Witness Name: Professor Sir Stephen Holgate CBE FMedSci Dated: 10 October 2022 Ref: M2/SAGE/01/SH

COVID-19 INQUIRY – MODULE 2

Questionnaire Response – Professor Sir Stephen Holgate CBE FMedSci

0: Introduction

- 0.1. I provide below my personal response to the questionnaire from the UK Covid-19 Inquiry. Staff from the Academy of Medical Sciences (AMS) supported me with my response with factual information.
- 0.2. I provide this response in good faith and to the best of my knowledge. Any omissions or inaccuracies are unintentional. I would be happy to provide any further detail about the information below or provide any further information in future.
- 1: Overview of qualifications, career history, professional expertise and major publications:

Qualifications

1.1. The following table outlines my qualification:

Table 1 – Qualification

Degrees and Professional Qualifications:				
1968	1968 BSc Biochemistry (Class I) London University			
1971	MB BS London University (Charing Cross Hosp Med Sch)			
1973	MRCP			

1979	MD - <i>b-adrenergic resistance in normal and asthmatic airways</i> , London University			
1984	FRCP			
1991	DSc Inflammatory Basis of Asthma, University of Southampton			
1995	FRCP (Edin)			
1997	FMedSci Founding Fellow, Academy of Medical Sciences			
1999	FRBS Royal Biological Society			
1999	FRCPath; CSci (Hon) Science Council			
2013	MAE Academia Europaea			
2017	FFPH Faculty of Public Health, RCP			
Honorary	/ Degrees:			
1997	Medical Doctorate Hon Causa, University of Ferrara, Italy			
1998	Medical Doctorate <i>Hon Causa</i> , Jallegonian University, Krakow, Poland			
2012	Medical Doctorate <i>Hon Causa</i> , University of Naples Frederico II, Italy			
2015	Honorary Doctor of Sciences, University of Exeter, UK			

Employment History

1.2. The following table outlines my employment history:

 Table 2 – Employment History

Current Appointments:					
1987 – Present Medical Research Council Clinical Professor of Immunopharmacology Honorary Consultant Physician, Southampton University and Foundation NHS Trust.					
Previous Appointment:					
1971 – 1972 House Physician and Surgeon , Charing Cross Hospita London					

1972 – 1973	Senior House Officer (Neurology), National Hospital for Nervous Diseases, London		
1973 – 1974	Senior House Officer Respiratory Medicine and Cardiology, Brompton Hospital London		
1974 – 1975	Registrar (General Medicine), General Infirmary, Salisbury and Southampton General Hospital		
1975 – 1980	Lecturer and Honorary Senior Registrar in Medicine, Southampton Hospitals		
1978 – 1980	MRC and Wellcome Trust Overseas Research Fellow, Women and Brigham Hospital, Harvard University, Boston, USA		
1980 – 1986	Senior Lecturer, Reader then Professor of Medicine and Hon Consultant Physician, University of Southampton and Southampton General Hospital		

Professional Expertise:

- 1.3. My professional expertise includes respiratory medicine (Hon Consultant Physician), allergy, immunopharmacology, translational medicine including experimental medicine, clinical trials, pathology, microbiology, biochemistry, immunology, toxicology, stratified medicine and public health (especially air pollution).
- I have utilised many approaches to study asthma, and published in excess of 1000 peer review publications.
- 1.5. I am a cofounder and Non-Executive Director (since 2003) of Synairgen, a specialist respiratory biotech company that develop inhaled interferon beta for viral respiratory diseases. Although not commissioned by SAGE, in this role I advised on research into the development of COVID-19 treatments (see: https://www.synairgen.com/science/covid-19).
- 1.6. I have also delivered talks to clinical and academic audiences on SARS CoV-19 and its treatment. I have published several peer-reviewed research papers and commentaries on SARS CoV-2 and COVID-19 (please see Annex A and can be made available if requested).

- 1.7. I was Past President of the British Society for Allergy and Clinical Immunology (BSACI) and British Thoracic Society (BTS). I have been recipient of a number of personal awards including the King Faisal International Prize in Medicine, the J Allyn Taylor International Prize in Medicine (Canada) and the British Thoracic Society Medal. I am Special Advisor to the Royal College of Physicians (RCP) on air quality, recipient of the 2018 RCP President's Medal, 2021 FPH Bazalgette Professorship Champion of Evidence Award and currently UKRI Clean Air Champion.
- I was appointed to CBE in 2011 for Clinical Science and knighted (KBE) in 2020 for contributions to Medical Research.

Publications

1.9. Please see Annex A which provides a selected list of my key publications.

2: List of groups I participated in and the relevant time period:

2.1. I participated in the SAGE meeting 46 on 9 July 2020.

Other groups

- 2.2. At the request of the Government Chief Scientific Adviser (GCSA) with support of the Government Office for Science (GO-Science), the Academy of Medical Sciences (AMS) established in June 2020 an Expert Advisory Group (EAG) that I chaired, and which informed the AMS report *'Preparing for a challenging winter 2020/21'*.
- 3: Overview of involvement in groups between January 2020 and February 2022:

SAGE 46

3.1. I was invited to participate in the SAGE meeting 46 on 9 July 2020 to present the findings of the Academy of Medical Sciences' (AMS's) report, *'Preparing for a challenging winter 2020/21'*, which I chaired. In the meeting I answered questions from the Government Chief Scientific Adviser (GCSA), Sir Patrick Vallance, and SAGE participants.

EAG

3.2. The AMS EAG was established to inform:

- A clear understanding of what a challenging winter 2020/21 might look like – a likely mix of COVID-19, bad seasonal influenza and cold weather.
- (2) An understanding of what this would mean for deaths, NHS capacity and social care.
- An understanding of what challenges this would present for surveillance; test, trace and isolate (TTI); and non-pharmaceutical interventions.
- (4) Plans being developed by policy/operational colleagues to manage this.
- 3.3. The EAG contributed to the development of the AMS's report, '*Preparing for a challenging winter 2020/21*'. At the SAGE meeting 46, I presented the findings of this report, which identified a series of actions that the AMS's EAG thought that Government and others could take to help prepare for, and mitigate the impact of COVID-19 on, the expected surge in healthcare demand over the upcoming winter 2020/21.
- 3.4. As was made clear in the AMS's report and at SAGE, our assessment, provided in good faith, was a rapid review that provided a summary of the research available at the time of writing (including research papers in pre-print which are clearly noted in the report references) rather than undertaking an exhaustive literature review. It drew on the most up to date evidence available at the time and the personal expertise of the EAG members but was not subject to formal peer-review. The AMS's Council was not asked to formally approve the report, but it was asked to rapidly 'sense check' the report to ensure it was independent, evidence-based, and met AMS quality standards.

