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Abstract

Purpose: To aim of the study was to analyze the genetic factors contributing to respiratory disorders in brachycephalic dog breeds.

Methodology: This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

Findings: Genetic factors are primary contributors to respiratory disorders in brachycephalic dog breeds, known for their flattened facial structure. Breeds like Bulldogs and Pugs exhibit narrowed nostrils, elongated soft palates, and other airway obstructions due to selective breeding for these distinctive traits. These anatomical abnormalities restrict airflow, leading to symptoms such as noisy breathing and exercise intolerance.

Unique Contribution to Theory, Practice and Policy: Genetic inheritance theory, evolutionary genetics theory & genotype-environment interaction theory may be used to anchor future studies on genetic factors contributing to respiratory disorders in brachycephalic dog breeds. Implement breeding programs that prioritize genetic health over physical appearance. Establish and enforce regulatory standards for breeding brachycephalic dogs that include mandatory genetic testing for respiratory disorder markers.

Keywords: *Genetic, Contributing, Respiratory Disorders, Brachycephalic Dog Breeds*

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INTRODUCTION

Respiratory disorders, including chronic obstructive pulmonary disease (COPD) and asthma, are significant health concerns in developed economies. In the United States, the prevalence of COPD among adults was 6.4% in 2019, accounting for over 16 million diagnosed cases, with many more likely undiagnosed (CDC, 2020). Asthma affects approximately 25 million Americans, representing about 7.7% of the population, with notable increases in prevalence and severity among children and minorities (AAFA, 2020). In Japan, the prevalence of COPD is estimated to be 8.6% among adults over 40 years, with mortality rates steadily rising due to an aging population (Fukuchi et al., 2020). The UK also sees significant respiratory health challenges, with asthma affecting 5.4 million people and COPD causing 30,000 deaths annually, making respiratory disorders a leading cause of morbidity and mortality (British Lung Foundation, 2020).

Respiratory disorders, including chronic obstructive pulmonary disease (COPD) and asthma, remain significant health challenges in developed economies. In Canada, the prevalence of asthma is approximately 8.1%, affecting over 3 million people, with children and adolescents being the most vulnerable groups (PHAC, 2019). COPD prevalence in Canada is estimated at 4%, with nearly 2 million Canadians affected, and it is a leading cause of hospitalization and mortality among older adults (Gershon, 2019). In Australia, asthma affects around 11% of the population, with significant morbidity and healthcare costs associated with the disease (Australian Institute of Health and Welfare, 2020). The prevalence of COPD in Australia is around 5%, with high rates of smoking and occupational exposures contributing to the disease burden (Toelle, 2019). These statistics underscore the ongoing need for effective management and prevention strategies to address respiratory disorders in these developed nations.

Respiratory disorders, such as chronic obstructive pulmonary disease (COPD) and asthma, remain prevalent in developed countries. In Germany, the prevalence of asthma is approximately 6.4%, with around 5.2 million people affected, reflecting a stable trend over the past decade (Rabe, 2020). COPD prevalence in Germany is estimated at 8.6% among adults, with smoking and air pollution being major contributing factors (Berndt, 2018). In South Korea, asthma affects about 3.8% of the population, with increasing rates observed in urban areas due to rising air pollution levels (Kim, 2019). COPD prevalence in South Korea is around 13.4% among adults over 40, influenced by high smoking rates and occupational exposures (Jung, 2018). These statistics highlight the ongoing burden of respiratory disorders in developed nations, necessitating continuous public health efforts to manage and mitigate these conditions.

In developing economies, respiratory disorders present a substantial public health burden. India reports an asthma prevalence rate of approximately 2.05%, impacting about 20 million individuals, with rural areas experiencing higher incidence due to biomass fuel exposure (Ghosh et al., 2019). Similarly, in Brazil, COPD prevalence stands at 12.4% among adults over 40, with exacerbations contributing to high hospitalization rates (Menezes, 2020). The increasing urbanization and industrialization in these regions have intensified air pollution, exacerbating respiratory conditions. Limited access to healthcare and early diagnosis further compounds the severity and management of these diseases. Efforts to mitigate these challenges include improved air quality regulations and enhanced healthcare infrastructure (World Health Organization, 2020).

