

Global Health: What Does it Mean for ENT?

Introduction

Global health is a term to describe the conduction of transnational research to identify variables that influence health, and the use of information gathered to inform evidence-based decisions which aim to improve health across the world.⁽¹⁾

In 2007, the World Health Organisation (WHO) outlined the main threats to global human health in the 21st Century.⁽²⁾ These include a rise in epidemic-prone diseases, foodborne diseases, accidental or deliberate outbreaks of infectious disease, toxic chemicals and radionuclear materials, and finally environmental disasters which influence health through multiple avenues.⁽²⁾

An acute threat to global health is climate change.^(3,4) Research demonstrates its direct and indirect influence on health. The greatest effect on health will arise from limited access to safe food and water, and dirtier air. Climate change is estimated to contribute to an additional 12.6 million death each year.⁽⁵⁾

Otorhinolaryngology and Global health

Ear, Nose and Throat (ENT) surgery, also called Otorhinolaryngology, is the surgical specialty concerned with the diagnosis, evaluation and management of head, neck, ear, nose and throat diseases.⁽⁶⁾ ENT encompasses a vast disease spectrum, much of which is treatable through manoeuvres and medical management but equally, surgical intervention is often indicated.

ENT disease prevalence, risk factors and treatment vary between developed and developing countries. Health provision, particularly surgery, in developing countries is poor and their healthcare systems are unstable.⁽⁷⁾ Technological advances provide ENT surgery with novel diagnostic and treatment opportunities, however new technology is inaccessible to developing countries which further contributes to the great difference in ENT practice between the developed and developing world.^(2,8)

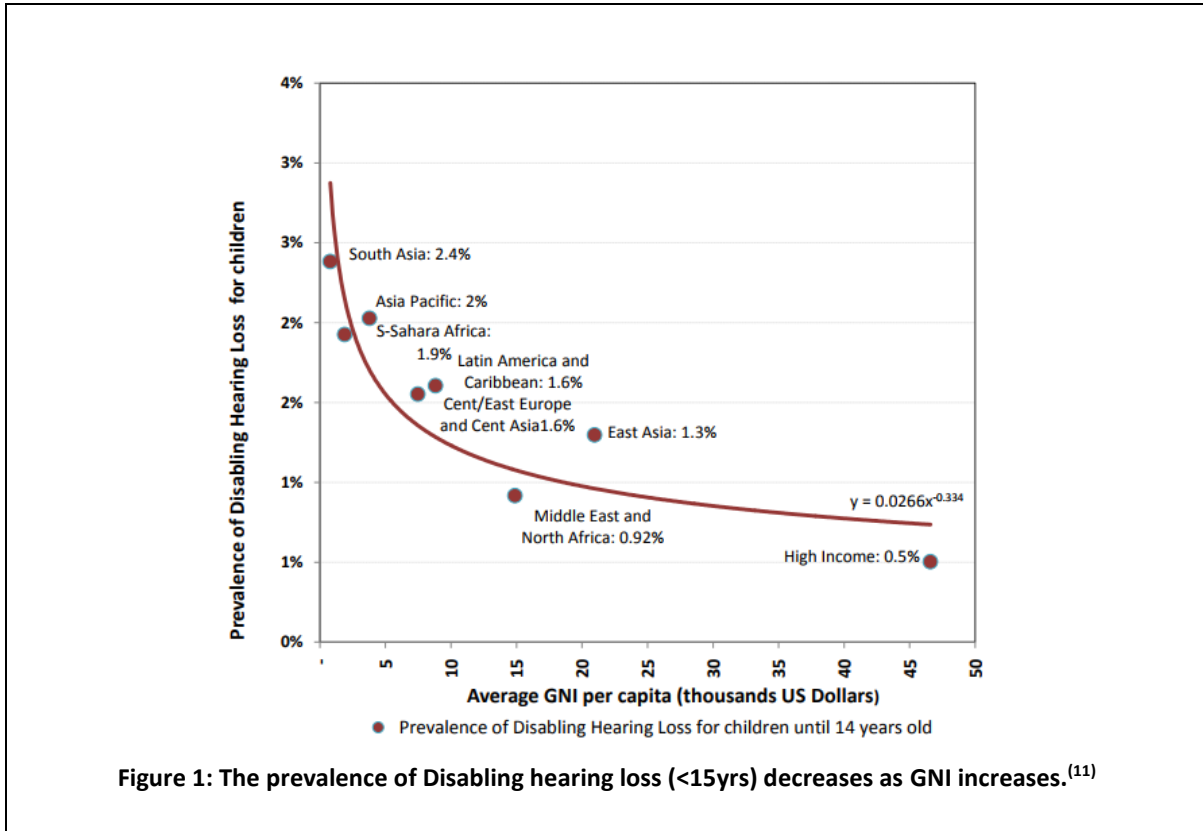
The American Academy of Otolaryngology has outlined the main ENT diseases requiring intervention in low- and middle-income countries (LMIC). These include thyroid and parathyroid disease, hearing loss, chronic ear disease, tracheostomy care and paediatric airway pathologies.⁽⁸⁾

In this essay, I will outline key global health concerns in otorhinolaryngology, discuss why discrepancies in ENT services between developed and developing countries exist, provide an insight into future challenges for global otorhinolaryngology, and finally suggest methods to minimise ENT's global burden.