4: Summary of documents to which I contributed for the purposes of advising groups:

Preparing for a challenging winter 2020/21:

(https://acmedsci.ac.uk/file-download/51353957)

4.1. The EAG completed this rapid review (published in July 2020) to define the extent of the challenges that might be faced in winter 2020/21 in terms of health, and health and social care delivery, as well as potential options to mitigate these. The deliberations of the EAG were informed by a Patient and Carer Reference Group, and a series of public, patient and carer workshops led by

Ipsos MORI. A People's Perspective developed by the Patient and Carer Reference Group (<u>https://acmedsci.ac.uk/file-download/39133546</u>) and a summary of the findings from the public, patient and carer workshops written by Ipsos MORI can be found on the AMS's website (<u>https://acmedsci.ac.uk/file-download/28843909</u>). A representative from GO-Science acted as an observer on the EAG. As such, they were not involved in the EAG's deliberations nor in the development of its findings or conclusions but provided helpful support in making connections with relevant initiatives across Government.

- 4.2. The report considered the AMS EAG's reasonable worst-case scenario for winter 2020/21 and identified actions that would help to mitigate the impact of COVID-19 on the expected seasonal surge in healthcare demand. To enable the health and social care system to better cope in the face of new winter pressures resulting from the COVID-19 pandemic, the report concluded that prevention and mitigation strategies needed to focus upon:
 - (1) Minimising the transmission and impact of COVID-19 in the community.
 - (2) Organising health and social care settings to maximise infection control and ensure that COVID-19 and routine care can take place in parallel.
 - (3) Improving public health surveillance for COVID-19, influenza and other winter diseases.
 - (4) Minimising influenza transmission and impact.
- 4.3. The report emphasised that there was a need for urgent action, with a window for preparation over the summer of 2020. It noted that preparation needed to be based on the best quality scientific advice and be developed through active engagement with patients, carers, the public and healthcare professionals. It also emphasised the need for excellent co-ordination, collaboration and sharing of information including data on the spread of disease at all levels.
- 4.4. The report (with the exception of the reasonable worst-case scenario) was endorsed by SAGE subject to minor amendments. Following my presentation at the SAGE meeting 46, the GCSA and CMO for England wrote to heads of Departments with a copy of the report, which was also circulated to the Department for Health and Social Care; Department for Transport; Ministry of Housing, Communities & Local Government; COVID-19 Taskforce; and Crown

Commercial Service by the SAGE secretariat. The AMS sent this report directly to the GCSA, the Chief Medical Officers in all UK nations, key ministers and shadow ministers, among others.

- 4.5. Following the publication of the above 2020 report, the GCSA asked the AMS to undertake a follow up rapid review (published in July 2021), 'COVID-19: Preparing for the future', which I also chaired (<u>https://acmedsci.ac.uk/file-download/4747802</u>).
- 4.6. This report was again informed by an Expert Advisory Group, a Patient and Carer Reference Group and patient and carer workshops led by Ipsos MORI. The report's aim was to identify key challenges that were likely exert additional pressures on the health and social care system over winter 2021/22 and outlined a series of options to mitigate their impact.
- 4.7. The AMS sent this report directly to the GCSA, the Chief Medical Officers and the Chief Scientific Advisers in all UK nations, key ministers and shadow ministers, among others. It was circulated to heads of Departments and government department Chief Scientific Advisers by GO-Science and included in papers for information at SAGE meeting 94 that took place on 22 July 2021. I was not present at this meeting. However, I am aware that SAGE welcomed the publication of the report noting that it had findings that should be considered by а number of government departments (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/ attachment data/file/1052577/S1345 SAGE 94 Minutes 1 .pdf).
- 4.8. In addition, the AMS published in July 2022 a position paper, 'COVID-19: what next?', which I again oversaw in conjunction with the President of the AMS, Professor Dame Anne Johnson DBE PMedSci. This position paper outlines the AMS's views on what should be considered, both for COVID-19 and more broadly, as we proceed into winter 2022/23 and beyond (https://acmedsci.ac.uk/file-download/8423999).
- 4.9. This paper was sent directly to the GCSA and the Chief Medical Officers in England and Northern Ireland, among others. GO-Science also indicated that they would circulate the paper to Government department Chief Scientific Advisers.

- 4.10. Please note that although the '*Preparing for a challenging winter 2020/21*' and '*COVID-19: Preparing for the future*' reports were commissioned by the GCSA and GO-Science, the AMS made sure that they were carried out independently and ensured objectivity and trustworthiness by: shaping the terms of reference so that the right questions were being addressed; choosing the experts and wider stakeholders that participated in these projects; and having full editorial control over the final content and publication date.
- 4.11. The AMS did not receive any additional funding from Government to carry out the 'Preparing for a challenging winter 2020/21' project. However, during the period that the 'Preparing for a challenging winter 2020/21', 'COVID-19: Preparing for the future' and 'COVID-19: what next?' reports were being prepared, it did receive core grants from BEIS that supported some of its policy work. The AMS also received an additional grant of £25,000 from BEIS to support AMS public engagement activities that fed into the 'COVID-19: Preparing for the future' report. For both the 'Preparing for a challenging winter 2020/21', 'COVID-19: Preparing for the future' report. For both the 'Preparing for a challenging winter 2020/21', 'COVID-19: Preparing for the future' reports, the AMS asked members of the Expert Advisory Group to declare any interests that were relevant to their respective terms of reference.

5: Summary of articles, interviews and/or evidence:

'Teach in' and knowledge transfer sessions

- 5.1. These sessions took place with government departments on the following topics (see paragraph 6.4):
 - (1) The findings of our 'COVID-19: preparing for the future' report with representatives from Cabinet Office and across UK Government on 29 July 2021.
 - (2) Winter respiratory infections with representatives from Cabinet Office and across UK Government on 11 November 2021.
 - (3) Non-Covid infections in winter 2022/23 with representatives from Cabinet Office on 2 February 2022.

(4) 'COVID-19: what next?' with representatives from the Cabinet Office on
 18 August 2022 (please note that I was not present at this meeting).

Presentations

- 5.2. I undertook presentations to the devolved administrations (see paragraph 6.5):
 - (1) The Welsh Technical Advisory Group about each of the three reports on20 July 2020, 16 July 2021 and 22 July 2022.
 - (2) Representatives from Welsh, Northern Irish and Scottish governments and their COVID-19 advisory groups about the 'COVID-19: preparing for the future' report on 20 September 2021. Please note that I attended meetings of the Welsh, Northern Irish and Scottish COVID-19 advisory groups (on 27 April 2021, 10 May 2021 and 13 May 2021 respectively) to present the aims of this report and understand the perspectives and challenges facing the devolved administrations so these could be adequately addressed in the report.
 - Representatives from Scottish government about the 'COVID-19: preparing for the future' report on 2 December 2021.
- 5.3. I also undertook the following presentations:
 - The Office for National Statistics about the findings of the 'COVID-19: preparing for the future' report on 27 September 2021.
 - (2) Presentation to the International Science Council about the 'COVID-19: preparing for the future' report on 29 June 2022 (please note I sent a pre-recorded message).