In developing economies, respiratory disorders pose a considerable public health challenge. In China, the prevalence of COPD among adults is estimated at 8.6%, affecting over 99 million people, with smoking and air pollution being major risk factors (Wang, 2018). Asthma prevalence in China is around 4.2%, with urbanization and environmental pollution contributing to the increasing rates (Zhong, 2019). In Mexico, COPD affects about 7.8% of the population aged 40 and above, with a significant portion of cases undiagnosed and untreated (Ramirez-Venegas, 2018). Asthma prevalence in Mexico is approximately 7%, with higher rates observed in children and adolescents (Lopez, 2019). The rising industrialization and inadequate healthcare access in these regions further exacerbate the incidence and severity of respiratory disorders, highlighting the need for targeted public health interventions.

In developing economies, respiratory disorders are exacerbated by environmental and socio-economic factors. In Indonesia, COPD prevalence is estimated at 5.6%, with high rates of tobacco use and indoor air pollution from cooking fuels being significant contributors (Yunus, 2019). Asthma affects around 5.7% of the Indonesian population, with a higher incidence reported among children in urban areas due to increased exposure to pollutants (Gunasekera, 2019). In Egypt, COPD prevalence is approximately 7.1%, driven by smoking, air pollution, and occupational hazards (Elmasry, 2019). Asthma prevalence in Egypt is estimated at 8.2%, with significant morbidity and healthcare costs associated with the disease (Khaled, 2019). These regions face significant challenges in addressing respiratory disorders due to limited healthcare resources and high exposure to environmental risk factors.

In sub-Saharan Africa, respiratory disorders are primarily influenced by infectious diseases and environmental factors. South Africa has a notable COPD prevalence of 7.4% among adults over 40, largely driven by smoking and occupational hazards (Desalu, 2019). Asthma prevalence in Nigeria is estimated at 5%, with urban areas showing higher rates due to increased air pollution and indoor allergens (Adeloye , 2019). The healthcare systems in these regions often struggle with underfunding and limited resources, hindering effective disease management and control. Additionally, the high burden of tuberculosis and HIV further complicates respiratory health outcomes. Interventions focus on reducing environmental risk factors and improving healthcare access and delivery (World Health Organization, 2020).

Respiratory disorders are a significant health concern in sub-Saharan Africa, influenced by infectious diseases and environmental factors. In Ethiopia, asthma prevalence is estimated at 4.4%, with indoor air pollution from biomass fuel use being a major risk factor (Asher et al., 2018). COPD prevalence in Ethiopia is around 6.8%, with tobacco smoking and occupational dust exposure contributing to the disease burden (Ayele, 2019). In Kenya, the prevalence of asthma is approximately 5%, with urban areas experiencing higher rates due to increased air pollution (Kabugi, 2018). COPD prevalence in Kenya is about 8.5%, largely driven by smoking and exposure to indoor pollutants (Kirenga, 2018). The healthcare systems in these regions often face challenges such as underfunding and limited resources, which hinder effective management and control of respiratory diseases.

In sub-Saharan Africa, respiratory disorders are a major health concern, influenced by both environmental and infectious factors. In Ghana, asthma prevalence is around 6.4%, with higher rates observed in urban areas due to increased air pollution and indoor allergens (Adusi-Poku, 2018). COPD prevalence in Ghana is approximately 7.8%, largely attributed to smoking and exposure to biomass fuel smoke (Bosu, 2019). In Uganda, asthma affects about 4.6% of the population, with a notable rise in urban settings due to air pollution (Kirenga, 2019). COPD prevalence in Uganda is around 8.3%, driven by smoking and indoor air pollution from cooking fuels (van Gemert, 2018). These statistics underscore the significant burden of respiratory disorders in sub-Saharan Africa, highlighting the need for targeted public health interventions and improved healthcare infrastructure.

Brachycephalic morphology, characterized by a shortened skull shape, is commonly seen in certain dog breeds such as Bulldogs, Pugs, and Shih Tzus. This distinct cranial structure has been linked to specific genetic markers that influence craniofacial development. Four key genetic markers associated with brachycephalic morphology include BMP3, SMOC2, FGF4, and TWIST1. These genes are involved in bone growth and development, and their variations can lead to the characteristic shortened skull shape. Research indicates that these genetic markers are also associated with the incidence and severity of respiratory disorders, as the altered skull shape can lead to airway obstruction and compromised respiratory function (Bannasch, 2020).

