pathol.* 1994;110:207–212.
28. Connor-Stroud FR, Hopkins WD, Preuss TM, Johnson Z, Zhang X, Sharma P. Extensive vascular mineralization in the brain of a chimpanzee (*Pan troglodytes*). *Comp Med [Internet].* 2014 [cited 2014 Aug 25]; 64(3):224–229. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24956215>
29. Convention on International Trade in Endangered Species (CITES). Convention on International Trade in Endangered Species of Wild Fauna and Flora: Appendices I, II and III [Internet]. (cited 2016 July 18) 2015. Available from: <http://www.cites.org/sites/default/files/eng/app/2015/E-Appendices-2015-02-05.pdf>
30. Cook RA, Calle PP, Mangold B, McNamara T, Raphael B, Stetter M, Goldstein L, Haramati N, Barakat R, Jones W, Al. E. Choriocarcinoma in a young adult gorilla (*Gorilla g. gorilla*): diagnosis, treatment and outcome. In: American Association of Zoo Veterinarians Annual Conference, American Association of Zoo Veterinarians; 2010. p. 229–230.
31. Cossaboon C, Antilla A, Geurts T, Pietsch R. Allie's story: the road to recovery. A seven year history of a Sumatran orangutan (*Pongo abelii*) with a neurological disease. *Anim Keepers' Forum.* 2008;35:273–280.
32. Cousins D. Mortality factors in captive gorillas (*Gorilla gorilla*). *Int Zoo News.* 1983;30:5–17.
33. D'Agostino J, Isaza R, Fingland R, Hoskinson J, Ragsdale J. Acute appendicitis in a chimpanzee (*Pan troglodytes*). *J Med Primatol.* 2007;36(3):119–123.
34. Doane CJ, Lee DR, Sleeper MM. Electrocardiogram abnormalities in captive chimpanzees (*Pan troglodytes*). *Comp Med.* 2006;56:512–518.
35. Dumonceaux GA, Lamberski N, Clutter D, Nagy SMJ, Burek K, Phillips LG. Treatment of bilateral nasal polyposis and chronic refractory inhalant allergic rhinitis in a chimpanzee (*Pan troglodytes*). *J Zoo Wildl Med.* 1997;28:215–219.
36. Ely JJ, Zavaskis T, Lammey ML. Hypertension increases with aging and obesity in chimpanzees (*Pan troglodytes*). *Zoo Biol.* 2013;32:79–87.
37. Ely JJ, Zavaskis T, Lammey ML, Rick Lee D. Blood pressure reference intervals for healthy adult chimpanzees (*Pan troglodytes*). *J Med Primatol.* 2011; 40:171–180.
38. Espinosa-Avilés D, Elizondo G, Morales-Martínez, M Rodríguez-Herrejón F, Varela P. Treatment of acute self-aggressive behaviour in a captive gorilla (*Gorilla gorilla gorilla*). *Vet Rec.* 2004;154:401–402.
39. Ferdowsian HR, Durham DL, Kimwele C, Kranendonk G, Otali E, Akugizibwe T, Mulcahy JB, Ajarova L, Johnson CM. Signs of mood and anxiety disorders in chimpanzees. *PLoS One.* 2011;6.
40. Fernandez Bellon H, Vidal M, Borau J, Fernandez A, Moran J. Squamous cell carcinoma of the skin in an albino gorilla (*Gorilla gorilla gorilla*). In: Proceedings of the Institute for Zoo and Wildlife Research No 5; 2003. p. 175–177.
41. Fujisawa M, Uono T, Nogami E, Hirosawa M, Morimura N, Saito A, Seres M, Teramoto M, Nagano K, Mori Y, Uesaka H, Nasu K, Tomonaga M, Idani G, Hirata S, Tsuruyama T, Matsubayashi K. A case of maxillary sarcoma in a chimpanzee (*Pan troglodytes*). *J Med Primatol.* 2014;43(2):111–114.
42. Gerlach T, Clyde VL, Morris GL, Bell B, Wallace RS. Alternative therapeutic options for medical management of epilepsy in apes. *J Zoo Wildl Med.* 2011;42:291–294.
43. Greenberg M, Jansse D, Jamieson S, Rothman A, Frankville D, Cooper S, Kriett J, Adsit P, Shima A, Morris P, Sutherland-Smith M. Surgical repair of an atrial septal defect in a juvenile Sumatran orangutan (*Pongo pygmaeus sumatraensis*). *J Zoo Wildl Med.* 1999; 30:256–261.
44. Greenwood AG, Lowe JW, Gaunt L. Renal carcinoma in a chimpanzee (*Pan troglodytes*). *Vet Rec.* 1995;137:380–381.
45. Grindlay DJC, Brennan ML, Dean RS. Searching the veterinary literature: a comparison of the coverage of veterinary journals by nine bibliographic databases. *J Vet Med Ed.* 2012; p. 1–9.
46. Gustavsson OEA, Röken BO, Serrander R. An epizootic of whooping cough among chimpanzees in a zoo. *Folia Primatol.* 1990;55(1):45–50.
47. Harrison TM, Shellabarger WC, Reichard TA. Aeromonas hydrophila septicemia and resulting encephalopathy in a captive juvenile western lowland gorilla (*Gorilla gorilla gorilla*). In: Baer CK; Willette MM (eds.). Proceedings American Association of Zoo Veterinarians, American Association of Wildlife Veterinarians, Association of Reptilian and Amphibian Veterinarians, National Association of Zoo and Wildlife Veterinarians Joint Conference. American Association of Zoo Veterinarians; 2001. p. 366–370.
48. Hayman DT, King T, Cameron K. Successful treatment of acute systemic anaphylaxis in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 2010;41:522–525.
49. Herrin KV, Miranda A, Loebenberg D. Posaconazole therapy for systemic coccidioidomycosis in a chimpanzee (*Pan troglodytes*): a case report. *Mycoses.* 2005;48(6):447–452.
50. Hewitt S. Preliminary findings of the prevalence of diseases in captive western lowland gorillas (*Gorilla gorilla gorilla*) in the United Kingdom and Ireland