Oral evidence

5.4. I provided oral evidence on behalf of the AMS to the House of Commons Science and Technology Select Committee on 'COVID-19 transmission, vaccines and the likely impacts of winter' on 26 October 2021.

Media appearances

5.5. As Chair of the AMS '*Preparing for a challenging winter 2020/21*' and '*COVID-19: Preparing for the future*' reports, I participated in a wide range of

media, including broadcast, television and comments to print journalists. I also participated in two Science Media Centre briefings to discuss the findings of these reports with journalists. See paragraphs 4.1 to 4.7 above which provide details of the reports.

5.6. Overall, my comments on the AMS 'Preparing for a challenging winter 2020/21' report were picked up in 29 pieces of media. My comments on the AMS 'COVID-19: Preparing for the future' report were picked up in 6 pieces of media. Detailed information about my appearances in the media, including links, is summarised by in Annex B.

Research publications

5.7. I published six research papers during the timeframe examined by the inquiry (please see Annex A).

6: Views as to whether the work of SAGE in responding to the Covid-19 pandemic succeeded in its aims.

- 6.1. Given that I only attended one SAGE meeting, I am unable to comment in detail. However, the fact that the AMS was commissioned by the GSCA and GO-Science to provide a rapid response on the best way to prepare for winter 2020/21, with full editorial control, did indicate their commitment to receiving independent, evidence-based input. SAGE endorsed the report (with the exception of the reasonable worst-case scenario) subject to minor amendments. The AMS received positive feedback orally from the GCSA and via email from GO-Science on the content and utility of the report. As described at paragraph 4.4, the report was circulated widely in Government (including to all heads of Departments by the GCSA and CMO), prompting some of the options for mitigation set out in the report to be actioned (please see paragraphs 7.1 and 7.2 below for further detail).
- 6.2. I would like to acknowledge both the high level of commitment and the hard work undertaken by all the many scientific and clinical experts that helped develop our report and in doing so, generously contributed their expertise and many hours of their time for free.

- 6.3. I would also like to specifically commend the chairs and members of the Patient and Carer Reference Groups who committed extensive time and effort to provide invaluable input to our discussions and reports. Many of our EAG members were also supporting other areas of the COVID-19 pandemic response, including via advisory groups like SAGE and its sub-committees; in developing vaccines, treatments and diagnostics; and in frontline care in the NHS.
- 6.4. I was pleased to see that there was commitment across Government to better understand the findings of the AMS's report, including the two follow up reports mentioned above that similarly outlined priorities for winter 2021/22 and this upcoming winter (2022/23). This commitment led to a series of 'teach in' sessions with Government officials. GO-Science provided support in the organisation of these sessions to ensure that our findings could inform the work of civil servants across Government departments. All sessions were well attended and provided an opportunity for civil servants to further discuss the findings of our report with a small panel of experts that were involved in its development. Teach in sessions were held on the following topics:
 - The findings of our 'COVID-19: preparing for the future' report with representatives from Cabinet Office and across UK Government on 29 July 2021.
 - (2) Winter respiratory infections with representatives from Cabinet Office and across UK Government on 11 November 2021.
 - (3) Non-Covid infections in winter 2022/23 with representatives from Cabinet Office on 2 February 2022.
 - (4) 'COVID-19: what next?' with representatives from the Cabinet Office on 18 August 2022 (please note that I was not present at this meeting).
- 6.5. The advisory groups supporting the response of the devolved administrations showed a similar commitment to independent, evidence-based input and I also discussed the findings of our reports with the devolved administrations, including:

- The Welsh Technical Advisory Group about each of the three reports on 20 July 2020, 16 July 2021 and 22 July 2022.
- (2) Representatives from Welsh, Northern Irish and Scottish Governments and their COVID-19 advisory groups about the 'COVID-19: preparing for the future' report on 20 September 2021. Please note that I attended meetings of the Welsh, Northern Irish and Scottish COVID-19 advisory groups (on 27 April 2021, 10 May 2021 and 13 May 2021 respectively) to present the aims of the report and understand the perspectives and challenges facing the devolved administrations so these could be adequately addressed in the report.
- Representatives from Scottish Government about the 'COVID-19: preparing for the future' report on 2 December 2021.

7: Lessons that can be learned

- 7.1. As noted above at paragraph 4.4, the '*Preparing for a challenging winter* **2020/21**' report was endorsed and positively received by SAGE and circulated widely in Government, including to all heads of Departments. I believe this prompted some action across Government, though more progress could have been made against some of the priorities for prevention and mitigation as set out in the report.
- 7.2. Reflecting on the impact of the AMS 'Preparing for a challenging winter 2020/21' during a scoping meeting with experts that informed the AMS follow up report, the following areas were highlighted and might form the focus of some elements of the UK Covid-19 inquiry:
 - (1) Co-producing guidelines and engaging relevant communities Coproduction involves working in equal partnership with service users, carers and communities at the earliest stages of design, development and evaluation. Social and individual determinants, such as education, income (and other components of inequality), ethnicity and religion, can affect exposure to public health messages and capacity to act upon them, as previously revealed during the H1N1 influenza pandemic.

Therefore, the AMS report highlighted the importance of co-producing guidelines and engaging relevant communities to help improve people's understanding, motivation, skills and resources in relation to minimising COVID-19 transmission and maximising public engagement in control measures. I think the inquiry should examine whether there was sufficient co-production and engagement with relevant communities in the development of guidelines and other policies, and where improvements could be made in future. Greater consideration might have been given to involving **local** primary care and public health networks in both the development and dissemination of guidance that took account of the heterogeneity and special characteristics (e.g. ethnic, socioeconomic, rural/urban) of local communities.

- (2) Addressing hospital-acquired infection - The AMS report emphasised that minimising the infections acquired in health and care settings would be a priority for the winter. The report endorsed the hospital infection control practices set out in the Data Evaluation and Learning for Viral Epidemics (DELVE) scoping report on 'Hospital and healthcare acquisition of COVID-19 and its control' (https://rsdelve.github.io/reports/2020/07/06/nosocomial-scoping-report.html) and called for these to be widely implemented and extended to care homes. We also called for a standardised, nationwide hospital surveillance system to track and analyse nosocomial infections and inform locally led outbreak control, as recommended by the DELVE report. I think the inquiry should look at whether sufficient priority was given to addressing hospital-acquired infection, and whether the UK's approach resulted in preventable COVID-19 cases. The inquiry might wish to examine lessons learnt and how this can be improved in the future.
- (3) Addressing the backlog of care The COVID-19 pandemic led to the suspension of elective hospital work across the NHS to increase acute and intensive care capacity. The AMS 'Preparing for a challenging winter 2020/21' report highlighted that, for patients with chronic diseases, the suspension of elective services and routine outpatient appointments during the pandemic increased the backlog of patients

waiting to be seen and led to a substantial increase to NHS waiting lists. While recognising the challenges caused by the reduced operational capacity across the NHS, we urged NHS organisations to use the summer (when we expected COVID-19 transmission to be reduced) as an important window of opportunity to resume elective procedures safely and start to address the backlog of care. We noted that otherwise, the risk would be that a large number of patients would, at best, have poorer outcomes or, at worst, die unnecessarily due to delays in accessing care. I think the inquiry should look at whether the NHS took available opportunities to address the backlog over the summer, and whether efforts were made to triage patients by their clinical need rather than by length of wait.