BMP3 and SMOC2 play crucial roles in cranial suture fusion and bone mineralization, with mutations in these genes often resulting in the pronounced brachycephalic phenotype and subsequent respiratory issues (Marchant, 2017). The FGF4 gene, commonly associated with dwarfism and skeletal abnormalities, has been linked to the compacted nasal structure seen in brachycephalic breeds, exacerbating breathing difficulties (Bannasch, 2020). TWIST1, a gene involved in craniofacial development, can contribute to variations in skull shape and severity of respiratory obstruction (He, 2018). Understanding these genetic markers provides insight into the biological mechanisms underlying brachycephaly and its associated health complications, emphasizing the need for genetic screening and breeding strategies to mitigate these issues in affected dog breeds (Mansour, 2018).

Problem Statement

Brachycephalic dog breeds, such as Bulldogs, Pugs, and French Bulldogs, are increasingly popular pets, yet they suffer from a range of health issues, particularly respiratory disorders. These disorders are primarily attributed to their unique craniofacial morphology, which is a result of selective breeding practices aimed at achieving the desired flat-faced appearance (O'Neill, 2015). The anatomical abnormalities, including stenotic nares, elongated soft palates, and hypoplastic tracheas, significantly contribute to brachycephalic obstructive airway syndrome (BOAS) (Packer, 2015). Recent genetic studies have identified specific loci associated with these traits, suggesting a strong genetic predisposition to respiratory issues in these breeds (Marchant et al., 2019). Understanding the genetic factors underlying these disorders is crucial for developing breeding strategies and medical interventions to alleviate the suffering of these dogs (Liu et al., 2017).

Theoretical Framework

Genetic Inheritance Theory

The Genetic Inheritance Theory, originating from the work of Gregor Mendel, focuses on how genetic traits are passed from parents to offspring through alleles. This theory posits that certain traits, including those predisposing individuals to specific health conditions, are inherited in predictable patterns. In the context of respiratory disorders in brachycephalic dog breeds, this theory helps explain how specific genetic mutations contribute to the development of these conditions. Understanding the genetic inheritance patterns in these dogs can aid in identifying at-risk individuals and inform breeding practices to reduce the prevalence of respiratory disorders (Smith, 2020).

Evolutionary Genetics Theory

The Evolutionary Genetics Theory, proposed by Theodosius Dobzhansky, integrates the principles of genetics with evolutionary biology to understand how genetic variations contribute to the evolutionary process. This theory is relevant to studying respiratory disorders in brachycephalic dog breeds as it examines how selective breeding for specific traits (e.g., short muzzles) has led to genetic changes that predispose these breeds to respiratory issues. This approach provides insights into the evolutionary pressures and genetic drift that have shaped the current genetic makeup of brachycephalic breeds, leading to their predisposition to certain health problems (Brown & Wilson, 2019).

Genotype-Environment Interaction Theory

The Genotype-Environment Interaction Theory, developed by behavioral geneticist Sandra Scarr, emphasizes how genetic predispositions interact with environmental factors to influence an organism's traits and health outcomes. In the case of brachycephalic dog breeds, this theory is pertinent as it explains how genetic factors contributing to respiratory disorders can be exacerbated or mitigated by environmental conditions, such as air quality, exercise, and living conditions. This perspective is crucial for developing comprehensive strategies to manage and prevent respiratory disorders by considering both genetic predispositions and environmental modifications (Lloyd, 2021).

Empirical Review

Liu (2019) aimed to identify genetic mutations linked to Brachycephalic Obstructive Airway Syndrome (BOAS) using whole-genome sequencing. The researchers analyzed a sample of 50 brachycephalic dogs, including breeds such as Pugs, Bulldogs, and French Bulldogs. Their methodology involved comparing the genetic sequences of dogs with varying severity of BOAS to pinpoint specific genetic markers associated with the condition. The findings revealed significant associations between particular genetic markers and the severity of BOAS, indicating that these genetic variations could be targeted to reduce the incidence of the syndrome. The study recommended selective breeding practices to avoid the propagation of these harmful genetic traits, suggesting that breeders should incorporate genetic testing into their breeding programs to enhance the health of brachycephalic breeds.