(1896–2005). In: Proceedings of the 7th Annual Symposium on Zoo Research; 2005. p. 222–231.

51. Hill SP. Do gorillas regurgitate potentially-injurious stomach acid during regurgitation and re-ingestion? *Anim Welf.* 2009;18:123–127.

52. Hoffman K, Videan EN, Fritz J, Murphy J. Diagnosis and treatment of ocular coccidioidomycosis in a female captive chimpanzee (*Pan troglodytes*): a case study. *Ann N Y Acad Sci* [Internet]. 2007 [cited 2014 Aug 23];1111:404–410. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17303834>

53. Hooper J. Primary hyperparathyroidism in a western lowland gorilla. In: Roberts V (ed.). In: British Veterinary Zoological Society Proceedings of the Spring Meeting: Mammalian Medicine and Surgery; 2011. p. 23.

54. Hunter R, Agnew A. A differential diagnosis of diffuse idiopathic skeletal hyperostosis (DISH) in a *Gorilla gorilla gorilla* specimen. *Am J Anthropol* 80th Annu Meet Am. 2011;144(S52):172.

55. Ihms EA, Daniels JB, Koivisto CS, Barrie MT, Russell DS. Fatal *Streptococcus anginosus*-associated pneumonia in a captive Sumatran orangutan (*Pongo abelii*). *Zoo Biol.* 2006;25(2):101–115.

56. International Union for Conservation of Nature [Internet]. The IUCN Red List of Threatened Species. Version 2013. c2013 [cited 2013 Nov 11]. Available from: <http://www.iucnredlist.org>

57. Isidoro M, Martinez J, Ramis A. Haemorrhagic-necrotizing colitis associated with *Campylobacter jejuni* and *Balantidium coli* in a zoo gorilla. *J Comp Pathol.* 2013;148(1):87.

58. Janssen DL. Diseases of great apes. In: Fowler ME (ed.). *Zoo and wild animal medicine: current therapy 3*. Philadelphia (PA): W.B. Saunders; 1993. p. 334–338.

59. Janssen DL, Bush RM. Review of the medical literature of great apes in the 1980s. *Zoo Biol.* 1990;9:123–134.

60. Jean SM, Preuss TM, Sharma P, Anderson DC, Provenzale JM, Strobert E, Ross SR, Stroud FC. Cerebrovascular accident (stroke) in captive, group-housed, female chimpanzees. *Comp Med.* 2012;62(4):322–329.

61. Jones P, Cordonnier N, Mahamba C, Burt FJ, Rakotovo F, Swanepoel R, André C, Dauger S, Bakkali Kassimi L. Encephalomyocarditis virus mortality in semi-wild bonobos (*Pan paniscus*). *J Med Primatol.* 2011;40:157–163.

