Short Period Incidence Study of Severe Acute Respiratory Infection (SPRINT SARI)

Rob Fowler on behalf of the SPRINT SARI Management Committee
Management Committee

- Steve Webb (AU)
- Yaseen Arabi (SA)
- Kenneth Baillie (GB)
- Gail Carson (GB)
- Michael Christian (CA)
- J Perren Cobb (US)
- Jake Dunning (GB)
- Robert Fowler (CA)
- Peter Horby (GB)
- John Marshall (CA)
- Colin McArthur (NZ)

- Laura Merson (VN)
- Srinivas Murthy (CA)
- Alistair Nichol (IE)
- Genevieve O’Neill (AU)
- Rachael Parke (NZ)
- Tim Uyeki (US)
- Juan Francisco Galán Herrera (MX, LaRed)
- Plus a representative from each participating networks
Emerging and Re-emerging Infectious Diseases

Increased Risks

- Globalisation
- Air Travel
- Farming Practices
- Climate Change

Every 23 years
Figure 1. A Timeline of Major Public Health Emergencies Worldwide (2001–2012).
SARS denotes severe acute respiratory syndrome.
Uncertainties...

When?
Where?
How much critical illness?
Age-specific critical illness incidence?
Risk factors for critical illness?
Infectivity ($R_0$)?
Case-fatality?
Even with best ICU research infrastructure in the world...

Ethics Application

Commenced

Submitted

Approval obtained

Patients Admitted to ICU (no. per million inhabitants)

End Date of Study Week

NEJM 2009: 361

Courtesy of Peter Kruger
If we Wait until Outbreaks Start to Initiate Outbreak Research – we will Fail to Improve Care
Effective pandemic research must be ‘shovel ready’

- 3 components
- Each component necessary but not sufficient

Pre-planned

Pre-approved

Research infrastructure in place
**Severe Acute Respiratory Infection**

- **2009 H1N1 pandemic (mild)**
  Estimated >200,000 respiratory &
  >80,000 cardiovascular deaths globally

- **Multiple outbreaks of novel SARI continue.**
  SARS-CoV, H7N9, H5N1, MERS-CoV
International preparedness activities

USA
- Develop and pre-position influenza treatment protocol and test the data collection and reporting system during peak times.
- Objective is to facilitate development of medical counter measures to protect against threats.

EUROPE
- ‘PREPARE’
- European Union FP7-Health 2014-2019, € 24M
- Objective is to mount a rapid, coordinated deployment of Europe’s clinical investigators, within 48 hours of a severe outbreak.

AUSTRALIA/NEW ZEALAND
- NHMRC to fund $5-10M ‘PREPARE’
- pre-planned & pre-approved protocol & support for central coordination infrastructure
- Objective is to coordinate a national approach to preventing & responding to emerging health threats.

The Goal is to be better prepared

SPRINT SARI
The primary aim of this study is to establish a research response capability for a future epidemic and pandemic through a global SARI observational study.

- Obtain and maintain ethical and other approvals for this study so that it can be rapidly activated in the event of a future outbreak of SARI in as many locations as possible;

- Generate research capacity in regions and hospitals traditionally under-served by clinical research, including formal mentoring and education initiatives;

- Assist ISARIC in developing an operational plan for a future pandemic; and

- Identify potential topics & patient populations for future studies.
Secondary Aim

The secondary aim of this study is to investigate the descriptive epidemiology and microbiology profiles of patients with SARI.

- Period *Incidence* of SARI
- Disease severity and *risk factors for severe disease* due to SARI
- *Case Fatality Proportion* of SARI
- *Duration* of ICU/hospital stay due to SARI
- *Microbiology & virology* of SARI, including variability in testing
- Describe *treatments* received during hospitalization for SARI
- Evaluate the impact of *alternative case-definitions* of SARI
Tertiary Aim

To assess the Ethics, Administrative, Regulatory and Logistic (EARL) ‘barriers’ to conducting pandemic research on a global level.