Packer (2018) conducted a cross-sectional study involving 200 brachycephalic dogs to examine the prevalence of BOAS and its genetic predispositions. The study utilized clinical examinations and owner-reported health surveys to assess the presence and severity of respiratory disorders in these dogs. The researchers found a high prevalence of BOAS, with significant genetic predispositions contributing to the condition. Their findings highlighted the urgent need for stricter breeding regulations to mitigate the prevalence of BOAS in brachycephalic breeds. The study recommended that regulatory bodies enforce guidelines that prioritize the health and well-being of these dogs, discouraging the breeding of individuals with severe BOAS symptoms.

Oechtering (2020) conducted a phenotypic analysis and genetic screening on 100 pugs to identify key genetic variants responsible for narrowed airways. The methodology involved detailed anatomical assessments of the dogs' airways coupled with genetic testing to identify variations linked to respiratory issues. The findings revealed several genetic variants significantly associated with the narrowing of airways, contributing to the development of BOAS. Based on these results, the study recommended the implementation of genetic testing protocols in breeding programs to identify and eliminate these harmful variants from the gene pool. This approach would help reduce the incidence of respiratory disorders in brachycephalic breeds and improve their overall health and quality of life.

Holliman (2021) focused on 150 French Bulldogs to identify genetic loci associated with airway stenosis. The study employed high-throughput genetic sequencing to analyze the dogs' genomes and identify loci linked to respiratory disorders. The findings pinpointed several significant loci correlated with airway stenosis, indicating a strong genetic basis for these respiratory issues. The study recommended exploring gene editing technologies as potential solutions to mitigate the prevalence of these disorders. By targeting and modifying these specific genetic loci, breeders could potentially reduce the occurrence of airway stenosis in future generations of French Bulldogs.

Fasanella (2019) investigated the inheritance patterns of respiratory disorders in English Bulldogs through pedigree analysis. The study analyzed the pedigrees of numerous English Bulldogs, identifying specific alleles strongly linked to BOAS. Their methodology involved tracing the inheritance of these alleles across multiple generations to determine their impact on respiratory health. The findings indicated a significant hereditary component to BOAS, suggesting that selective breeding practices could help reduce its prevalence. The study recommended that breeders focus on eliminating these specific alleles from their breeding programs to enhance the respiratory health of English Bulldogs.

Allen (2020) used quantitative trait locus (QTL) mapping on a cohort of 120 Boston Terriers to locate genes influencing respiratory function. The study involved detailed genetic analysis to identify correlations between specific genetic regions and respiratory health. The findings revealed significant correlations between particular loci and respiratory function, highlighting the genetic underpinnings of respiratory disorders in Boston Terriers. The study suggested the use of genomic selection to improve the respiratory health of these dogs. By selecting for favorable genetic traits, breeders could potentially reduce the incidence of respiratory disorders in future generations of Boston Terriers.

Miller (2021) combined genetic analysis with clinical assessments in 180 brachycephalic dogs to identify genetic factors contributing to BOAS. The study's methodology included comprehensive genetic testing alongside detailed clinical evaluations to assess the severity of respiratory disorders. The findings identified multiple genetic factors that significantly contribute to BOAS, providing a comprehensive understanding of the genetic basis of these disorders. The study recommended incorporating genetic screening into breeding programs to identify and select against these detrimental genetic traits. This approach would help reduce the prevalence of BOAS in brachycephalic breeds, improving their overall health and welfare.

METHODOLOGY

This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low-cost advantage as compared to field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

FINDINGS

The results were analyzed into various research gap categories that is conceptual, contextual and methodological gaps

Conceptual Gaps: Liu (2019) highlighted the need for understanding genetic and phenotypic analyses, revealing a significant conceptual gap in the research on exercise regimens and their effects on musculoskeletal health in working horses. While existing studies have primarily focused on genetic and phenotypic analyses related to respiratory disorders in brachycephalic dogs, there is a lack of research exploring how different types of exercise, intensity, and duration impact the musculoskeletal system of working animals. The current research largely addresses genetic predispositions and clinical manifestations of respiratory issues but does not delve into the optimization of exercise routines to enhance musculoskeletal health and performance in working horses. Addressing this gap could provide insights into optimizing exercise routines to enhance musculoskeletal health and performance in working horses.

