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Consensus document on the epidemiology of severe acute respiratory syndrome (SARS)

DEPARTMENT OF COMMUNICABLE DISEASE
SURVEILLANCE AND RESPONSE

Acknowledgement

This document has been produced by the Severe Acute Respiratory Syndrome (SARS) Epidemiology Working Group and the participants at the Global Meeting on the Epidemiology of SARS, 16-17 May 2003.

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I. Introduction

On 16-17 May 2003, the World Health Organization held the first global meeting on the epidemiology of SARS in Geneva, Switzerland. The objectives of the meeting were to:

- Produce a WHO consensus document on our current understanding of the epidemiology of SARS **as it informs public health practice.**
- Identify gaps in our knowledge for the planning of additional epidemiological studies if required.

There are still considerable gaps in our knowledge of the global epidemiology of SARS, which is the first severe and readily transmissible new disease to emerge in the twenty-first century. WHO is coordinating the synthesis and interpretation of the body of work that is being produced around the world and is promoting the sharing of data and experience in containing and controlling this epidemic.

Participants were asked to present data and analysis relevant to answering the epidemiological questions in the agenda (Annex 1) either from their experience of SARS outbreaks in their countries and territories or based on the analysis of data from countries reporting cases of SARS. The final list of participants is attached as Annex 2.

Participants were representatives of the Centres (institutions, national and regional public health authorities and other health protection agencies) that have experienced outbreaks of SARS and also included leading international experts in the fields of public health and communicable disease epidemiology, mathematical modelling and clinical virology. Seven topics for discussion (see below) were selected on the basis of their importance as epidemiological indicators of the potential impact of the SARS epidemic and the potential for prevention, containment, elimination or eradication. Participants presented their findings to a broad audience on Friday 16 May and a smaller group met on Saturday 17 May to review the data and formulate draft recommendations for wider dissemination.

Professor Angus Nicoll (Health Protection Agency, Colindale, London England), the invited chair, opened the meeting, welcomed the participants and outlined the meeting's objectives. Dr David Heymann (Executive Director, Communicable Diseases Cluster, WHO) also welcomed the participants and thanked them on behalf of Dr Brundtland (Director-General, WHO) for their participation. Dr Guénäel Rodier (Director, Communicable Disease Surveillance and Response Department, WHO) highlighted the importance of sharing data and experience and the need to reach a consensus on the epidemiology of SARS to enable evidence-based public health action.

Discussions at this meeting focused on seven main topics:

- Incubation period
- Infectious period
- Case-fatality ratios
- Routes of transmission, exposure dose and risk factors for transmission
- The presence and significance of subclinical infection
- Reproduction number in different transmission settings and under different control strategies
- Animal and environmental reservoirs

The main findings and recommendations arising from the meeting are summarized by topic followed by the studies under way. However, given the rapid evolution of our knowledge about SARS, the document also incorporates published data and data presented at the SARS Clinical Management Workshop, 13-14 June 2003, Hong Kong, Special Administrative Region of China, the WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17-18 June 2003 and during teleconferences of the WHO Ad Hoc Working

Group on the Epidemiology of SARS. It therefore provides a synthesis of our current understanding of the epidemiology of SARS and the priorities for public health research.

II. Recommendations from the global meeting on the epidemiology of SARS

The participants recognized that striking progress had been made in global understanding of the science of SARS, and the coronavirus[1] that is its cause (SARS-CoV), since the first information began to be gathered in March. The experience in affected areas has already shown that the transmission of the SARS-CoV can be prevented by adherence to basic public health measures, including rapid case detection, case isolation, contact tracing and good infection control, including hand washing and the use of personal protective equipment (PPE). However they also recognized that much more needs to be known so as to protect the public and achieve WHO's goal of containing and pushing back SARS out of its human host. To help achieve this, the participants made the following **recommendations** that have been updated in light of new data:

1. Incubation period

1.1. Refined estimates of the incubation period can rapidly be achieved by combining data internationally on the approximately 200 cases with clearly defined exposure histories. WHO to coordinate a global analysis of the incubation period by defining a minimum data set, with a data dictionary and coding sheet.