Hearing Loss

In 2012 it was estimated that 5.3% of the world's population were living with disabling hearing loss (DHL), defined as a hearing impairment greater than 40db when 15years or older, or greater than 30dB when younger than 15years.⁽⁹⁾ The burden of hearing loss predominates in LMICs, particularly

Sub-Saharan Africa (SSA), south Asia, and the Asian pacific.⁽⁹⁾ The prevalence of hearing loss decreases exponentially as gross national income (GNI) increases, both for adults and children.⁽¹⁰⁾(figure 1) 48% of adults over 65years in south Asia have DHL, compared with 18% of those from high-income countries (HIC).^(10,11)



Why does hearing loss matter?

Whether from a developed or underdeveloped country, chronic hearing loss in children impairs speech and language development.⁽¹²⁾ Disability and handicap results, for example through poor educational and vocational attainment. Unemployment rates are higher in deaf adults, and those that do achieve employment, usually receive a lower grade than the general population.⁽¹²⁾ Children whose hearing is impaired are more prone to experiencing emotional, sexual and physical abuse, including murder.^(12,13)

WHO estimates that unaddressed hearing loss has a global cost of 750 billion international dollars.⁽¹⁰⁾ Many causes of DHL are preventable and owing to its negative consequences, prevention is paramount.

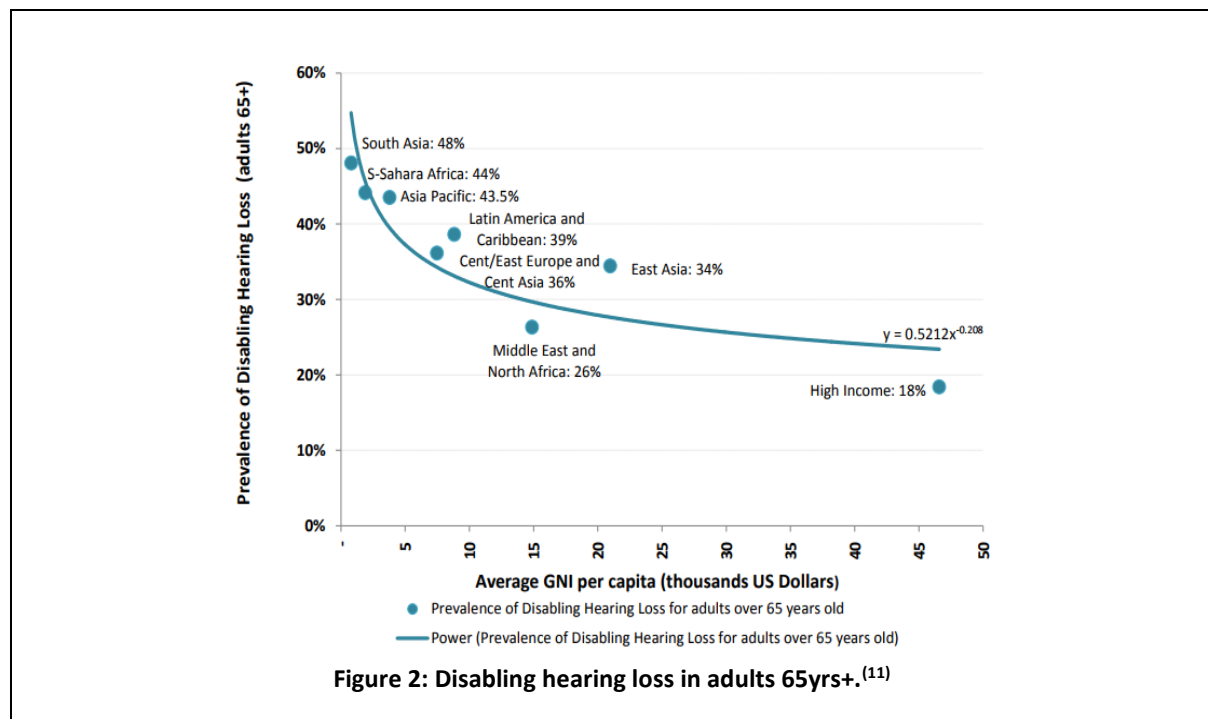
Hearing loss in developing countries

The prevalence of childhood DHL is higher in developing countries. 2.4% of children under 15 years of age have DHL in South Asia, a low-income country, compared with 0.5% in HICs.⁽¹¹⁾ 80% of the world’s deaf population receive no education, particularly skewed towards LMICs where almost all deaf people don’t, causing devastating consequences for deaf childrens’ futures.⁽¹⁴⁾

Causes of hearing loss in children and adolescents

60% of DHL in children under 15yrs is preventable with a disproportionately high burden in LMICs where 75% are preventable, compared with 49% in HICs.⁽¹⁰⁾

Infections are the main preventable cause.⁽¹⁵⁾ They occur antenatally (rubella and syphilis) or during infancy (mumps, measles and rubella). Persistent middle ear infections cause chronic suppurative otitis media (CSOM), a condition affecting 330 million people worldwide. It is more common in LMICs, accounting for roughly 25% of the ENT workload, where it is associated with higher complication rates too.^(10,15-17) Secondly, complications from childbirth may cause sensorineural hearing loss, usually secondary to cerebral damage, which may result from birth asphyxia and hyperbilirubinaemia; complications more commonly affect premature neonates.⁽¹⁰⁾ Finally, ototoxicity is the third main cause, most commonly arising from medication use in babies or pregnant mothers.⁽¹⁰⁾



Hearing loss in adults

Although the proportional difference between LMICs' and developed countries' DHL prevalence is largest in those under 15yrs old, adult populations differ too.(figure 2) Adult DHL is usually due to disease originating from childhood, degenerative changes, and noise-induced DHL.