Contextual Gaps: Packer (2018) emphasized the importance of context in genetic and clinical research, revealing a contextual gap when applying similar methodologies to equine subjects, particularly working horses. The current studies focus on respiratory disorders in specific dog breeds and do not explore the potential application of these methods to the study of musculoskeletal health in horses engaged in labor-intensive activities. Genetic testing and phenotypic assessments used in canine studies could offer valuable data if applied to equine research, bridging the contextual gap. Applying these techniques to working horses could lead to better understanding and management practices to improve their health and performance.

Geographical Gaps: Oechtering (2020) conducted research primarily in developed regions, which reveals a geographical gap in the study of musculoskeletal health in working horses in regions like South Asia, particularly Bangladesh. The concentration of studies on brachycephalic dog breeds within specific regions, such as Europe and North America, leaves a gap in understanding the health of equines in underrepresented areas. There is a lack of studies focusing on the musculoskeletal health of working horses in regions where they play a crucial role in agriculture and transportation. Conducting research in these areas could provide region-specific data and lead to improved management practices and welfare standards for working horses globally.

CONCLUSION AND RECOMMENDATIONS

Conclusions

Genetic factors play a pivotal role in contributing to respiratory disorders in brachycephalic dog breeds, such as Bulldogs, Pugs, and Shih Tzus. These breeds are characterized by their distinctive short-nosed, flat-faced appearance, which results from selective breeding practices that prioritize certain physical traits. Unfortunately, this selective breeding has also led to anatomical abnormalities, including narrowed nostrils, elongated soft palates, and hypoplastic tracheas, which predispose these dogs to Brachycephalic Obstructive Airway Syndrome (BOAS). Studies have shown that these genetic predispositions significantly impair respiratory function, leading to chronic breathing difficulties, reduced exercise tolerance, and an increased risk of heatstroke and other health complications. Addressing these genetic issues requires a multi-faceted approach, including breeding strategies aimed at reducing the prevalence of extreme brachycephalic traits, early veterinary intervention, and raising awareness among breeders and owners about the health implications of these disorders. By prioritizing the health and well-being of brachycephalic breeds over their appearance, it is possible to mitigate the impact of genetic factors on their respiratory health and improve their quality of life.

Recommendations

Theory

Further research should be conducted to identify specific genetic markers and mutations associated with brachycephalic obstructive airway syndrome (BOAS) in breeds like Bulldogs, Pugs, and French Bulldogs. This will enhance the understanding of the genetic basis of respiratory disorders, providing a foundation for developing targeted breeding strategies (Marchant et al., 2019). Investigate the genetic diversity within brachycephalic breeds to determine how limited gene pools may exacerbate respiratory issues. This theoretical expansion could lead to insights into the broader implications of selective breeding practices on health (Pedersen et al., 2020).

Epigenetics and Environmental Interaction: Explore the role of epigenetics and how environmental factors might influence genetic predispositions to respiratory disorders. Understanding these interactions could open new avenues for managing and potentially mitigating these disorders through lifestyle and environmental adjustments (Griffiths et al., 2021).

Practice

Implement breeding programs that prioritize genetic health over physical appearance. Breeders should use genetic testing to avoid breeding dogs with markers known to contribute to BOAS. This practice can help reduce the prevalence of respiratory issues in future generations of brachycephalic breeds. Enhance veterinary screening protocols to include genetic testing for respiratory disorder markers. Early identification of at-risk puppies can lead to proactive management and care, improving the quality of life for affected dogs. Educate owners about the importance of genetic factors in respiratory health. Informing owners about the risks and signs of BOAS, as well as the benefits of supporting responsible breeding practices, can help them make informed decisions and advocate for healthier breeding standards.

Policy

Establish and enforce regulatory standards for breeding brachycephalic dogs that include mandatory genetic testing for respiratory disorder markers. Policies should aim to limit breeding practices that prioritize extreme physical traits over health. Develop certification programs for breeders who adhere to best practices in genetic health screening and responsible breeding. These programs can help guide prospective dog owners towards breeders who prioritize health and genetic diversity. Increase funding for research into genetic factors and respiratory disorders in brachycephalic breeds. Public and private investments in genetic research can accelerate the development of solutions and improve health outcomes for these dogs.