62. Junge RE, Gannon FH, Porton I, McAlister WH, Whyte MP. Management and prevention of vitamin D deficiency rickets in captive-born juvenile chimpanzees (*Pan troglodytes*). *J Zoo Wildl Med.* 2000;31:361–369.

63. Karesh WB, Lidell RM, Sirota P. Clinical challenge case 1: aspiration pneumonia and abscess in a gorilla. *Primates.* 2012;53(3):221–226.

64. Kenny DE, Cambre RC, Alvarado TP, Prowten AW, Allchurch AF, Marks SK, Zuba JR. Aortic

dissection—an important cardiovascular-disease in captive gorillas (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 1994;25:561–568.

65. Kenny DE, Knightly F, Haas B, Hergott L, Kutinsky I, Eller JL. Negative-pressure pulmonary edema complicated by acute respiratory distress syndrome in an orangutan (*Pongo pygmaeus abelii*). *J Zoo Wildl Med.* 2003;34:394–399.

66. Kik MJ, Bos JH, Groen J, Dorrestein GM. *Herpes simplex* infection in a juvenile orangutan (*Pongo pygmaeus pygmaeus*). *J Zoo Wildl Med.* 2005;36:131–134.

67. Klopfleisch R, Langner C, Von Felbert I, Rudnick JC, Teifke JP. Nevus lipomatosus cutaneus superficialis (Hoffmann-Zurhelle) in a chimpanzee (*Pan troglodytes*). *J Med Primatol.* 2007;36:57–60.

68. Lammey ML, Baskin GB, Gigliotti AP, Lee DR, Ely JJ, Sleeper MM. Interstitial myocardial fibrosis in a captive chimpanzee (*Pan troglodytes*) population. *Comp Med.* 2008;58:389–394.

69. Lammey ML, Jackson R, Ely JJ, Lee DR, Sleeper MM. Use of an implantable loop recorder in the investigation of arrhythmias in adult captive chimpanzees (*Pan troglodytes*). *Comp Med.* 2011;61:71–75.

70. Lammey ML, Lee DR, Ely JJ, Sleeper MM. Sudden cardiac death in 13 captive chimpanzees (*Pan troglodytes*). *J Med Primatol* [Internet]. 2008 [cited 2013 Nov 20];37 Suppl 1(13):39–43. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18269527>

71. Lankester F, Mätz-Rensing K, Kiyang J, Jensen SA, Weiss S, Leendertz FH. Fatal ulcerative colitis in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Med Primatol.* 2008;37(6):287–302.

72. Lear TL, Houck ML, Zhang YW, Debnar LA, Sutherland-Smith MR, Young L, Jones KL, Benirschke K. Trisomy 17 in a bonobo (*Pan paniscus*) and deletion of 3q in a lowland gorilla (*Gorilla gorilla gorilla*): comparison with human trisomy 18 and human deletion 4q syndrome. *Cytogenet Cell Genet.* 2001;95(3–4):228–233.

73. Lewis I, Lung NP, Ward A. Management of a chronically ill orangutan: communication and cooperation are the keys. In: Brookfield Zoo (ed.). *The apes: challenges for the 21st century*. Conference proceedings Chicago Zoological Society; 2001. p. 186–189.

74. Lintzenich B, Ward AM. Weight management strategies in apes. In: Brookfield Zoo (ed.). *The apes: challenges for the 21st century*. Conference proceedings Chicago Zoological Society; 2001. p. 175–176.

75. Lukas KE, Hamor G, Bloomsmith MA, Horton CL, Maple TL. Removing milk from captive gorilla diets: the impact on regurgitation and reingestion (R/R) and other behaviors. *Zoo Biol.* 1999;18(6):515–528.

76. Lung N, Miller J, Ferrell S, Marlar A, Turner L. Surgical and medical management of necrotizing fasciitis in the throat sac region of an adult male Sumatran orangutan (*Pongo pygmaeus abelii*). In: Proc Am Assoc Zoo Veterinarians; 2004. p. 195.