Noise-induced hearing loss is particularly prevalent in LMICs. Many LMICs are experiencing rapid urbanisation and therefore increased noise exposure with minimal regulation.⁽¹⁸⁾ Residents and workers are exposed to high noise levels which contributes to the high prevalence of noise-induced DHL.⁽¹²⁾

How can we minimise preventable causes of hearing loss in LMICs?

As many DHL cases in LMICs are preventable, we can intervene in various ways to reduce its incidence. Self- and herd-immunity can be induced through providing childhood immunisations, particularly against measles, mumps, rubella and bacterial meningitis.^(10,12) Contraceptive access in LMICs is poor. Therefore immunising women of reproductive age against rubella, screening pregnant females for

syphilis, and improving antenatal care all help reduce neonatal DHL.^(10,12) HIV prevention would reduce its influence on CSOM complication rates (OR 4.3, 95% CI; 1.17–15.6; $p=0.028$).⁽¹⁷⁾ Implementing newborn hearing screening programmes in LMICs would improve the early diagnosis and treatment of sensorineural hearing loss. High quality ENT training for professionals, accessible primary health care services, and up-to-date technology could prevent unsafe prescribing of ototoxic medication and would allow disease to be identified at an early stage. Early disease identification would reduce the prevalence of CSOM-associated complications that occur at an increased rate in prolonged and untreated disease (OR 1.03, 95% CI; 1.007–1.05; $p=0.01$).⁽¹⁷⁾

Minimising noise exposure is essential. In the UK, The Control of Noise at Work Regulations 2005 ensures that employers reduce occupational noise to prevent it impairing their employees' hearing.⁽¹⁹⁾ Pressure must be put on LMIC governments to create similar legislation, which often is lacking. If environments and occupations cannot be altered, personal protective equipment must be available.

LMICs carry a larger proportion of DHL than developed countries but care is minute in comparison.^(20,21) Although small, progress has been made over the last decade, particularly primary care health service expansion in LMICs with a focus on educating local people in the effective management of ear diseases.^(20–22)

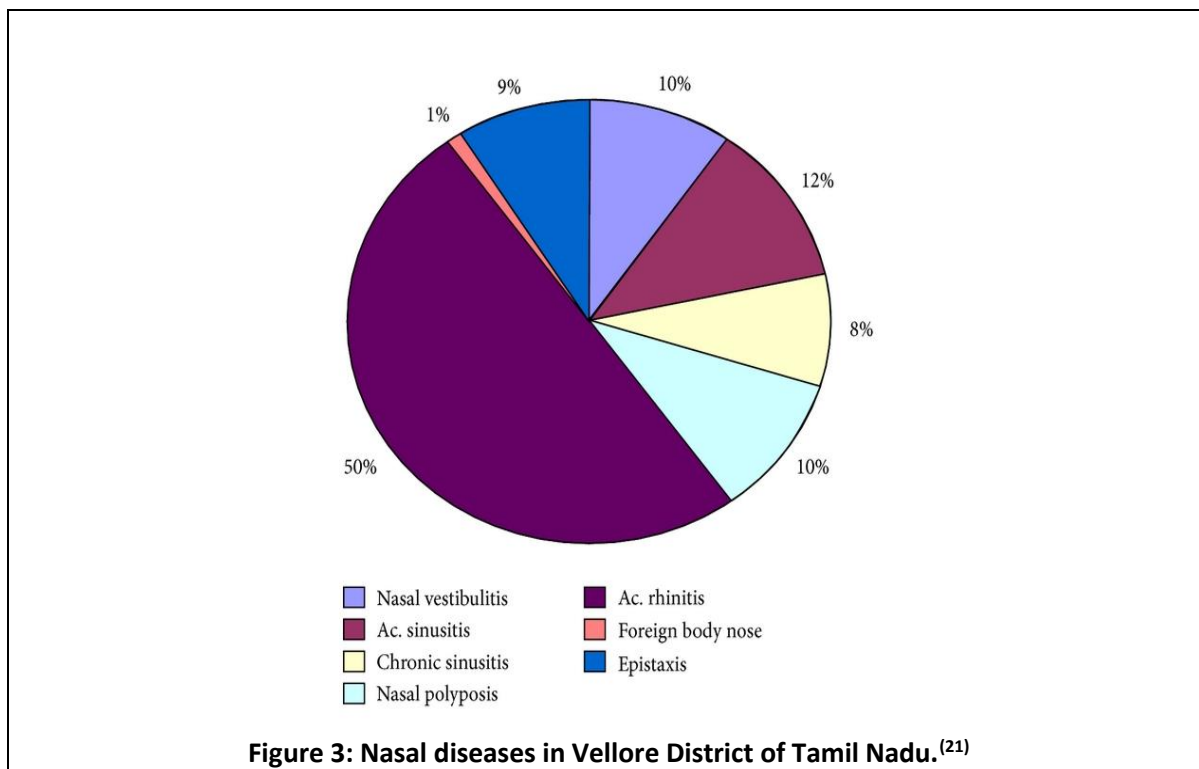
Disease of the Nose, Pharynx and Larynx

A prospective cohort study assessed the burden of ENT disease in LMICs. Roughly 2600 patients were assessed and followed-up for three years, all of whom presented to secondary care outpatient departments and healthcare camps in an Indian farming community with high poverty rates.⁽²¹⁾ All diagnoses were made by trained professionals who decided whether ENT referral was indicated.