- Determine requirements of ethical approval at each site
- Determine the time required to obtain ethical approval
- Determine additional EARL barriers using questionnaires to investigators
- Identify solutions for future observational and interventional studies
Study Design

Annual, Multi-centre, Prospective, Short Period Incidence Study

- Hospitalised SARI patients during a (flexible) 5- to 7-day study period
- Northern Hemisphere winter 2015/2016
- Southern Hemisphere winter 2016
- Tropical regions in between these times

- 20 to 40 Hospital / ICU Networks to participate globally
  - ICU networks only collect in ICU
  - Hospital networks collect in ward +/- ICU
Inclusion Criteria

A suspected or proven acute respiratory infection requiring new inpatient admission with:

• Onset within the past 14 days;

& one or more of the following:

• A history of feverishness or measured fever of $\geq 38^\circ$C;
• Cough;
• Dyspnoea (shortness of breath) OR Tachypnoea*

No Exclusion Criteria
Data Collection

ISARIC - WHO SARI Case Report Forms

- Globally standardised CRFs
- **3 Tiers** of data collection depending on site capacity & infrastructure
  - Tier 0: “Rapid” CRF
  - Tier 1: CORE & Daily CRF on 1st day ICU & hospital admission
  - Tier 2: CORE & Daily CRF on 1st & 2nd day ICU & hospital admission

- Site makes choice about Tier
  - But commits for all SARI patients during the study period
### 1. SITE

**Clinical centre:**

**Country:**

**Date of study enrolment:**

### 2. DEMOGRAPHICS

**Sex at Birth:**
- [ ] Male
- [ ] Female

**Date of birth:**

**If date of birth unknown:**
- Estimated age: [__] years OR [__] months

**Pregnant:**
- [ ] Yes
- [ ] No
- [ ] Unknown
- [ ] N/A

**If YES: Gestation age of fetus:** [__] weeks

### 3. ONSET & ADMISSION

**Date of onset of first/earliest symptom:**

**Date of admission to this facility:**

### 4. INTENSIVE CARE OR HIGH DEPENDENCY CARE UNIT ADMISSION

**Admitted to ICU (or high dependency unit)?**
- [ ] Yes (complete the rest of this section)
- [ ] No (skip the rest of section 5)

**Date of first ICU admission:**

**Record the lowest value in first 24 hours of first ICU admission:**

- **Mechanical ventilation:**
  - [ ] Yes
  - [ ] No
  - [ ] N/A

- **FiO₂ (0.21-1.0):** [__] % or [__] L/min

- **PaO₂:** [__] mmHg

- **Platelet Count:** [__] x 10⁹/L

- **Mean arterial pressure:** [__] mmHg

- **Glasgow Coma Score (out of 15):** [__]

- **Urine output:** [__] mL/24 hours - check if estimated

**Record the highest value in first 24 hours of first ICU admission:**

- **Bilirubin:** [__] µmol/L or [__] mg/dL

- **Creatinine:** [__] µmol/L or [__] mg/dL

**Any vasopressor/inotropic support on 1st day of ICU admission?**
- [ ] Yes
- [ ] No (if NO, answer the next 3 questions NO)
- [ ] N/A

<table>
<thead>
<tr>
<th>Vasopressor/Inotropic Support</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine +5 μg/kg/min OR Dobutamine OR Milrinone OR Levosimendan</td>
<td>[ ]</td>
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</tr>
<tr>
<td>Dopamine 5-15 μg/kg/min OR Epinephrine/Norepinephrine &lt;0.2 μg/kg/min OR Vasopressin OR Phenylephrine</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Dopamine &gt;15 μg/kg/min OR Epinephrine/Norepinephrine &gt;0.1 μg/kg/min</td>
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</tbody>
</table>

**Date of last ICU discharge:**

**Total time admitted to ICU:** [__] days

### 5. INFECTIOUS RESPIRATORY DIAGNOSIS

**Influenza:**
- [ ] YES- Confirmed
- [ ] YES- Probable
- [ ] NO

**If YES:**
- [ ] H7N9
- [ ] H5N1
- [ ] H1N1
- [ ] Other: [__]

**Coronavirus:**
- [ ] YES- Confirmed
- [ ] YES- Probable
- [ ] NO

**If YES:**
- [ ] MERS-CoV
- [ ] Other: [__]

**Other:**
- [ ] YES- Confirmed
- [ ] YES- Probable
- [ ] NO

**If YES:**
- [ ] Other: [__]

**Clinical pneumonia:**
- [ ] YES
- [ ] NO

**If none of the above: Unknown/Non-infective:**
- [ ] Yes

### 6. OUTCOME

**During hospital admission did the patient at any time receive:**

<table>
<thead>
<tr>
<th>Ventilation</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
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<tbody>
<tr>
<td>Supplemental O₂</td>
<td>[ ]</td>
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<tr>
<td>Invasive ventilation</td>
<td>[ ]</td>
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<tr>
<td>Non-invasive ventilation</td>
<td>[ ]</td>
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<td>[ ]</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ECMO/ECLS</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
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</thead>
<tbody>
<tr>
<td>Dialysis</td>
<td>[ ]</td>
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</table>