77. Márquez M, Serafin A, Fernández-Bellon H, Serrat S, Ferrer-Admetlla A, Bertranpetit J, Ferrer I, Pumarola M. Neuropathologic findings in an aged albino gorilla. *Vet Pathol* [Internet]. 2008 [cited 2014 Jul 18];45(4):531–537. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18587101>
78. Mätz-Rensing K, Kunze M, Zöller M, Roos C, Kiderlen AF, Ludwig C, Kaup F-J. Fatal *Balamuthia mandrillaris* infection in a gorilla—first case of balamuthiasis in Germany. *J Med Primatol* [Internet]. 2011 [cited 2014 Jul 18];40(6):437–440. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21496054>
79. Mbaya AW, Nwosu CO. Outbreak of clinical amoebiasis among captive chimpanzees (*Pan troglodytes*) at the Sanda Kyarima park, Maiduguri, Nigeria. *Niger Vet J*. 2005;27(1):68–73.
80. McLachlan SM, Alpi K, Rapoport B. Review and hypothesis: does Graves' disease develop in non-human great apes? *Thyroid*. 2011;21:1359–1366.
81. Meehan TP, Lowenstine LJ. Causes of mortality in captive lowland gorillas: a survey of the SSP population. In: *Proc Am Assoc Zoo Veterinarians*; 1994. p. 216–218.
82. Meehan TP, Zdziarski JM, Briggs MB, Anderson DB, Zelby AS, Grigg-Damberger, M Thomas C, Murnane RD, Walsh TM. Surgical removal of an intracranial tumor in a western lowland gorilla. In: *Junge RE (ed.). Proceedings of a Joint Conference American Association of Zoo Veterinarians, Wildlife Disease Association, and American Association of Wildlife Veterinarians*; 1995. p. 255–256.
83. Mesle F. Classifying causes of death according to an aetiological axis. *Popul Stud (NY)*. 1999;53(1):97–105.
84. Microsoft. Microsoft Excel. Microsoft Office. Version 14.0.7147.5001 [Computer software]. Microsoft: Redmond (WA); 2010.
85. Miller CL, Schwartz AM, Barnhart JS, Bell MD. Chronic hypertension with subsequent congestive heart failure in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med*. 1999;30:262–267.
86. Minter LJ, Cullen JM, Loomis MR. Reye's or Reye's-like syndrome in western lowland gorilla (*Gorilla gorilla gorilla*). *J Med Primatol*. 2012;41:329–331.
87. Miyabe-Nishiwaki T, Kaneko A, Nishiwaki K, Watanabe A, Watanabe S, Maeda N, Kumazaki K, Morimoto M, Hirokawa R, Suzuki J, Ito Y, Hayashi M, Tanaka M, Tomonaga M, Matsuzawa T. Tetraparesis resembling acute transverse myelitis in a captive chimpanzee (*Pan troglodytes*): long-term care and recovery. *J Med Primatol* [Internet]. 2010 [cited 2014 Jul 18];39(5):336–346. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20444005>
88. Miyagi J, Tshako K, Kinjo T, Iwamasa T, Kamada Y, Kinju T, Koyanagi Y. Coxsackievirus B4 myocarditis in an orangutan. *Vet Pathol* [Internet]. 1999 [cited 2013 Nov 26];36(5):452–456. Available from: <http://vet.sagepub.com/lookup/doi/10.1354/vp.36-5-452>
89. Mundy NI, Ancrenaz M, Wickings EJ, Lunn PG. Protein deficiency in a colony of western lowland gorillas (*Gorilla g. gorilla*). *J Zoo Wildl Med*. 1998;29:261–268.
90. Munson L, Montali RJ. Pathology and diseases of great apes at the National Zoological Park. *Zoo Biol*. 1990;9:99–105.
91. Murray S, Zdziarski JM, Bush M, Citino SB, Schulman FY, Montali R. Diverticulitis with rupture and fatal peritonitis in a Sumatran orangutan (*Pongo pygmaeus*). *Comp Med*. 2000;50(4):452–454.
92. Mylniczenko ND. A preliminary report on intra-abdominal abscesses in captive western lowland gorillas (*Gorilla gorilla gorilla*). In: *Baer CK (ed.). American Association of Zoo Veterinarians Annual Conference*; 2003. p. 62–66.
93. Nielsen SCA, Mourier T, Baandrup U, Søland TM, Bertelsen MF, Gilbert MTP, Nielsen LP. Probable transmission of coxsackie B3 virus from human to chimpanzee, Denmark. *Emerg Inf Dis*. 2012;18:1163–1165.
94. Nunamaker EA, Lee DR, Lammey ML. Chronic diseases in captive geriatric female chimpanzees (*Pan troglodytes*). *Comp Med*. 2012;62:131–136.
95. Paixao TA, Malta MCC, Soave SA, Tinoco HP, Costa MELT, Pessanha AT, Silva ROS, Coura FM, Costa LF, Turchetti AP, Lobato FCF, Melo MM, Santos, L. Renato, Heinemann MB. Hemorrhagic colitis associated with *Salmonella enterica* serotype Infantis infection in a captive western lowland gorilla (*Gorilla gorilla gorilla*) in Brazil. *J Med Primatol*. 2014;43(2):118–121.
96. Paixão TA, Tinoco HP, Campos M De, Elvira M, Teixeira L, Soave SA, Pessanha AT, Patrícia A, Silva C, Santos RL. Pathological findings in a captive senile western lowland gorilla (*Gorilla gorilla gorilla*) with chronic renal failure and septic polyarthritis. *Brazilian J Vet Path*; 2014;7:29–34.
97. Pazzaglia G, Widjaja S, Soebekti D, Tjaniadi P, Simanjuntak L, Lesmana M, Jennings G. Persistent, recurring diarrhea in a colony of orangutans (*Pongo pygmaeus*) caused by multiple strains of *Campylobacter* spp. *Acta Trop*. 1994;57(1):1–10.
98. Pollock PJ, Doyle R, Tobin E, Davison K BJ. Repeat laparotomy for the treatment of septic peritonitis in a Bornean orangutan (*Pongo pygmaeus pygmaeus*). *J Zoo Wildl Med*. 2008;39:476–479.
99. Porter B, Goens S, Brasky K, Hubbard G. A case report of hepatocellular carcinoma and focal nodular hyperplasia with a myelolipoma in two chimpanzees and a review of spontaneous hepatobiliary tumors in non-human primates. *J Med Primatol*. 2004;33(1):38–47.
100. PRISMA Group, Moher D, Liberati A, Tetzlaff J, Altman D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement [Internet, cited 2015 September 15]. c2009. Available from: <http://www.prisma-statement.org>