Roughly 8% had a nasal disorder, 50% attributable to acute rhinitis, likely due to working in masonry, with paint, and around dust.⁽²¹⁾(figure 3) Seasonality showed an increasing incidence in winter.

8% had recurrent sinusitis, becoming chronic in all patients after three years or less.⁽²¹⁾ Nasal polyposis requiring surgery affected 10% of patients.⁽²¹⁾

19% of those with swallowing difficulty or hoarseness had chronic laryngitis and tonsillitis caused 49% of throat pain.⁽²¹⁾ Iron deficiency is epidemic in many LMICs due to diet, worm infections, malaria and poor antenatal care.⁽²³⁾ As a result, Plummer Vinson's syndrome - a triad of iron deficiency, atrophic glossitis and oesophageal webs or strictures - was diagnosed in 23% of those with swallowing difficulty.⁽²¹⁾



Air pollution and LMICs

Air pollution is the contamination of any environment by substances (chemical, biological or physical) that modify its natural characteristics.⁽²⁴⁾ With in-depth knowledge of the adverse impacts of air pollution, developed countries have made successful efforts to reduce levels.⁽²⁵⁾ This is not the case in LMICs. As industry has expanded, air pollution has remained high, and efforts have either minimally reduced levels or they have remained static.⁽²⁵⁾

Previous research has demonstrated a positive correlation between disease incidence and air pollution concentrations. Respiratory and cardiovascular diseases particularly are associated, with morbidity and mortality rates increasing.⁽²⁵⁾ NO₂ and SO₂, affect the upper airway and middle ear causing inflammation, irritation and infection.^(26,27) Higher levels of air pollution is associated with increased incidence of head and neck cancer, which is discussed later.^(28,29)

A study in Beijing evaluated the influence of air pollution on otolaryngology outpatient attendance.⁽²⁷⁾ NO₂ and SO₂ concentrations showed positive associations with outpatient attendance.⁽²⁷⁾ Exposure to air pollution early in life increases the risk to both upper and lower respiratory tract infections in children, including middle ear infection.^(30,31) Exposure to a combination of pollutants accelerates the onset of allergic rhinitis, particularly inducing exacerbations.⁽²⁷⁾ These findings are consistent with other studies.⁽³⁰⁻³²⁾

Data on air pollution's influence on ENT disease is limited. Higher air pollutant concentrations in developing countries may suggest that LMICs suffer greater air pollution associated ENT disease burden than HICs. Further research is required for confirmation.

Head and Neck Cancer

Head and neck cancers (HNC) are the sixth most common cancer worldwide.⁽³³⁾ Two thirds of the global burden of HNCs occur in LMICs, and the Indian subcontinent alone is responsible for one third of lip and oral cavity cancers.⁽²⁹⁾

The incidence of HNCs is increasing globally, particularly among women, likely due to increased alcohol and tobacco use, and improved diagnostic capabilities.^(29,34) Alcohol and tobacco use remain the greatest risk factors for laryngeal cancer. Tobacco primarily influences disease at the vocal cords and glottis, and alcohol mainly in the supraglottic region. Synergism is evident between HNC risk factors, particularly tobacco use (smoking and smokeless), Gutka chewing as it contains Areca nut, alcohol consumption, and oral Human papillomavirus (HPV) infections.⁽³⁵⁾

Smoking

Over the last 10yrs tobacco use has been increasing by 2-3% per year in India, and is expected to be responsible for 13% of all deaths there by 2020.⁽³⁶⁾ In LMICs, cancer of the oral cavity and throat is one of the commonest causes of death; the Aizawl district has the highest incidence of pharyngeal and tongue cancer in the world, 11.5/100,000 and 7.6/100,000 respectively.⁽³³⁾

Alcohol

In most LMICs, alcohol is consumed infrequently but heavily.⁽³⁷⁾ Moderate and heavy alcohol use increases the risk to cancers, including cancer of the larynx, with a systematic review demonstrating a risk-ratio of 1.44 (95% CI 1.25–1.66) for moderate consumption and 2.65 (95% CI 2.19–3.19) for heavy consumption.^(37,38) Through lack of education, LMIC inhabitants are less aware of alcohol's negative consequences and alcohol cessation strategies tend to fail.⁽³⁷⁾

Air pollution and HNC

High levels of air pollution is associated with an increased risk to developing HNC.⁽²⁸⁾ 74% of the Indian population relies on solid fuels, greatly contrasting that of HICs, where in April 2017 Britain generated all electricity without using any coal.⁽³⁹⁾ India is using increasing quantities of coal, rising at a rate of 2.8% each year.^(28,40)

A retrospective case-control study investigated how exposure to air pollution from solid fuels affects the incidence of laryngeal and hypopharyngeal cancer.⁽²⁸⁾ Exposure to burning coal indoors for over 50yrs increased the risk of developing hypopharyngeal (OR 3.47, CI 0.95–12.69) and laryngeal (OR 3.65, CI 1.11–11.93) cancers.⁽²⁸⁾ Other solid fuels such as wood increased the risk to hypopharyngeal cancer too (OR 1.62, CI 1.14–2.32) but not in never-smokers.⁽²⁸⁾

Human Papillomavirus (HPV) and HNC

HPV is present in 50% of Squamous cell carcinomas (SCC) of the head and neck, particularly affecting the tongue and tonsils.⁽³³⁾ Changing oral sexual practices and the presence of high-risk HPV genotypes increase the frequency of HPV-associated HNCs in LMICs. These particularly affect younger patients and aren't sex-specific.⁽³³⁾ HPV is present in 16% of oral and laryngeal cancers in HICs; this is fewer than in LMICs, especially India where prevalence ranges from 33.6% to 67%.⁽⁴¹⁾