1.2. Centres to prioritize laboratory testing of the approximately 200 SARS cases with clearly defined exposure histories. These cases should be tested for SARS coronavirus by one or more assays[2] to identify cases with laboratory evidence of infection, and ideally with evidence of seroconversion as the laboratory gold standard.[3]

1.3. WHO to establish and achieve agreement on a protocol to investigate "outliers" in both tails of the incubation period distribution.

1.4. WHO to review its public health recommendations informed by the incubation period immediately after the analysis of the combined data set is completed.

1.5. WHO to facilitate the development of an applied research plan to evaluate the public health policies for SARS containment and control that are based on a 10-day incubation period.

2. Infectious period

2.1. Centres to relate clinical data on the onset and/or change in the symptoms and signs of SARS (fever, cough, dyspnoea, and diarrhoea and chest X-ray changes) to viral shedding studies both retrospectively and prospectively.

2.2. WHO to encourage Centres to analyse linked clinical and laboratory data sets in order to better describe the infectious period and other clinical epidemiology.

2.3. WHO to facilitate modelling and data analytic studies to estimate infectiousness by time since onset from detailed epidemiological data sets.

2.4. WHO to encourage Centres to carry out detailed case-studies on "superspreading events"[i] (this terminology was considered more accurate than "super spreaders") and to coordinate collection and synthesis of these data. A review of "superspreading

[i] A "superspreading event " is a transmission event that generates many more than the average number of secondary cases.

events" should explore the connectedness of social networks that may facilitate transmission and the current infection control and other public health measures that need to be improved to prevent future "superspreading events".

2.5. Based on current evidence and experience, WHO to re-affirm that hospital discharge and follow-up recommendations published on 28 March 2003 are acceptable public health practice.

2.6. WHO to revise the *Management of Contacts of Probable SARS Cases* (11 April 2003)[4] to indicate that where SARS, is present or there is a reasonable suspicion that an individual is infected (for example on the basis of travel history), the need for prompt isolation of the individual and investigation of relevant contacts after onset of any symptoms suggestive of SARS.

2.7. WHO to publish a statement on what is currently known about the infectious period of SARS.

2.8. Centres to undertake quantitative studies of SARS-CoV shedding, wherever possible before and after the onset of symptoms suggestive of SARS, and continuing beyond resolution of these symptoms to determine the time period of potential infectiousness in relation to onset and resolution of symptoms, as a basis for appropriate isolation procedures.

3. Case-fatality ratios

3.1. Simple methods for calculating case-fatality ratios (CFRs) from aggregate data will not give reliable estimates during the course of an epidemic. Centres to review CFRs using statistical methods that provide valid and robust estimates such as non-parametric and/or parametric survival analyses. These methods require case-based data, preferably with laboratory confirmation.

3.2. The effects of factors such as age, sex, the presence of co-morbidities and the effectiveness of clinical management on the CFR for SARS need to be determined at the global level. WHO to facilitate the systematic collection of data on co-morbidities, including underlying immunosuppression, cardiorespiratory disease and other chronic diseases, clinical management and clinical outcome.

3.3. WHO to analyse data on the CFR for health care workers as a specific population at risk of SARS.

3.4. WHO to establish criteria for cause of death in relation to SARS through collaboration with the WHO Update Reference Committee for the International Classification of Diseases and Vital Statistics unit. There is a need to distinguish between SARS as the cause of death and dying of other causes with SARS as co-morbidity.

4. Routes of transmission, exposure dose and risk factors for transmission

4.1. WHO to review *Definition of a SARS Contact* in *Management of Contacts of Probable SARS Cases* in Web document [4] to include:

- analysis of SARS cases by probable route of transmission, including the proportion of cases currently unexplained by established chains of transmission
- explicit reference to exposure during the symptomatic period of a SARS case while investigating the role, if any, of infectivity in the pre-clinical period
- that special consideration should be given to confined spaces (such as within aircraft, taxis, other vehicles, some work environments) and hospital settings

- that there is a need for flexibility and judgement in the assessment of the risk of SARS transmission to contacts
- that current evidence indicates casual contacts are not at risk for SARS except when there has been sustained, close contact with a case of SARS or in high-risk transmission settings, such as health care settings and households
- that Centres report unusual transmission events to WHO to help build the evidence for as yet unrecognized routes of transmission and better define risky environments and behaviours such as clinical procedures that result in aerosols, including the use of nebulizers and difficult intubations.