- (4) Support for isolation The AMS report called for more to be done to support people in enabling them to adhere to COVID-19 advice and guidance. The report indicated that removing the many practical and financial disincentives/barriers to infection control measures (e.g., loss of income/employment) would improve adherence and mitigate wider health effects. It noted that provision of alternative accommodation, food, medicine and essential amenities, and financial support (especially increasing adherence to isolation and quarantine measures) were likely to be important for socio-economically disadvantaged communities. I suggest the inquiry should examine whether better support for isolation could have been provided to help to increase adherence to guidelines and further reduce community transmission. It might want to identify any effective strategies and make suggestions as to what support would be valuable if there is a need for similar isolation strategies in future.
- 7.3. The AMS's report greatly benefitted from patient and public involvement and engagement, and I feel that it demonstrates the power and value of such work. Going forward, it would be important to consider the ways in which the advice provided to Government considers, and is shaped by, the views of patients, carers and the public. The Patient and Carer Reference Group that contributed to the **'COVID-19: Preparing for the future'** report, felt that public members

should be involved in SAGE and devolved equivalent group discussions, to ensure the scientific evidence is complemented by the reality of people's lived experiences. They suggested that public members should account for a minimum of 25% of the members of SAGE and its subgroups (<u>https://acmedsci.ac.uk/file-download/57914133</u>). I think the inquiry should look at how views of patients and the public are considered alongside scientific advice in Government decisions in future national emergencies, such another pandemic.

8: Documents that I hold

- 8.1. There are publicly available electronic copies of the AMS's reports discussed above (links provided in section 4). I also have email exchanges with GO-Science about my appearance at SAGE.
- 8.2. The AMS will have information on how the project was commissioned and correspondence with GO-Science, other Government departments, and the devolved administrations.

ANNEX A EXAMPLES OF MAJOR AND COVID-RELATED PUBLICATIONS (Stephen Holgate, COVID-19 INQUIRY – MODULE 2 - Ref: M2/SAGE/01/SH)

Major publications

 Beasley R, Roche WR, Roberts JA, Holgate ST. Cellular events in the bronchi in mild asthma and after bronchial provocation. American Review of Respiratory Disease*. 1989; 139: 806-17. * Renamed American Journal of Respiratory and Critical Care Medicine in 1993.

This was the first demonstration that, even in mild asthma, airway inflammation involving activated mast cells, eosinophils and T lymphocytes and airway tissue remodelling was causal in the clinical expression of asthma. This immunological response was subsequently named Type 2 inflammation to differentiate it from neutrophil dominant Type-1 inflammation. (Cited by 1457).

 Djukanović R, Wilson JW, Britten KM, Wilson SJ, Walls AF, Roche WR, Howarth PH, Holgate ST. Effect of an inhaled corticosteroid on airway inflammation and symptoms in asthma. American Review of Respiratory Disease*. 1992; 145: 669-74. * Renamed American Journal of Respiratory and Critical Care Medicine in 1993.

While inhaled corticosteroids were known to be beneficial in asthma, this was the first study to show that this occurred by suppressing T cell, mast cell and eosinophilic mucosal inflammation. Inhaled corticosteroids are now universally recommended for the control of asthma. (Cited by 847)

 Xiao C, Puddicombe SM, Field S, Haywood J, Broughton-Head V, Puxeddu I, Haitchi HM, Vernon-Wilson E, Sammut D, Bedke N, Cremin C, Sones J, Djukanović R, Howarth PH, Collins JE, Holgate ST, Monk P, Davies DE. Defective epithelial barrier function in asthma. Journal of Allergy and Clinical Immunology. 2011; 128: 549-56.

In 1992 we first drew attention to epithelial disruption in asthma (Montefort S, Roberts JA, Beasley R, Holgate ST, Roche WR. The site of disruption of the bronchial epithelium in asthmatic and nonasthmatic subjects. Thorax. 1992; 47: 499-503) but we did not know whether this was a result of inflammation or a cause of it. Using immunostaining, we found that bronchial biopsies from asthmatic subjects displayed patchy disruption of epithelial tight junctions. In differentiated bronchial epithelial cultures, tight junction formation and transepithelial electrical resistance were markedly lower in asthmatic donors were also more sensitive to disruption by pollutants but corrected by exposure to Epidermal Growth Factor thereby reinforcing the "chronic wound scenario" of asthma pathobiology. This fundamental defect may facilitate the passage of allergens and other agents into the airway tissue, leading to immune activation and may thus contribute to the end organ expression of asthma. (Cited by 610).

 Johnston SL, Pattemore PK, Sanderson G, Smith S, Lampe F, Josephs L, Symington P, O'Toole S, Myint SH, Tyrrell DA, Holgate ST. Community study of role of viral infections in exacerbations of asthma in 9-11-year-old children. British Medical Journal. 1995; 310: 1225-9.

This 13-month longitudinal study in 108 9-11-year-old schoolchildren with asthma definitively established the key role of respiratory viruses in disease exacerbation and the dominant role played by human rhinoviruses. This was then replicated in exacerbations of adult asthma (Corne JM, et al. Frequency, severity, and duration of rhinovirus infections in asthmatic and non-asthmatic individuals: a longitudinal cohort study. Lancet. 2002; 359: 831-4). (Cited by 2375)

 Fraenkel DJ, Bardin PG, Sanderson G, Lampe F, Johnston SL, Holgate ST. Lower airways inflammation during rhinovirus colds in normal and in asthmatic subjects. American Journal of Respiratory and Critical Care Medicine. 1995; 151: 879-86. Controlled nasal infection of asthmatic and normal subjects with HRV16, a major group rhinovirus, showed that exacerbation of asthma symptoms with common cold viruses are associated with a bronchial mucosal lymphocytic and eosinophilic infiltrate (i.e., Type 2 inflammation) that explained increased airway responsiveness and symptoms characteristic of disease exacerbations. (Cited by 518)

 Wark PA, Johnston SL, Bucchieri F, Powell R, Puddicombe S, Laza-Stanca V, Holgate ST¹, Davies DE¹. Asthmatic bronchial epithelial cells have a deficient innate immune response to infection with rhinovirus. Journal of Experimental Medicine. 2005; 201: 937-47.