By understanding the biology of HPV-associated cancers, there is no reason to suggest that the HPV vaccine's protective properties would differ in efficacy between HNC and anogenital cancer.⁽⁴²⁾ HPV

vaccinations for genotypes 16 and 18 could prevent over 90% of HPV-associated oropharyngeal cancers, supporting the argument that males should be vaccinated too, owing to their higher risk for HPV-associated HNC.^(42,43)

HPV vaccines are widely available in high-income and some middle-income countries. Although one of the most-cost effective methods for disease prevention, vaccines are rarely available in low-income countries.^(44,45) For vaccines to become widely available, substantial financial subsidies must be provided. Recently, Ministries of Health and non-governmental organisations (NGO) have used donated vaccinations to try and improve conditions.⁽⁴⁴⁾ Although a good effort, governmental and international projects are essential otherwise HPV-associated HNC rates are unlikely to fall.

HNC care improvements in the developing world

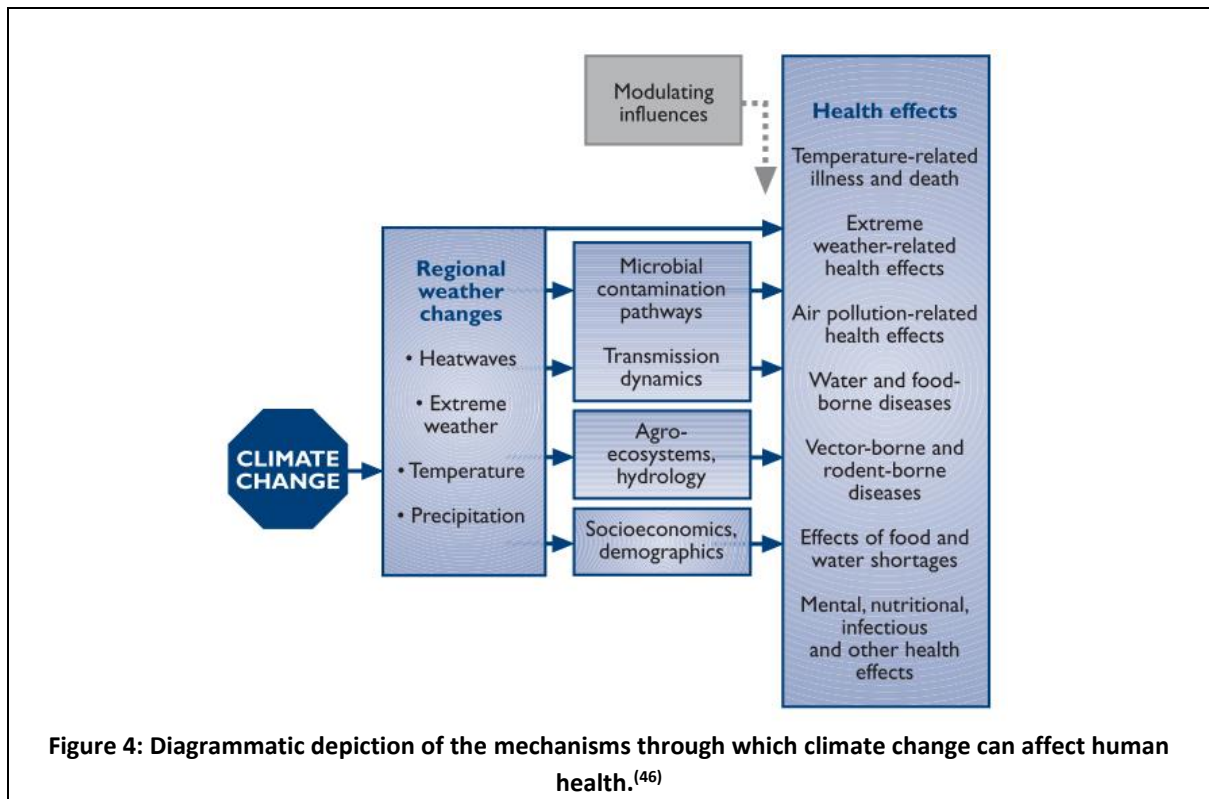
Steps must be taken to both prevent and manage HNC in LMICs. Primary preventative initiatives such as international media campaigns to raise awareness of the current HNC crisis, taxing tobacco and alcohol use, designating smoke-free areas, vaccinations, ventilation for buildings, and safe-sex programmes are essential. Secondary prevention by appropriately training professionals to manage HNCs and encouraging smoking cessation would help too.

Climate change and ENT

With the beginning of the industrial revolution, humans have released gases into the lower atmosphere that trap energy and contribute to global warming by amplifying the Earth's natural greenhouse effect.⁽⁴⁶⁾ As the Earth continues to warm our climate changes, and its effect on human life and health already is evident.

Climate change has been referred to as one of the greatest risks to human health, and between 2030 and 2050 is predicted to cause around 250000 deaths per year.⁽⁴⁷⁾ Figure 4 outlines how climate change affects human health.

Climate change's health impact will be felt across the globe, most prominently however, in LMICs. LMICs already have weak health infrastructures, particularly for ENT services, and damage for example through loss of land and overcrowding, will impair its ability to cope.⁽⁴⁷⁾ Changes in air pollution and aeroallergen concentrations will affect otorhinolaryngeal disease, and changes in the distribution of vector organisms will predispose to infectious disease, including those of the nasopharynx, ear, and paediatric airway.^(3,46,48)



How can we improve ENT Global Health for the future?