4.2. Centres to undertake or continue detailed epidemiological, laboratory and environmental investigations on unusual transmission events, including transmission that cannot be explained by close, sustained contact (defined as having cared for, lived with or having had direct contact (<1 metre) with respiratory secretions or other body fluids of a suspect or probable case of SARS).

4.3. WHO to recommend that persons who have an acute febrile respiratory illness should not travel until their symptoms have resolved.

4.4. Centres in collaboration with WHO to undertake careful evaluation of all aspects of exit and entry screening.

4.5. WHO to review overall guidelines for cleaning and disinfection of hospitals and other settings after the presence of people with SARS.

4.6. WHO to facilitate a collaborative international study on SARS in pregnancy to understand the role of vertical transmission if any, the impact of SARS on pregnancy outcomes for both the mother and the fetus and the impact of pregnancy on the clinical course and outcome of SARS.

4.7. Centres to design and carry out immunological studies and surveys among children for evidence of infection and transmission in this age group where virus has been circulating. The use of methodologies for rapid serological assessment should be considered while awaiting the design and approval of formal epidemiological studies.

5. The presence and significance of subclinical infection

5.1. Centres to complete serological testing of cohorts of contacts of probable and suspect SARS cases to determine the proportion of contacts who developed symptomatic and asymptomatic infection.

5.2. WHO to synthesize the results of serologic testing of SARS contacts at a global level.

5.3. WHO to facilitate Centres pooling data and experience on unusual laboratory findings (for example isolated SARS-CoV positive serology or positive polymerase chain reaction (PCR) in individuals with no or minimal symptoms) so as to determine the public health significance of these events and the action they should trigger.

6. Reproduction number in different transmission settings and under different control strategies

6.1. WHO to introduce additional data variables in the global line listing of SARS cases to facilitate the ongoing determination of the reproduction number and impact of control measures as the epidemic evolves (see also recommendation 8.3).

6.2. WHO to facilitate modelling and other studies to estimate the impact of different control measures on the effective reproduction number in different countries.

6.3. WHO to access the International Connectance Database (air travel statistics) in order to more accurately assess the risk of international spread of SARS.

6.4. WHO to support or assist in the analysis of detailed epidemiological data from mainland China and Taiwan province to evaluate the effectiveness of public health measures by assessing the effective reproduction number.

6.5. The WHO Western Pacific Regional Office to negotiate China's participation in data sharing including the synthesis of global data via the global minimum data set.

7. Animal and environmental reservoirs

7.1. Centres to undertake urgent studies to determine whether animal reservoirs exist based on epidemiological evidence of exposure risk and laboratory evidence of infection and transmission potential.

7.2. WHO to collaborate with Centres on studies of viral inactivation to develop additional guidance on environmental decontamination in the context of SARS, particularly for the cleaning of hospitals and residential buildings (see also recommendation 4.5).

8. Cross-cutting issues

8.1. Those responsible for the health of the public need to ensure that clinical, laboratory, and epidemiological resources are efficiently coordinated to best respond and manage an outbreak and to evaluate these activities. This includes the undertaking of well-coordinated, priority studies to generate the information needed for public health action, and the timely access by public health decision-makers to this information.

8.2. WHO to facilitate closer collaboration between clinical, laboratory and epidemiology networks to address public health priorities in the diagnosis, containment and control of SARS.

8.3. WHO to achieve consensus from Centres on their participation in developing a global minimum data set for international analysis in order to better describe the epidemiology of SARS, especially for uncommon events to increase sample size and the power of any study.

8.4. WHO to leverage a data sharing agreement between Centres which addresses issues of confidentiality, use of data and publication rights.

8.5. WHO to work with Centres to analyse the global data set and to present these findings as a consensus statement by the partnership at the WHO Global Conference on Severe Acute Respiratory Syndrome, Kuala Lumpur, Malaysia, 17–18 June 2003.

8.6. WHO to review published clinical data collection tools and define a minimum clinical data set.

8.7. WHO to facilitate the development of an applied research plan to evaluate the public health policies for SARS containment and control that are based on findings such as