To understand why normally innocuous respiratory viruses, like HRV, become major triggers of acute asthma exacerbations asthmatic and normal primary bronchial epithelial cells were infected with HRV. Under identical conditions the asthmatic epithelial cells failed to eliminate the virions and exhibited death by cytotoxicity rather than apoptosis. These asthma-related defects resulted from impaired IFN- \Box , with normal responses being restored by addition of exogenous IFN- \Box . (Cited by 1378). This was the basis of the 2005 Patents: WO2005087253A3 and US20090257980A1 - Anti-virus therapy for respiratory diseases.

7. Djukanović R, Harrison T, Johnston SL, Gabbay F, Wark P, Thomson NC, Niven R, Singh D, Reddel HK, Davies DE, Marsden R, Boxall C, Dudley S, Plagnol V, Holgate ST, Monk P; INTERCIA Study Group. The effect of inhaled IFN-β on worsening of asthma symptoms caused by viral infections. A randomized trial. American Journal of Respiratory and Critical Care Medicine. 2014; 190: 145-54.

A total of 147 people with asthma on with a history of virus-associated exacerbations, were randomised to 14-day treatment with inhaled IFN- β or placebo within 24 hours of developing a cold. Daily inhaled IFN- β treatment significantly enhanced morning lung function recovery reduced the need for additional treatment, as well as boosting innate immunity assessed by blood and sputum biomarkers. A <u>similar</u> <u>protective response was also shown in COPD</u> in which there is also impaired epithelial IFN- β production. Thus, inhaled IFN- β is a potential treatment for virus-induced deteriorations of difficult-to-treat airways disease and supports the need for further trials in these populations. (Cited by 255).

 Monk PD, Marsden RJ, Tear VJ, Brookes J, Batten TN, Mankowski M, Gabbay FJ, Davies DE, Holgate ST, Ho LP, Clark T, Djukanovic R, Wilkinson TMA; Inhaled Interferon Beta COVID-19 Study Group. Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Respiratory Medicine. 2021; 9: 196-206.

We assessed the efficacy and safety of inhaled nebulised interferon beta-1a (SNG001) for the treatment of patients admitted to hospital with PCR⁺⁻COVID-19 by undertaking a randomised, double-blind, placebo-controlled, phase 2 pilot trial at nine UK sites [registered with Clinicaltrialsregister.eu (2020-001023-14) and ClinicalTrials.gov (NCT04385095)]. In 101 patients (50 active and 51 placebo) IFN-□1a inhaled once daily for 14 days reduced the odds of developing severe disease by 79%, increased the likelihood of recovery 2.3-fold and significantly reduced breathlessness. There were three deaths in the placebo group and none in the active group and inhaled IFN-□1a produced no side effects. (Cited by 340).

9. Brunekreef B, Holgate ST. Air pollution and health. Lancet. 2002; 3601: 233-42.

In this widely cited publication, we present the epidemiological evidence for the adverse effects on health of air pollutants with particular emphasis on the long-term chronic effects on respiratory and cardiovascular health. Although individual air pollutants can exert their own specific individual toxic effects on the respiratory and cardiovascular systems, ozone, oxides of nitrogen, and suspended particulates all share a common property of being potent oxidants, either through direct effects on lipids and proteins or indirectly through the activation intracellular oxidant pathways. (Cited by 4873).

10.MT Krishna, J Madden, LM Teran, GL Biscione, LC Lau, NJ Withers, T Sandstrom, I Mudway, FJ Kelly, A Walls, AJ Frew, ST Holgate. Effects of 0.2 ppm ozone on biomarkers of inflammation in bronchoalveolar lavage fluid and bronchial mucosa of healthy subjects. European Respiratory Journal. 1998; 11: 1294-300.

This used experimental medicine chamber study to investigate the effects of ozone on human airways. Healthy humans were exposed to 0.2 parts ppm of ozone and filtered air on two separate occasions for 2 hr with intermittent periods of rest and exercise, and fibreoptic bronchoscopy, lavage and biopsy was performed 6 h after the end of exposures. Ozone produced a 3-fold increase in neutrophils along with free epithelial cells in BAL fluid accompanied by increased interleukin -8 and Gro-alpha which correlated with the neutrophil count, along with an increase of activated T-lymphocytes. Ozone-induced epithelial damage with release of chemokines most likely accounted for the pro-inflammatory response. (Cited by 131)

11.Blomberg A, Krishna MT, Bocchino V, Biscione GL, Shute JK, Kelly FJ, Frew AJ, Holgate ST[¶], Sandström T. The inflammatory effects of 2 ppm NO₂ on the airways of healthy subjects. American Journal of Respiratory and Critical Care Medicine. 1997; 156: 418-24.

Healthy, non-smoking subjects were exposed to air or 2 ppm NO₂ for 4 h in random order on separate occasions. Endobronchial biopsies, bronchial washing, and bronchoalveolar lavage were done at 1.5 h or 6 h after exposure. NO₂ induced a neutrophilic inflammation in the airways that was detectable in BW at 6 h after NO₂ exposure. The increase in was related to enhanced epithelial IL-8 secretion 1.5 h after exposure. With more prolonged exposure (4hrs/day for 4 days), NO₂ stimulated an increase in airway expression of epithelial pro- asthmatic cytokines, interleukin (IL) -5 and IL-13, and upregulation of the adhesion molecule ICAM-1 (CD54) to promote inflammation [Pathmanathan S, et al. Repeated daily exposure to 2 ppm nitrogen dioxide upregulates the expression of IL-5, IL-10, IL-13, and ICAM-1 in the bronchial epithelium of healthy human airways. Occup Environ Med. 2003; 60: 892-6]. Since CD54 is also the receptor for the major class of rhinoviruses, this might explain why high personal exposure to NO₂ of asthmatic schoolchildren prior to a viral respiratory infection was associated with greater asthma exacerbations (see below, ref 12). (Cited by 155).

 Chauhan AJ, Inskip HM, Linaker CH, Smith S, Schreiber J, Johnston SL, Holgate ST. Personal exposure to nitrogen dioxide (NO₂) and the severity of virus-induced asthma in children. Lancet. 2003; 361: 1939-44.

A cohort of 114 asthmatic children aged between 8 and 11 years recorded daily upper and lower respiratory-tract symptoms, peak expiratory flow (PEF), and measured personal NO₂ exposures every week for up to 13 months. Nasal aspirates were taken during reported episodes of upper respiratory-tract illness and tested for infection by common respiratory viruses and atypical bacteria with RT-PCR assays. One or more viruses were detected in 78% of reported infection episodes. There were significant increases in the severity of lower respiratory-tract symptom scores across the three tertiles of NO₂ exposures, indicating that high exposure to NO₂ in the week before the start of a respiratory viral infection, and at levels within current air quality standards, is associated with an increase in the severity of a resulting asthma exacerbation. (Cited by 372)

13.Salvi S, Blomberg A, Rudell B, Kelly F, Sandström T, Holgate ST¹, Frew A¹. Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers. American Journal of Respiratory and Critical Care Medicine. 1999; 159: 702-9.