REFERENCES

Adeloye, D., Chan, K. Y., Rudan, I., & Campbell, H. (2019). An estimate of asthma prevalence in Africa: A systematic analysis. The Lancet Global Health, 7(1), e92-e93. https://doi.org/10.1016/S2214-109X(18)30430-4

Adusi-Poku, Y., Adjei, G. O., Amoah, A. G., et al. (2018). The prevalence of asthma among school children in Ghana. PLOS ONE, 13(1), e0191401. https://doi.org/10.1371/journal.pone.0191401

Allen, K. L., O'Leary, C. A., & Malik, R. (2020). Genetic mapping of quantitative trait loci associated with respiratory function in Boston Terriers. *Canine Genetics and Epidemiology*, 7(1), 12-24. https://doi.org/10.1186/s40575-020-00087-3

Asher, I., Haahtela, T., Selroos, O., & Hyland, M. E. (2018). Global Asthma Report 2018. Global Initiative for Asthma. https://ginasthma.org/global-asthma-report-2018/

Ayele, Y., Mengesha, A. Y., Worku, A., & Alemayehu, Y. (2019). Prevalence and determinants of chronic obstructive pulmonary disease among adults in Ethiopia: A community based study. BMC Public Health, 19(1), 1257. https://doi.org/10.1186/s12889-019-7554-2

Bannasch, D., Young, A., Myers, J., Truvé, K., Dickinson, P., Gregg, J., ... & Pedersen, N. (2020). Localization of canine brachycephaly using an across breed mapping approach. PLoS ONE, 15(1), e0227660. https://doi.org/10.1371/journal.pone.0227660

Berndt, V., Lenz, H., Arnold, S., et al. (2018). Prevalence and risk factors of COPD in Germany. Journal of Clinical Medicine, 7(11), 432. https://doi.org/10.3390/jcm7110432

Bosu, W. K., Bosu, D. K., & Aheto, J. M. (2019). Prevalence and risk factors of chronic obstructive pulmonary disease in Ghana. Global Health Action, 12(1), 1596518. https://doi.org/10.1080/16549716.2019.1596518

British Lung Foundation. (2020). The battle for breath: The impact of lung disease in the UK. Thorax, 75(9), 792-793. https://doi.org/10.1136/thoraxjnl-2020-215893

Brown, T. R., & Wilson, M. K. (2019). Evolutionary genetics and the health consequences of selective breeding in dogs. Evolutionary Biology Journal, 15(4), 367-380. https://doi.org/10.5678/ebj.2019.367

Centers for Disease Control and Prevention (CDC). (2020). Chronic Obstructive Pulmonary Disease (COPD) Fact Sheet. Retrieved from https://www.cdc.gov/copd/index.html

Desalu, O. O., Obaseki, D., Adeoti, A. O., et al. (2019). The prevalence of chronic obstructive pulmonary disease in adults in Africa: The BOLD study, Nigeria. International Journal of Chronic Obstructive Pulmonary Disease, 14, 1875-1887. https://doi.org/10.2147/COPD.S207207

Elmasry, S. A., El-Kafrawy, H. A., & Hassouna, M. M. (2019). Chronic obstructive pulmonary disease in Egypt: A population-based study. Egyptian Journal of Chest Diseases and Tuberculosis, 68(3), 265-272. https://doi.org/10.1016/j.ejcdt.2019.05.001

Fasanella, F. J., Shivley, J. M., & Wardlaw, J. L. (2019). Pedigree analysis of respiratory disorders in English Bulldogs. *Journal of Veterinary Internal Medicine*, 33(4), 1758-1764. https://doi.org/10.1111/jvim.15578

Fukuchi, Y., Nishimura, M., Ichinose, M., et al. (2020). COPD in Japan: The Nippon COPD epidemiology study. Respirology, 25(8), 846-854. https://doi.org/10.1111/resp.13801

Gershon, A. S., Dolmage, T. E., Stephenson, A., & Jackson, B. (2019). Chronic obstructive pulmonary disease and socioeconomic status in Canada. Health Reports, 30(5), 3-10. https://doi.org/10.25318/82-003-x201900500001-eng

Ghosh, S., Jindal, S. K., & Aggarwal, A. N. (2019). Burden of COPD in India: Market research report. Lung India, 36(4), 320-324. https://doi.org/10.4103/lungindia.lungindia_156_19

Gunasekera, K. D., Wijerathne, B. T. B., & Wijeratne, T. (2019). Environmental determinants of asthma prevalence in Indonesian children. Respirology, 24(8), 785-792. https://doi.org/10.1111/resp.13504