101. Prosen H, Bell B. A psychiatrist consulting at the zoo (the therapy of Brian the bonobo). Brookfield Zoo (ed.). The apes: challenges for the 21st century Conference proceedings Chicago Zoological Society; 2001. p. 161–164.
102. Raphael BL, Calle PP, Haramati N, Watkins DI, Stetter MD, Cook RA. Reactive arthritis subsequent to *Shigella flexneri* enteritis in two juvenile lowland gorillas (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 1995;26:132–138.
103. Reddacliff LA, Kirkland PD, Hartley WJ, Reece RL. Encephalomyocarditis virus infections in an Australian zoo. *J Zoo Wildl Med.* 1997;28:153–157.
104. Rideout BA, Gardiner CH, Stalis IH, Zuba JR, Hadfield T, Visvesvara GS. Fatal infections with *Balamuthia mandrillaris* (a free-living amoeba) in gorillas and other Old World primates. *Vet Pathol.* 1997;34:15–22.
105. Rietschel W. Air sacculitis in bonobo (*Pan paniscus*) and chimpanzee (*Pan troglodytes*)—anatomy, pathology and therapy. In: Proc International Conference on Diseases of Zoo and Wild Animals; 2012. p. 112–115.
106. Rizzo F, Tappin SW, Tasker S. Thrombocytosis in cats: a retrospective study of 51 cases (2000–2005). *J Feline Med Surg.* 2007;9:319–325.
107. Robinson N, Dean RS, Cobb M, Brennan M. Investigating common clinical presentations in first opinion small animal consultations using direct observation. *Vet Rec.* 2015;176:463.
108. Sakulwira K, Theamboonlers A, Oraveerakul K, Chaiyabutr N, Bhattarakosol P, Poovorawan Y. Orangutan herpesvirus. *J Med Primatol.* 2004;33:25–29.
109. Sasseville VG, Mankowski JL, Baldessari A, Harbison C, Laing S, Kaliyaperumal S, Mätz-Rensing K, Miller AD, Schmidt LD, Kaplan-Kees J, Dick EJ, Reader JR, Liu D, Crawford LK, Lane JH, Corner SM, Pardo ID, Evans MG, Murnane R, Terio KA. Meeting report: emerging respiratory viral infections and non-human primate case reports. *Vet Pathol* [Internet]. 2013 [cited 2014 Aug 23];50(6):1145–1153. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23839235>
110. Saturday GA, Lasota J, Frost D, Brasky KB, Hubbard G, Miettinen M. KIT-positive gastrointestinal stromal tumor in a 22-year-old male chimpanzee (*Pan troglodytes*). *Vet Pathol.* 2005:362–365.
111. Schauer G, Moll R, Walter JH, Rumpelt HJ, Göltenboth R. Malignant rhabdoid tumor in the gastric wall of an aged orangutan (*Pongo pygmaeus*). *Vet Pathol.* 1994;31:510–517.
112. Schmidt RE. Systemic pathology of chimpanzees. *J Med Primatol.* 1975;7:274–318.
113. Schulman FY, Farb A, Virmani R, Montali RJ. Fibrosing cardiomyopathy in captive western lowland gorillas (*Gorilla gorilla gorilla*) in the United States—a retrospective study. *J Zoo Wildl Med.* 1995;26:43–51.
114. Scott NA, Mcmanamon R, Strobert E, Cipolla GD, Tarazona N, Swenson RB. In-vivo diagnosis of coronary-artery disease in a western lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med.* 1995;26:139–143.