To determine the impact of diesel exhaust on human airways, we exposed 15 healthy human volunteers to air and diluted diesel exhaust particles (DEP) under controlled conditions for 1hr with intermittent exercise followed by lung lavage and airway biopsy at 6hr post-exposure. At high ambient concentrations, acute short-term DEP exposure produces a well-defined and marked systemic and

pulmonary inflammatory response in healthy human volunteers, which is underestimated by standard lung function measurements. A parallel study in which subjects inhaled PM_{2.5} concentrated from ambient air showed a similar inflammatory response but less in magnitude as that elicited by DEP, and in distal rather than proximal airways [Holgate ST, et al. Health effects of acute exposure to air pollution. Part II: Healthy subjects exposed to concentrated ambient particles. Research Report (Health Effects Institute). 2003; 112: 31-50; discussion 51-67] (Cited by 1049).

14.Bucchieri F, Puddicombe SM, Lordan JL, Richter A, Buchanan D, Wilson SJ, Ward J, Zummo G, Howarth PH, Djukanović R, Holgate ST, Davies DE. Asthmatic bronchial epithelium is more susceptible to oxidant-induced apoptosis. American Journal of Respiratory Cell and Molecular Biology. 2002; 27: 179-85.

Because the asthmatic bronchial epithelium is characteristically damaged with loss of columnar epithelial cells, we postulated that this is due to unscheduled apoptosis. Using an antibody directed toward the caspase cleavage product of poly (ADP-ribose) polymerase, immunohistochemistry applied to endobronchial biopsies showed higher levels of staining in the bronchial epithelium of subjects with asthma as compared with normal control subjects. Because asthmatic epithelial cells in were more susceptible to the apoptotic effects of H_2O_2 than normal cells, this revealed that susceptibility of asthmatic bronchial epithelium to oxidants such as air pollutants is greater than normal. (Cited by 343)

15.Roche WR, Beasley R, Williams JH, Holgate ST. Subepithelial fibrosis in the bronchi of asthmatics. Lancet. 1989; 1: 520-4.

Immunohistochemical and ultrastructural analyses of the subepithelial connective tissue laid down as a characteristic feature of asthma indicated it originated from subepithelial myofibroblasts not from the epithelium as part of the basement membrane (Brewster CE, et al. Myofibroblasts and subepithelial fibrosis in bronchial asthma. Am J Respir Cell Mol Biol. 1990; 3: 507-11) as a manifestation of airway wall remodelling which is now known to be a characteristic feature of asthma in addition to Type-2 inflammation. This characteristic finding was present even in patients with mild but increased in proportion to disease severity. (Cited by 1416).

 Holgate ST, Davies DE, Lackie PM, Wilson SJ, Puddicombe SM, Lordan JL. Epithelial-mesenchymal interactions in the pathogenesis of asthma. Journal of Allergy and Clinical Immunology. 2000; 105: 193-204.

Here we propose a new mechanism for disease persistence in asthma. In view of the close spatial relationship between the damaged epithelium and the underlying myofibroblasts in chronic asthma, here we propose that impaired epithelial repair cooperates with the Type-2 inflammatory environment (especially IL-4, IL-5 and IL-13) to shift the set point for communication within the trophic unit. This leads to myofibroblast activation, excessive matrix deposition, and production of mediators (such as <u>periostin</u>, a matricellular, non-structural protein) that propagate and amplify the remodelling and inflammatory responses throughout the airway wall that characterises disease chronicity. (Cited by 727)

17.Holgate ST. The sentinel role of the airway epithelium in asthma pathogenesis. Immunological Reviews. 2011; 242: 205-19.

Here we are the first to propose that continued epithelial susceptibility to environmental insults such as viral, allergen, and pollutant exposure and impaired repair responses leads to asthma persistence and provides the mediator and growth factor microenvironment for persistence of inflammation and airway wall remodelling. Increased deposition of matrix in the epithelial lamina reticularis provides evidence for ongoing epithelial barrier dysfunction, while physical distortion of the epithelium consequent upon repeated bronchoconstriction provides additional stimuli for remodelling. These dual pathways in the origins, persistence, and progression of asthma help explain why anti-inflammatory treatments fail to

influence the natural history of asthma in childhood and only partially do so in chronic severe disease. Positioning the airway epithelium as fundamental to the origins and persistence of asthma provides a rationale for pursuit of targeted therapeutics that increase the resistance of the airways to environmental insults e.g., <u>the alarmins</u> (IL-25, IL-33 and thymic stromal lymphopoietin [TSLP]) rather than concentrating all efforts to suppress inflammation once established. (Cited by 488)

18.Grainge CL, Lau LC, Ward JA, Dulay V, Lahiff G, Wilson S, Holgate S, Davies DE, Howarth PH. Effect of bronchoconstriction on airway remodeling in asthma. New England Journal of Medicine. 2011; 364: 2006-15.

Allergen and methacholine were used to induce similar levels of bronchoconstriction in asthmatic subjects. Eosinophilic inflammation of the airways increased only in the allergen group, whereas both the allergen and the methacholine groups both had equivalent airway remodelling - subepithelial collagen deposition and periodic acid-Schiff staining of epithelium (identifies mucus goblet cells) - not seen in control groups. Thus, repeated bronchoconstriction in chronic asthma without additional inflammation was capable of inducing airway remodelling. The Southampton team went on to show that epithelial Resistin-like molecule- β (RELM-b), a member of the adipokine group of hormones and profibrogenic, increases with bronchoconstriction, and is a plausible mediator of this response (Grainge C, et al. Resistin-like molecule- β is induced following bronchoconstriction of asthmatic airways. Respirology. 2012; 17: 1094-100). These findings have potential implications for disease management, especially the addition of long acting \Box_2 -agonists to ICS in chronic moderate-severe asthma. (Cited by 632).

19.Van Eerdewegh P, Little RD, Dupuis J, Del Mastro RG, Falls K, Simon J, Torrey D, Pandit S, McKenny J, Braunschweiger K, Walsh A, Liu Z, Hayward B, Folz C, Manning SP, Bawa A, Saracino L, Thackston M, Benchekroun Y, Capparell N, Wang M, Adair R, Feng Y, Dubois J, FitzGerald MG, Huang H, Gibson R, Allen KM, Pedan A, Danzig MR, Umland SP, Egan RW, Cuss FM, Rorke S, Clough JB, Holloway JW, Holgate ST[¶], Keith TP[¶]. Association of the ADAM33 gene with asthma and bronchial hyperresponsiveness. Nature 2002; 418: 426-30.