The ENT disease burden predominates in developing countries, unfortunately being a prime example of the inverse care law in action. Although not to the same extent as in developed countries, the population in LMICs is ageing. Along with ageing comes an increased disease burden, increasing demands on health services, rationing of treatment, and longer waiting times. Although interventions such as an ENT training programme established in SSA showed promise, there was minimal improvement in the population’s ENT health as the community’s population grew at a rate that overwhelmed new services after just six years.⁽⁴⁹⁾ It seems that improved education and communication, humanitarian efforts, and introducing self-sustaining healthcare infrastructures are necessary approaches to reduce the global burden of ENT diseases.

Education and communication

Both public and staff in LMICs are insufficiently educated in the prevention, diagnosis, treatment, and rehabilitation of ENT disease. Public behaviours increase the population’s risk to disease and health care is of insufficient quality and quantity.⁽⁵⁰⁾ This is due to poor local training and the migration of professionals.⁽⁵⁰⁾ Therefore, LMICs become dependent on the importation of external practitioners who they cannot afford.⁽⁵⁰⁾ International bodies must help to fund training programmes for local people, as done rather successfully in Malawi by Mulwafu *et al.*⁽²²⁾ Being trained to deliver preventative healthcare, such as vaccinations and contraception, is essential.

Innovative low-cost methods for training are needed. Clark *et al.*⁽⁵¹⁾ developed an ear trainer for low-resource settings which recently has been validated as a realistic representation of the ear for microsurgical training. GoogleGlass is a company that has streamed live surgical operations online using a camera attached to spectacles.⁽⁵²⁾ In 2014, its first operation was live-streamed to 13000

surgical students from 115 different countries. Students had their questions answered by the surgeon in real-time, representing a cornerstone in transnational education and providing promise for future training in LMICs.⁽⁵³⁾

Telemedicine, the use of electronic information and technology to provide healthcare when distance separates the patient from the professional, should be utilised as an affordable way to communicate with, and provide care to, LMICs which often have limited transport opportunities.^(54,55)

Humanitarian efforts

Although most aid is provided vertically, when trying to establish a sustainable healthcare system, horizontal aid should predominate.⁽⁵⁶⁾ Financial cooperation from multiple bodies is required to establish a sustainable healthcare system in LMICs. Independent donors, universities, ministries, and both governmental and NGOs must contribute so healthcare professionals can be recruited and resources made available.⁽⁵⁷⁾

Healthcare infrastructure

A sustainable health system requires robust financing, a well-trained workforce who are paid appropriately, an evidence-base to assist in decision-making, technology sufficient to diagnose and treat disease, and a system to deliver medicine and technology to patients.⁽⁵⁰⁾ Most LMIC's healthcare systems underachieve in all of these categories for various reasons.⁽⁵⁰⁾

Healthcare systems operate in numerous ways. To maximise the population's health for the lowest cost, most funding should target high-quality primary care service provision with a focus on disease prevention.⁽⁵⁸⁾ This is difficult to implement however as privately-run services often provide treatment for established disease and thus prevention strategies are of little interest. The role of NGOs is not simply to 'fill gaps' in health care; they can provide large-scale innovative health programmes.⁽⁵⁹⁾ NGOs face challenges. They are dependent on donors, often lack a strategic plan and often have conflicting political governance. Governments are often focused on short-term public popularity with short-term objectives. Along with other political motives such as pressure from big businesses (pharmaceutical, tobacco and alcohol), convincing governments to prioritise the long-term commitment towards establishing an effective disease prevention strategy is challenging.

References:

1. Beaglehole R, Bonita R. What is global health? *Glob Health Action*. 2010 Apr 6;3: 10.3402/gha.v3i0.5142.
2. World Health Organization. World Health Report: Global Public Health Threats in the 21st Century. *WHO*; 2013
3. CDC. Climate Change and Public Health - Climate Effects on Health. *Centers for Disease control and Prevention*. 2016. Available from: <https://www.cdc.gov/climateandhealth/effects/default.htm> [cited 2017 Aug 24]
4. Balbus J, Crimmins A, Gamble JL. Human health the impacts of climate change on in the united states. *U.S. Global Change Research Program*. 2016
5. World Health Organization. Climate change and human health: Protecting health from climate change. *World Health Organization*; 2017
6. NHS Careers. Otorhinolaryngology (ear, nose and throat surgery, ENT) *Health Careers*. Available from: <https://www.healthcareers.nhs.uk/explore-roles/surgery/ear-nose-throat-surgery>. [cited 2017 Aug 24]
7. Chao TE, Mandigo M, Opoku-Anane J, Maine R. Systematic review of laparoscopic surgery in low- and middle-income countries: benefits, challenges, and strategies. *Surgical endoscopy*. 2016 Jan;30(1):1-10. doi: 10.1007/s00464-015-4201-2.
8. American Academy of Otolaryngology. Otolaryngology in Global Health. *American Academy of Otolaryngology - Head and Neck Surgery*. 2017. Available from: <http://www.entnet.org/content/otolaryngology-global-health> [cited 2017 Aug 24]
9. World Health Organisation. Prevention of Blindness and Deafness: Estimates. *World Health Organization*; 2012. Available from: <http://www.who.int/pbd/deafness/estimates/en/> [cited 2017 Aug 13].
10. World Health Organisation. Deafness and hearing loss. *WHO*. 2017. Available from: <http://www.who.int/mediacentre/factsheets/fs300/en/> [cited 2017 Aug 24]
11. World Health Organisation. WHO Global estimates on prevalence of hearing loss: mortality and Burden of Diseases and Prevention of Blindness and Deafness, *WHO*. 2012
12. Olusanya BO, Neumann KJ, Saunders JE. The global burden of disabling hearing impairment: a call to action. *WHO*; 2014;92:367-373.
13. Jones L, Bellis MA, Wood S, Hughes K, McCoy E, Eckley L.. Prevalence and risk of violence against children with disabilities: a systematic review and meta-analysis of observational studies. *Lancet*; 2 2012 Sep 8;380(9845):899-907.
14. WFD, Human Rights. *World federation of the deaf*. 2016. Available from: <https://wfdeaf.org/human-rights/> [cited 2017 Aug 24]
15. DeAntonio R, Yarzabal J-P, Cruz JP, Schmidt JE, Kleijnen J. Epidemiology of otitis media in children from developing countries: A systematic review. *International Journal of Pediatric*