**Final Outcome:**
- [ ] Discharged alive
- [ ] Died: [__]
- [ ] Still in hospital
- [ ] Transferred to other facility
- [ ] Palliative discharge
- [ ] N/A

**Date of final outcome:**

[Image of the RAPID CRF form]
4. COMPLICATIONS: At any time during hospitalisation did the patient experience:

<table>
<thead>
<tr>
<th>Complication</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral pneumonia</td>
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<tr>
<td>Bacterial pneumonia</td>
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<tr>
<td>Acute lung injury / ARDS</td>
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<tr>
<td>Pneumothorax</td>
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<td>Pleural effusion</td>
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<td>Bronchiolitis</td>
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<tr>
<td>Meningitis/Encephalitis</td>
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<tr>
<td>Seizure(s)</td>
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<tr>
<td>Stroke</td>
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<td>Congestive heart failure</td>
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<td>Endo/myo/peri-carditis</td>
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<tr>
<td>Cardiac arrhythmia</td>
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<tr>
<td>Cardiac ischaemia</td>
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</tbody>
</table>

Specify: ____________________________

5. PATHOGEN TESTING: Was pathogen testing done during this illness episode? YES (complete section)   NO  N/A

<table>
<thead>
<tr>
<th>Sample Collection Date (DD/MM/YYYY)</th>
<th>Sample Type</th>
<th>Method</th>
<th>Result</th>
<th>Pathogens Tested</th>
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<tbody>
<tr>
<td></td>
<td>Nasal/NP swab</td>
<td>PCR</td>
<td>Positive</td>
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<tr>
<td></td>
<td>Combined nasal/NP+throat swab</td>
<td>Culture</td>
<td>Negative</td>
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<tr>
<td></td>
<td>Throat swab</td>
<td>Other, Specify:</td>
<td>N/A</td>
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**Ethical Requirements**

- Ethics approval required for all Tiers (0 – 3)
  - As required ethics approval enabling ‘sleeper’ aspect
  - Enables epidemic / pandemic preparedness
  - Enables data collection at any tier during a pandemic / epidemic if desired

- No individual patient consent *anticipated*
  - Waiver-of-consent

- Submission of de-identified data only
Outcomes

Feasibility of a global observational study

- Number of sites; Data completeness; Barriers to data completion

Descriptive Information

- Incidence*; Disease severity; Case fatality; ICU/hospital Length of Stay; Treatments
- Evaluate impact of alternative SARI case definitions on incidence

EARL

- Sleeper REC approval; Barriers to EARL; Global EARL requirements & time
SPRINT SARI

Participating Networks

- CAPUCI 3 - Community-Acquired Pneumonia in Unidad de Cuidados Intensivos 3
- FLUCAN - The Influenza Complications Alert Network
- REVA - Research Network on Respiratory Failure and Artificial Ventilation
- SIDN – Singapore Infectious Diseases Network
- TIBDN - The Toronto Invasive Bacterial Diseases Network
- ACCCT - Asian Critical Care Trials Group
- ANZICS CTG – ANZ intensive care society clinical trials group
- BRICnet - Brazilian Research in Intensive Care Network
- CCCTG - Canadian Critical Care Trials Group
- ESICM - European Society of Intensive Care Medicine
- GABRIEL - Global Approach to Biology in Response to Infectious Epidemics in Low-income Countries
- GIViTI - Gruppo italiano per la Valutazione degli interventi in Terapia
- HSSG - Hellenic Sepsis Study Group
- ICCTG - Irish Critical Care Trials Group
- IP – Institut Pasteur
- La Red - The Mexican Emerging Infectious Diseases Clinical Research Network
- LACCTIN - Latin American Critical Care Trials Investigators’ Network
- OURCU - Oxford University Clinical Research Unit
- Scandinavian Informal Network
- SICP - Sino-International Severe Community-Acquired Pneumonia Consortium
- TRIGGERsep - TRIal Group for Global Evaluation and Research in Sepsis
- USCIIT/USCIIT Peds - U.S. Critical Illness and Injury Trials (USCIIT) Group
- Africa - Rwanda, Malawi, Kenya Informal Network
- Japan Informal Network
- Pakistan Informal Network
- Saudi Arabia Informal Network
Contact Details
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Project Manager

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Fax: +61 3 9903 0071
**FIGURE 1.** Conceptual time course of public health severity of a severe outbreak without (Panel 1) and with (Panel 2) an early effective clinical research response that provides information to clinicians on optimal diagnosis and management as well as information to public health authorities. Reproduced by courtesy of F. Deege.