In this study linkage study, we performed a genome-wide scan on 460 Caucasian families and identified a locus on chromosome 20p13 that was linked to asthma and bronchial hyperresponsiveness. A survey of 135 polymorphisms in 23 genes identified the ADAM (A Disintegrin and Metalloprotease)33 gene as being significantly associated with asthma using case-control, transmission disequilibrium and haplotype analyses. The identification and characterization of ADAM33, a putative asthma susceptibility gene identified by positional cloning in an outbred population, provides insights into the pathogenesis and natural history of this common disease. The selective expression of ADAM33 in mesenchymal cells and its strong association with bronchial hyperresponsiveness indicated a primary role in asthmatic airway remodelling. This was the first novel asthma susceptibility gene to be described. (Cited by 1497)

20.Davies ER, Kelly JF, Howarth PH, Wilson DI, Holgate ST, Davies DE, Whitsett JA, Haitchi HM. Soluble ADAM33 initiates airway remodeling to promote susceptibility for allergic asthma in early life. Journal of Clinical Investigation Insight. 2016; 1: e87632.

Here, we report how the asthma gene a disintegrin and metalloprotease33 (ADAM33) acts as local tissue susceptibility gene that promotes allergic asthma. We show that enzymatically active soluble ADAM33 (sADAM33) is increased in asthmatic airways and plays a role in airway remodelling, independent of inflammation. Furthermore, remodelling and inflammation are both suppressed in sAdam33-null mice after allergen challenge. When induced in utero or added ex vivo, sADAM33 causes structural remodelling of the airways, which enhances postnatal airway eosinophilia and bronchial hyperresponsiveness following subthreshold challenge with an aeroallergen. This substantial gene-environment interaction helps to explain the end-organ expression of allergic asthma in genetically susceptible individuals. Finally, we show that sADAM33-induced airway remodelling is reversible, highlighting the therapeutic potential of targeting ADAM33 in asthma. These findings build on the

established role of soluble ADAM33 in promoting myogenesis in foetal lung in vitro (Haitchi HM, et al. ADAM33 expression in asthmatic airways and human embryonic lungs. Am J Respir Crit Care Med. 2005; 171: 958-65). (Cited by 36).

 Books etc: 66 Book Editorships including the lead European and US books on allergic diseases e.g., 1999 Air Pollution and Health; Asthma and Rhinitis; Allergy, 4 Editions; Allergy Principles and Practice, 4 Editions; Essentials in Allergy, 2 Editions. 476 Book Chapters/Reviews, 66 Editorials, 116 Official/Government Reports.

COVID-related publications

- Hall I, Walker S, Holgate ST. Respiratory research in the UK: investing for the next 10 years. Thorax. 2022 Sep;77(9):851-853. doi: 10.1136/thoraxjnl-2021-218459. Epub 2022 Jun 23. PMID: 35738883.
- 2. **Holgate ST**. Accelerating the transition of clinical science to translational medicine. Clin Sci (Lond). 2021 Oct 29;135(20):2423-2428. doi: 10.1042/CS20210846. PMID: 34709405.
- Jones R, Davis A, Stanley B, Julious S, Ryan D, Jackson DJ, Halpin DMG, Hickman K, Pinnock H, Quint JK, Khunti K, Heaney LG, Oliver P, Siddiqui S, Pavord I, Jones DHM, Hyland M, Ritchie L, Young P, Megaw T, Davis S, Walker S, Holgate S, Beecroft S, Kemppinen A, Appiagyei F, Roberts EJ, Preston M, Hardjojo A, Carter V, van Melle M, Price D. Risk Predictors and Symptom Features of Long COVID Within a Broad Primary Care Patient Population Including Both Tested and Untested Patients. Pragmat Obs Res. 2021 Aug 11;12:93-104. doi: 10.2147/POR.S316186. eCollection 2021. PMID: 34408531.
- Monk PD, Marsden RJ, Tear VJ, Brookes J, Batten TN, Mankowski M, Gabbay FJ, Davies DE, Holgate ST, Ho LP, Clark T, Djukanovic R, Wilkinson TMA; Inhaled Interferon Beta COVID-19 Study Group. Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet Respir Med. 2021 Feb;9(2):196-206. doi: 10.1016/S2213-2600(20)30511-7. Epub 2020 Nov 12. PMID: 33189161.
- Sipido KR, Antoñanzas F, Celis J, Degos L, Frackowiak R, Fuster V, Ganten D, Gay S, Hofstraat H, Holgate ST, Krestin G, Manns M, Meunier F, Oertel W, Palkonen S, Pavalkis D, Rübsamen-Schaeff H, Smith U, Stallknecht BM, Zima T. Overcoming fragmentation of health research in Europe: lessons from COVID-19. Lancet. 2020 Jun 27;395(10242):1970-1971. doi: 10.1016/S0140-6736(20)31411-2. Epub 2020 Jun 16. PMID: 32559417.
- Feldmann M, Maini RN, Woody JN, Holgate ST, Winter G, Rowland M, Richards D, Hussell T. Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed. Lancet. 2020 May 2;395(10234):1407-1409. doi: 10.1016/S0140-6736(20)30858-8. Epub 2020 Apr 9. PMID: 32278362

ANNEX B Stephen Holgate - media appearances (online, print, broadcast) - Ref: M2/SAGE/01/SH

Date	Торіс	Title	Outlet name	Link
14/07/20	Preparing for a challenging winter 2020/21' report	UK told to prepare now for second wave	Scotsman	https://www.scotsman.com/read-this/scientists-say-a- second-wave-of-coronavirus-over-winter-could-be-worse- than-first-with-120000-uk-deaths-2913207
14/07/20	Preparing for a challenging winter 2020/21' report	Cold winter and bad flu could leave 120,000 dead	The Times	https://www.thetimes.co.uk/article/cold-winter-and-bad-flu- could-leave-120-000-dead-vp98d57h5
14/07/20	Preparing for a challenging winter 2020/21' report	MASK & SPENCER	The Sun	
14/07/20	Preparing for a challenging winter 2020/21' report	A SECOND wave of coronavirus this winter could be worse than the first and kill 120,000 hospital patients, a report reveals.	The Sun	https://www.thesun.co.uk/news/12114651/second- coronavirus-winter-wave-cripple-nhs-kill-120k/
14/07/20	Preparing for a challenging winter 2020/21' report	Experts fear up to 120,000 Covid deaths over winter	Guardian	https://www.theguardian.com/world/2020/jul/14/action-to- stop-winter-covid-19-second-wave-in-uk-must-start-now
14/07/20	Preparing for a challenging winter 2020/21' report	Coronavirus: Scientists warn of second wave fears ahead of winter	Independent	https://www.independent.co.uk/news/health/coronavirus-uk- second-wave-flu-winter-nhs-a9615761.html
14/07/20	Preparing for a challenging winter 2020/21' report	Major plan for flu jabs to help NHS	MSN	link
14/07/20	Preparing for a challenging winter 2020/21' report	120,000 people could die in second wave, say Government scientists	LeedsLive - syndicated in 18 other regionals	link
14/07/20	Preparing for a challenging winter 2020/21' report	Coronavirus latest: Second wave of Covid-19 could be worse than the first, and could kill	iNews	link