- Otorhinolaryngology*; 85;2016; 65–74.
16. Orji F. A survey of the burden of management of chronic suppurative otitis media in a developing country. *Annals of Medical and Health Sciences Research*; 2013 Oct;3(4):598-601.
 17. Mushi MF, Mwalutende AE, Gilyoma JM, Chalya PL, Seni J, Mirambo MM. Predictors of disease complications and treatment outcome among patients with chronic suppurative otitis media attending a tertiary hospital, Mwanza Tanzania. *BMC Ear, Nose and Throat Disorders*. 2016 Jan 7;16:1
 18. Schwela D, Finegold LS, Stewart J. A strategic approach on environmental noise management in developing countries. *9th International Congress on noise as a Public health Problem*. 2008
 19. HSE. The Control of Noise at Work Regulations. *Health and Safety Executive*. 2005. Available from: <http://www.hse.gov.uk/noise/regulations.htm> [cited 2017 Aug 24]
 20. Harris MS, Dodson EE. Hearing health access in developing countries. *Current Opinion in Otolaryngology and Head and Neck Surgery*. 2017; Jul 3.
 21. Emerson LP, Job A, Abraham V. A model for provision of ENT health care service at primary and secondary hospital level in a developing country. *Biomed Research International*; 2013;2013:562643
 22. Mulwafu W, Nyirenda TE, Fagan JJ, Bem C, Mlumbe K, Chitule J. Initiating and developing clinical services, training and research in a low resource setting: the Malawi ENT experience. *Tropical doctor*. 2014 Jul;44(3):135-9.
 23. World Health Organisation. Micronutrient deficiencies: Iron Deficiency Anaemia. *WHO*. 2015. Available from: <http://www.who.int/nutrition/topics/ida/en/> [cited 2017 Aug 24]
 24. World health organisation. Air pollution. *WHO*. 2016. Available from: http://www.who.int/topics/air_pollution/en/ [cited 2017 Aug 24]
 25. Chen B, Kan H. Air pollution and population health: a global challenge. *Environmental Health and Preventative Medicine*;2008 Mar;13(2):94-101.
 26. Njoroge GN, Bussmann RW. Traditional management of ear, nose and throat (ENT) diseases in Central Kenya. *Journal of Ethnobiology and Ethnomedicine*; 2006; 2: 54.
 27. Zhang F, Xu J, Zhang Z, Meng H, Wang L, Lu J. Ambient air quality and the effects of air pollutants on otolaryngology in Beijing. *Environmental Monitoring and Assessment*. 2015, 187:495.
 28. Sapkota A, Gajalakshmi V, Jetly DH, Roychowdhury S, Dikshit RP, Brennan P. Indoor air pollution from solid fuels and risk of hypopharyngeal/laryngeal and lung cancers: a multicentric case-control study from India. *International Journal of Epidemiology*. 2008 Apr;37(2):321-8
 29. Gupta B, Johnson NW, Kumar N. Global Epidemiology of Head and Neck Cancers: A Continuing Challenge. *Oncology*. 2016;91:13-23.
 30. Aguilera I, Pedersen M, Garcia-Esteban R, Ballester F, Basterrechea M, Esplugues A. Early-Life Exposure to Outdoor Air Pollution and Respiratory Health, Ear Infections, and Eczema in Infants from the INMA Study. *Environmental Health Perspectives*. 2012 Dec 5;121(3).