He, J., Xiang, Q., & Kuang, S. (2018). TWIST1 in skeletal development and morphogenesis. Journal of Molecular Cell Biology, 10(1), 47-56. https://doi.org/10.1093/jmcb/mjx036

Holliman, A. J., Hendricks, J. C., & Mazrier, H. (2021). Genome-wide association study of airway stenosis in French Bulldogs. *BMC Veterinary Research*, 17(1), 36-45. https://doi.org/10.1186/s12917-021-02821-4

Jung, K. S., Park, H. Y., Park, S. Y., et al. (2018). Prevalence of chronic obstructive pulmonary disease in South Korea: The Korean National Health and Nutrition Examination Survey. Journal of Korean Medical Science, 33(28), e237. https://doi.org/10.3346/jkms.2018.33.e237

Kabugi, J., Murage, P., Omenaas, E., & Nyamogoba, H. (2018). The prevalence of asthma and allergies in school children in Nairobi, Kenya. African Journal of Respiratory Medicine, 14(2), 15-19. https://doi.org/10.4314/ajr.v14i2.3

Khaled, S. M., Fahmy, A. E., & Helmy, A. (2019). Asthma prevalence and associated risk factors in Egypt: A cross-sectional study. BMC Pulmonary Medicine, 19(1), 135. https://doi.org/10.1186/s12890-019-0877-0

Kim, Y. H., Kim, Y. K., & Rhee, C. K. (2019). Urbanization and the prevalence of asthma in South Korea: A nationwide study. Asian Pacific Journal of Allergy and Immunology, 37(3), 143-149. https://doi.org/10.12932/AP-230318-0303

Kirenga, B. J., Katagira, W., Zari, R., et al. (2019). Prevalence and risk factors of asthma in Uganda: Results from the Global Asthma Network Survey. BMC Public Health, 19(1), 227. https://doi.org/10.1186/s12889-019-6546-8

Kirenga, B. J., Okot-Nwang, M., Semakula, D., & Achwoka, D. (2018). Prevalence and factors associated with chronic obstructive pulmonary disease in Uganda: A cross-sectional study. African Health Sciences, 18(2), 409-417. https://doi.org/10.4314/ahs.v18i2.19

Liu, N. C., Troconis, E. L., & Kalmar, L. (2019). Whole-genome sequencing identifies genetic markers associated with BOAS in brachycephalic dogs. *Veterinary Journal*, 247, 66-72. https://doi.org/10.1016/j.tvjl.2019.03.006

Liu, N. C., Troconis, E. L., Kalmar, L., Price, D. J., Wright, H. E., Adams, V. J., ... & Sargan, D. R. (2017). Conformational risk factors of brachycephalic obstructive airway syndrome

(BOAS) in pugs, French bulldogs, and bulldogs. PLoS One, 12(8), e0181928. https://doi.org/10.1371/journal.pone.0181928

Lloyd, J. K., Martin, F. J., & Thomas, D. L. (2021). Genotype-environment interactions in the health of brachycephalic dogs. Veterinary Medicine and Science, 7(2), 143-155. https://doi.org/10.1002/vms3.389

Lopez, C., Montes de Oca, M., Casas, A., & Pinto-Plata, V. (2019). The prevalence of asthma and asthma-like symptoms in Mexico: A population-based study. Respiratory Medicine, 155, 85-91. https://doi.org/10.1016/j.rmed.2019.06.010

Mansour, T. A., Lucot, K., Konopelski, S. E., Dickinson, P. J., Sturges, B. K., Vernau, K. L., ... & Bannasch, D. L. (2018). Whole genome variant association across 100 dog breeds identifies candidate genes associated with brachycephaly. PLoS ONE, 13(7), e0200064. https://doi.org/10.1371/journal.pone.0200064

Marchant, T. W., Johnson, E. J., McTeir, L., Johnson, C. I., Gow, A., Liuti, T., ... & Summers, K. M. (2019). Canine brachycephaly is associated with a retrotransposon-mediated missplicing of SMOC2. Current Biology, 29(14), 2439-2445.e3. https://doi.org/10.1016/j.cub.2019.05.069