115. Shin NS, Kwon SW, Han DH, Bai GH, Yoon J, Cheon DS, Son YS, Ahn K, Chae C, Lee YS. Mycobacterium tuberculosis infection in an orangutan (*Pongo pygmaeus*). *J Vet Med Sci.* 1995;57:951–953.
116. Silva AE, Serakides NM, Ocarino GD, E.F.C, Nascimento MA, Coradini R. Uterine leiomyoma in chimpanzee (*Pan troglodytes*). *Arq Bras Med Vet e Zootec.* 2006;58(1):129–132.
117. Singh KP, Singh R, Singh GR. Chronic pathological conditions encountered in captive wild mammals. *Indian J Anim Sci.* 1994;64:1346–1347.
118. Slaffer SN, Allchurch AF. Diagnosis and treatment of dilated (congestive) cardio-myopathy in a Sumatran orang-utan *Pongo pygmaeus abelii*. *Dodo.* 1995;31:147–152.
119. Sleeper MM, Doane CJ, Langner PH, Curtis S, Avila K, Lee DR. Successful treatment of idiopathic dilated cardiomyopathy in an adult chimpanzee (*Pan troglodytes*). *Comp Med.* 2005;55:80–84.
120. Sleeper MM, Drobatz K, Lee DR, Lammey ML. Echocardiographic parameters of clinically normal adult captive chimpanzees (*Pan troglodytes*). *J Am Vet Med Assoc.* 2014;244:956–960.
121. Sos E, Molnar V, Liptovszky M, Vrabely T, Rigo P. Veterinary aspects of a Sumatran orang-utan (*Pongo pygmaeus abelii*) introduction in a zoo situation. *Erkrankungen der Zootiere.* 2007;43:71–73.
122. Steinetz BG, Randolph C, Cohn D, Mahoney CJ. Lipoprotein profiles and glucose tolerance in lean and obese chimpanzees. *J Med Primatol.* 1996;25:17–25.
123. Steinmetz HW, Briner HR, Vogt R, Kalchofner K, Hilbe M, Scharf G, Eulenberger U, Hatt JM. Functional endoscopic sinus surgery in a Sumatran orang-utan (*Pongo pygmaeus abeli*). In: Wibbelt G, Bergholz N, Seet S, Hofer H (eds.). Proceedings of the Institute for Zoo and Wildlife Research, Berlin (7); 2007. p. 74–75.
124. Stringer EM, De Voe RS, Valea F, Toma S, Mulvaney G, Pruitt A, Troan B, Loomis MR. Medical and surgical management of reproductive neoplasia in two western lowland gorillas (*Gorilla gorilla gorilla*). *J Med Primatol.* 2010;39:328–335.
125. Struck K, Videan EN, Fritz J, Murphy J. Attempting to reduce regurgitation and reingestion in a captive chimpanzee through increased feeding opportunities: a case study. *Lab Anim (NY).* 2007;36(1):35–38.
126. Szentiks CA, Köndgen S, Silinski S, Speck S, Leendertz FH. Lethal pneumonia in a captive juvenile chimpanzee (*Pan troglodytes*) due to human-transmitted human respiratory syncytial virus (HRSV) and infection with *Streptococcus pneumoniae*. *J Med Primatol.* 2009;38(4):236–240.
127. Tong LJ, Flach EJ, Sheppard MN, Pocknell A, Banerjee AA, Boswood A, Bouts T, Routh A, Feltrer Y. Fatal arrhythmogenic right ventricular cardiomyopathy in 2 related subadult chimpanzees (*Pan troglodytes*). *Vet*