31. Altuğ H, Gaga EO, Döğeroğlu T, Brunekreef B, Hoek G, Van Doorn W. Effects of ambient air pollution on respiratory tract complaints and airway inflammation in primary school children. *Science of the Total Environment*. 2014 May 1;479-480:201-9
32. Bhattacharyya N, Shapiro NL. Air quality improvement and the prevalence of frequent ear infections in children. *Otolaryngology - Head and Neck Surgery*. 2010 Feb;142(2):242–6.
33. Joshi P, Dutta S, Chaturvedi P, Nair S. Head and neck cancers in developing countries. *Rambam Maimonides Medical Journal*. 2014 Apr;5(2):e0009.
34. Attar E, Dey S, Hablas A, Seifeldin IA, Ramadan M, Rozek LS. Head and neck cancer in a developing country: a population-based perspective across 8 years. *Oral Oncology*; 2010 Aug;46(8):591–6.
35. Hashibe M, Brennan P, Chuang SC., Boccia S, Castellsague X, Chen C. Interaction between Tobacco and Alcohol Use and the Risk of Head and Neck Cancer: Pooled Analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiology, Biomarkers & Prevention*. 2009 Feb 3;18(2):541–50.
36. Tarveen J, Mehrotra R. Anti-Tobacco Policies and Practices in the Past. *Asian Pacific Journal of Cancer Prevention*. 2008;9.
37. World Health Organization. Alcohol in Developing Societies: A Public Health Approach. *WHO*. 2002.
38. Islami F, Tramacere I, Rota M, Bagnardi V, Fedirko V, Scotti L. Alcohol drinking and laryngeal cancer: Overall and dose–risk relation – A systematic review and meta-analysis. *Oral Oncology*. 2010 Nov;46(11):802–10.
39. Brown G. British power generation achieves first ever coal-free day. *The Guardian*. 2017 Apr 22. Available from: <https://www.theguardian.com/environment/2017/apr/21/britain-set-for-first-coal-free-day-since-the-industrial-revolution> [cited 2017 Aug 24]
40. Penney Kate, Cronshaw Ian. Coal in India. Department of industry, innovation and science. 2015. Available from: <https://www.industry.gov.au/Office-of-the-Chief-Economist/Publications/Documents/Coal-in-India.pdf> [cited 2017 Aug 24]
41. Kreimer AR, Clifford GM, Boyle P, Franceschi S. Human Papillomavirus Types in Head and Neck Squamous Cell Carcinomas Worldwide: A Systematic Review. *Cancer Epidemiology, Biomarkers & Prevention*. 2005;14(2):467–75.
42. International Agency for Research on Cancer. Primary end-points for prophylactic hpv vaccine trials: Chapter 8. *WHO, International Agency For Research on cancer Working Group Reports Volume 7*, 2014.
43. Bogaards JA, Wallinga J, Brakenhoff RH, Meijer CJLM, Berkhof J. Direct benefit of vaccinating boys along with girls against oncogenic human papillomavirus: bayesian evidence synthesis. *British Medical Journal*. 2015;350.
44. Cervical Cancer Action. Strategies for HPV Vaccination in the Developing World. *Cervical Cancer Action Coalition*. Available from:

- http://www.rho.org/files/CCA_HPВ_vaccination_strategies.pdf [cited 2017 Aug 24]
45. Lahariya C. Vaccine epidemiology: A review. *Journal of Family medicine and Primary Care*. 2016;5(1):7–15.
 46. Mcmichael AJ, Campbell-Lendrum DH, Corvalán CF, Ebi KL, Githeko AK, Scheraga JD. Climate change and human health. *WHO*. 2003. Available from: <http://www.who.int/globalchange/publications/climchange.pdf> [cited 2017 Aug 24]
 47. World Health Organization. Climate change and health. *WHO*. 2017. Available from: <http://www.who.int/mediacentre/factsheets/fs266/en/> [cited 2017 Aug 24]
 48. Ebi KL, McGregor G. Climate Change, Tropospheric Ozone and Particulate Matter, and Health Impacts. *Environmental Health Perspectives*. 2008 Jul 10;116(11):1449–55. A
 49. Mulwafu W, Ensink R, Kuper H, Fagan J. Survey of ENT services in sub-Saharan Africa: little progress between 2009 and 2015. *Global Health Action*. 2017 Jan 9;10(1):1289736.
 50. EPRS. Strengthening Health Systems In Developing Countries [Internet]. European Parliamentary Research Service Blog. 2015; Available from: eprthinktank.eu/2015/02/10/strengthening-health-systems-in-developing-countries/ [cited 2017 Aug 24]
 51. Clark MPA, Westerberg BD, Mitchell JE. Development and validation of a low-cost microsurgery Ear Trainer for low-resource settings. *The Journal of Laryngology and Otology*; 2016 Oct 24;130(10):954–61.
 52. Developers G. Glass at Work. *GoogleGlass*. 2017; Available at: <https://www.x.company/glass/> [cited 2017 Aug 24]
 53. Smith R. First operation streamed live with surgeon wearing Google glass. *The Telegraph*. 2014. Available from: <http://www.telegraph.co.uk/news/health/news/10851116/First-operation-streamed-live-with-surgeon-wearing-Google-glass.html> [cited 2017 Aug 24]
 54. Field MJ. Telemedicine: A Guide to Assessing Telecommunications on Health Care. *Institute of Medicine (US) Committee on Evaluating Clinical Applications of Telemedicine*; 1996
 55. Combi C, Pozzani G, Pozzi G. Telemedicine for Developing Countries A Survey and Some Design Issues. *Application of Clinical Infectious Diseases*. 2016;718518(7):1025–50.
 56. World Health Organization. Vertical–horizontal synergy of the health workforce. *WHO*. Available from: <http://www.who.int/bulletin/volumes/83/4/editorial10405/en/> [cited 2017 Aug 24]
 57. Maeseneer J De, Weel C van, Egilman D, Mfenyana K, Kaufman A, Sewankambo N, et al. Funding for primary health care in developing countries. *British Medical Journal*. 2008 ;336(7643).
 58. World health Organization. What are the advantages and disadvantages of restructuring a health care system to be more focused on primary care services? *WHO*. 2004; Available from: http://www.euro.who.int/__data/assets/pdf_file/0004/74704/E82997.pdf [cited 2017 Aug 24]

59. Mercer A, Khan MH, Daulatuzzaman M, Reid J. Effectiveness of an NGO primary health care programme in rural Bangladesh: evidence from the management information system. *Health Policy and Planning*;2004;19(194):187–98.