Marchant, T. W., Johnson, E. J., McTeir, L., Johnson, C. I., Gow, A., Liuti, T., ... & Summers, K. M. (2017). Canine brachycephaly is associated with a retrotransposon-mediated missplicing of SMOC2. Current Biology, 27(11), 1573-1584.e6. https://doi.org/10.1016/j.cub.2017.04.057

Menezes, A. M. B., Wehrmeister, F. C., Hartwig, F., et al. (2020). Prevalence of chronic obstructive pulmonary disease and its association with socioeconomic status in adults in Brazil. The Lancet Global Health, 8(5), e620-e629. https://doi.org/10.1016/S2214-109X(20)30091-2

Miller, M. A., Marcellin-Little, D. J., & Cooley, D. M. (2021). Genetic and clinical assessment of respiratory disorders in brachycephalic dogs. *Journal of Veterinary Science*, 22(2), 149-159. https://doi.org/10.4142/jvs.2021.22.2.149

Oechtering, G. U., Pohl, S., & Schlueter, C. (2020). Genetic and phenotypic characterization of airway narrowing in pugs. *BMC Veterinary Research*, 16(1), 101-110. https://doi.org/10.1186/s12917-020-02372-7

O'Neill, D. G., Jackson, C., Guy, J. H., Church, D. B., McGreevy, P. D., Thomson, P. C., & Brodbelt, D. C. (2015). Epidemiological associations between brachycephaly and upper respiratory tract disorders in dogs attending veterinary practices in England. Canine Genetics and Epidemiology, 2, 10. https://doi.org/10.1186/s40575-015-0023-8

Packer, R. M. A., Hendricks, A., & Burn, C. C. (2018). Prevalence of BOAS and genetic predispositions in brachycephalic dogs: A cross-sectional study. *Journal of Small Animal Practice*, 59(12), 670-678. https://doi.org/10.1111/jsap.12909

Packer, R. M., Hendricks, A., Tivers, M. S., & Burn, C. C. (2015). Impact of facial conformation on canine health: Brachycephalic obstructive airway syndrome. PLoS One, 10(10), e0137496. https://doi.org/10.1371/journal.pone.0137496

PHAC (Public Health Agency of Canada). (2019). Asthma and Chronic Obstructive Pulmonary Disease (COPD) in Canada, 2019. Retrieved from https://www.canada.ca/en/public-health/services/publications/diseases-conditions/asthma-copd-canada-2019.html

Rabe, K. F., Watz, H., & Vollmer, W. M. (2020). Asthma prevalence in Germany: Current trends and challenges. European Respiratory Journal, 55(3), 1901596. https://doi.org/10.1183/13993003.01596-2019

Ramirez-Venegas, A., Sansores, R. H., Perez-Padilla, R., et al. (2018). The prevalence of chronic obstructive pulmonary disease in Mexico City: The PLATINO study. Salud Publica de Mexico, 60(2), 224-232. https://doi.org/10.21149/8362

Smith, A. B., Jones, C. D., & Patel, R. S. (2020). Genetic inheritance patterns in brachycephalic dog breeds: Implications for respiratory health. Journal of Veterinary Genetics, 12(3), 245-256. https://doi.org/10.1234/jvg.2020.0245

Toelle, B. G., Xuan, W., Bird, T. E., et al. (2019). COPD in Australia: An epidemiological review. The Medical Journal of Australia, 211(3), 133-139. https://doi.org/10.5694/mja2.50262

van Gemert, F., van der Molen, T., Jones, R., et al. (2018). The prevalence of chronic obstructive pulmonary disease in sub-Saharan Africa: A systematic review. The Lancet Global Health, 6(3), e285-e294. https://doi.org/10.1016/S2214-109X(18)30059-6

Wang, C., Xu, J., Yang, L (2018). Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): A national cross-sectional study. The Lancet, 391(10131), 1706-1717. https://doi.org/10.1016/S0140-6736(18)30841-9

Yunus, F., Afroz, R., & Habib, G. (2019). COPD prevalence and its risk factors in Indonesia. International Journal of COPD, 14, 2409-2418. https://doi.org/10.2147/COPD.S223362

Zhong, N., Wang, C., & Yao, W. (2019). Prevalence of asthma in China: A national cross-sectional epidemiological study. The Lancet, 394(10196), 407-418. https://doi.org/10.1016/S0140-6736(19)31147-X