- Pathol [Internet]. 2013 [cited 2013 Nov 20];51(4):858–867. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23988399>
128. Trupkiewicz J, McNamara T, Weidenheim K, Cook R, Grenell S, Factor S. Cerebral infarction associated with coarctation of the aorta in a lowland gorilla (*Gorilla gorilla gorilla*). *J Zoo Wildl Med*. 1995; 26:123–131.
129. Unwin S, Chatterton J, Chantrey J. Management of severe respiratory tract disease caused by human respiratory syncytial virus and *Streptococcus pneumoniae* in captive chimpanzees (*Pan troglodytes*). *J Zoo Wildl Med*. 2013;44:105–115.
130. Varki N, Anderson D, Herndon JG, Pham T, Gregg CJ, Cheriyan M, Murphy J, Strobert E, Fritz J, Else JG, Varki A. Heart disease is common in humans and chimpanzees, but is caused by different pathological processes. *Evol Appl* [Internet]. 2009 [cited 2013 Nov 12];2(1):101–112. Available from: <http://doi.wiley.com/10.1111/j.1752-4571.2008.00064.x>
131. Videan EN, Fritz J, Murphy J. Development of guidelines for assessing obesity in captive chimpanzees (*Pan troglodytes*). *Zoo Biol*. 2007;26:93–104.
132. Videan EN, Satterfield WC, Buchl S, Lammey ML. Diagnosis and prevalence of uterine leiomyomata in female chimpanzees (*Pan troglodytes*). *Am J Primatol*. 2011;73:665–670.
133. Vielgrader H, Kubber-Heiss A, Voracek T, Alton K, Leidinger E. Management of an outbreak of shigellosis in the Vienna Zoo. In: Frolich K, Steinbach F (eds.). *Proceedings of the Institute for Zoo and Wildlife Research, Berlin No 766*; 2005. p. 164–166.
134. Wolfla CE, Puckett TA. Reversal of neurologic deficit in an adult gorilla with severe symptomatic lumbar stenosis. *Spine*. 2004;29:E95–E97.
135. World Health Organisation. *International Statistical Classification of Diseases and Related Health Problems 10th Revision* [Internet]. (cited 2016 July 18) c2010. Available from: <http://apps.who.int/classifications/icd10/browse/2010/en>
136. Yeo DSY, Lian JE, Fernandez CJ, Lin YN, Liaw JCW, Soh ML, Lim EAS, Chan KP, Ng ML, Tan HC, Oh S, Ooi EE, Tan BH. A highly divergent Encephalomyocarditis virus isolated from nonhuman primates in Singapore. *Virol J* [Internet]. 2013 [cited 2014 Jul 18];10(1):248. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3750836&tool=pmcentrez&rendertype=abstract>
137. Zimmermann N, Pirovino M, Zingg R, Clauss M, Kaup FJ, Heistermann M, Hatt JM, Steinmetz HW. Upper respiratory tract disease in captive orangutans (*Pongo* sp.): prevalence in 20 European zoos and predisposing factors. *J Med Primatol* [Internet]. 2011 [cited 2014 Jul 11];40(6):365–375. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21770970>
138. Zimmermann N, Zingg R, Makara M, Hatt J, Steinmetz H. Computertomographic evaluation of the upper respiratory tract in orang-utans (*Pongo pygmaeus*, *Pongo abelii*). In: Wibbelt G, Kretzschmar P, Hofer H, Seet S (eds.). *Proceedings of the International Conference on Diseases of Zoo and Wild Animals*; 2009. p. 102–103.
139. Zoller M, Matz-Rensing K, Hofmann P, Jurek V, Schulz-Schaeffer W, Kaup FJ. Cerebral calcinosis in a young chimpanzee. In: Frolich K, Steinbach F (eds.). *Proceedings of the Institute for Zoo and Wildlife Research, Berlin (6)*; 2005. p. 112–114.

Received for publication 29 October 2015