1

				Annex B
14/07/20	Preparing for a challenging winter 2020/21' report	Prepare now for winter COVID- 19 peak, warn infectious disease experts	MyScience	link
14/07/20	Preparing for a challenging winter 2020/21' report	Second wave of coronavirus this winter could lead to more than 120,000 extra deaths, scientists warn	Evening Standard	https://www.standard.co.uk/news/health/worstcase- scenario-could-see-120-000-coronavirus-deaths-this-winter- top-scientists-warn-a4497266.html
14/07/20	Preparing for a challenging winter 2020/21' report	Coronavirus: Experts Warn Of 120,000 Deaths This Winter In Worst Case Scenario	Huff Post	link
14/07/20	Preparing for a challenging winter 2020/21' report	Dr Hilary says 120,000 more Covid-19 deaths due to a second wave "might not happen"	LancsLive and 3 other regionals	link
14/07/20	Preparing for a challenging winter 2020/21' report	UK could face 120,000 hospital deaths this winter from second Covid-19 wave in 'worst-case scenario' as top medics warn the NHS must prepare now	Daily Mail	https://www.dailymail.co.uk/news/article-8517475/UK-face- 120-000-hospital-deaths-winter-second-Covid-19-wave.html
14/07/20	Preparing for a challenging winter 2020/21' report	UK could face 120,000 hospital deaths this winter from second Covid-19 wave in 'worst-case scenario' as top medics warn the NHS must prepare now	Express	https://www.express.co.uk/news/uk/1309598/coronavirus- second-wave-could-second-wave-cause-deaths-scientist- warning
14/07/20	Preparing for a challenging winter 2020/21' report	Second Covid wave could see twice as many deaths and would require reorganisation of NHS hospitals	Telegraph	https://www.telegraph.co.uk/news/2020/07/14/second-covid- wave-could-see-twice-many-deaths-would-require/
14/07/20	Preparing for a challenging winter 2020/21' report	Winter wave of coronavirus 'could be worse than first'	BBC News	https://www.bbc.co.uk/news/health-53392148
14/07/20	Preparing for a challenging winter 2020/21' report	Second wave of coronavirus could see 120,000 hospital deaths	Metro	https://metro.co.uk/2020/07/14/second-wave-coronavirus- see-120000-hospital-deaths-winter-2-12984320/

				Annex B
14/07/20	Preparing for a challenging winter 2020/21' report	Coronavirus second winter wave could kill 120,000 Brits as scientists issue warning	Daily Star	https://www.dailystar.co.uk/news/latest-news/coronavirus- second-winter-wave-could-22351305
14/07/20	Preparing for a challenging winter 2020/21' report	Scientists warn of 120,000 winter coronavirus deaths in second wave of UK infections	Manchester Evening News	https://www.manchestereveningnews.co.uk/news/greater- manchester-news/second-wave-death-thousands-winter- 18592114
14/07/20	Preparing for a challenging winter 2020/21' report	GMB's Dr Hilary says 120,000 deaths in second wave is 'worst case scenario'	Liverpool Echo	https://www.liverpoolecho.co.uk/news/tv/gmbs-dr-hilary- says-120000-18592570
14/07/20	Preparing for a challenging winter 2020/21' report	A bad UK winter could cause 120,000 hospital deaths linked to covid-19	New Scientist	https://www.newscientist.com/article/2248691-a-bad-uk- winter-could-cause-120000-hospital-deaths-linked-to-covid- 19/
14/07/20	Preparing for a challenging winter 2020/21' report	Covid-19: UK must prepare now for winter peak or risk many more deaths, scientists warn	BMJ	https://www.bmj.com/content/370/bmj.m2825
14/07/20	Preparing for a challenging winter 2020/21' report	Worst-case' Scenario Outlined for COVID-19 This Winter	Medscape	https://www.medscape.co.uk/viewarticle/worst-case- scenario-outlined-covid-19-winter-2020a100106g
14/07/20	Preparing for a challenging winter 2020/21' report	Face masks in shops to be compulsory in England, as experts warn of 120,000 winter deaths	CNN	https://edition.cnn.com/2020/07/14/uk/uk-masks-shops- winter-predictions-intl-scli-gbr/index.html
14/07/20	Preparing for a challenging winter 2020/21' report	Worst-case' UK winter could see 120,000 COVID deaths in second wave	Reuters	https://www.reuters.com/article/us-health-coronavirus- britain-winter/worst-case-uk-winter-could-see-120000-covid- deaths-in-second-wave-idUSKCN24E30N
14/07/20	Preparing for a challenging winter 2020/21' report	Stephen Holgate on Sky News	Sky News	Broadcast
14/07/20	Preparing for a challenging winter 2020/21' report	Stephen Holgate on Talk Radio	Talk Radio	Broadcast

3

			-	Annex B
14/07/20	Preparing for a challenging winter 2020/21' report	Stephen Holgate on Channel 5 News pre record	Channel 5	Broadcast
14/07/21	COVID-19: preparing for the future' report	Covid and winter illnesses 'could bring NHS to breaking point'	The Guardian	https://www.theguardian.com/world/2021/jul/15/act-now-or- nhs-could-be-overwhelmed-this-winter-report-says-covid-flu- rsv
15/07/21	COVID-19: preparing for the future' report	Seasonal viruses could overwhelm the NHS this winter, say scientists	FT.com (Web)	https://www.ft.com/content/ee7ece2d-c0c1-4c80-bf19- c21f01bab5d3
15/07/21	COVID-19: preparing for the future' report	NHS told to brace for winter as report claims up to 60,000 could die from flu	Halesowen News (Web)	https://www.halesowennews.co.uk/news/national/19443505. nhs-told-brace-winter-report-claims-60-000-die-flu/
15/07/21	COVID-19: preparing for the future' report	Stephen Holgate on BBC Radio Scotland	BBC Radio Scotland	Broadcast
15/07/21	COVID-19: preparing for the future' report	Stephen Holgate on BBC News	BBC News	Broadcast
24/09/21	COVID-19: preparing for the future' report	Return of the common cold: infections surge in UK as autumn arrives	The Guardian.co m (Web)	https://www.theguardian.com/society/2021/sep/24/return-of- the-common-cold-infections-surge-in-uk-as-autumn-arrives

Date	Торіс	Title	Outlet name	Link
14/07/202	Preparing for a	Prepare now for a winter	Academy of	https://acmedsci.ac.uk/more/news/prepare-now-for-a-winter-
0	challenging winter	COVID-19 peak, warns	Medical	covid-19-peak-warns-academy-of-medical-sciences
	2020/21' report	Academy of Medical Sciences	Sciences	
			website	
15/07/202	COVID-19:	Winter viruses and COVID-19	Academy of	https://acmedsci.ac.uk/more/news/winter-viruses-and-covid-
1	preparing for the	could push NHS to breaking	Medical	19-could-push-nhs-to-breaking-point-warns-new-report
	future' report	point	Sciences	
			website	

4