HEPATITIS C CLUSTER IN THE RENAL WARD OF SINGAPORE GENERAL HOSPITAL

THE INDEPENDENT REVIEW COMMITTEE REPORT

5 December 2015
8 December 2015

Prof Leo Yee Sin  
Chairman  
Independent Review Committee

Dear Yee Sin,

REPORT OF THE INDEPENDENT REVIEW COMMITTEE'S INVESTIGATION INTO THE SINGAPORE GENERAL HOSPITAL HEPATITIS C CLUSTER

Thank you for chairing the Independent Review Committee (IRC) on the Singapore General Hospital (SGH) Hepatitis C Cluster.

2. The IRC has worked tirelessly over the past two months to investigate the outbreak thoroughly. I would like to express my appreciation to you and your members for the time and effort that has been given to this task. I also note with appreciation the contributions and inputs of the advisers and resource persons appointed to assist the IRC.

3. The IRC's investigation has highlighted that a combination of multiple overlapping factors was the most likely explanation for the outbreak. In addition, while MOH has a national surveillance system that works well for community outbreaks of known infectious diseases, and hospitals also have robust frameworks for common healthcare-associated infections (HAIs), the Hepatitis C outbreak was an unusual HAI outbreak that highlighted a gap in the current system.

4. The IRC made recommendations for SGH to review its standard operating procedures for infection prevention and control and to ensure staff compliance. It also recommended for MOH to review the structures for surveillance, investigation and management of outbreaks, and ensure adequate expertise and resources for this; and to strengthen processes for communication and escalation of potential outbreaks to the senior management of the hospital, healthcare cluster, and MOH.

5. The Ministry of Health accepts the findings and recommendations of the IRC in full, and will act on them expeditiously.

Yours sincerely,

GAN KIM YONG
MINISTER FOR HEALTH
Mr Gan Kim Yong  
Minister for Health  

A/Prof Benjamin Ong  
Director of Medical Services  
Ministry of Health  

5 December 2015  

Dear Minister and DMS,  

REPORT OF THE INDEPENDENT REVIEW COMMITTEE  

It is my committee's pleasure to submit the report of the Independent Review Committee (IRC) for a hepatitis C cluster in the renal ward of the Singapore General Hospital (SGH).  

2. The IRC was convened on 28 September 2015 to provide an independent, objective and critical review of the Hepatitis C Cluster in SGH Renal Ward and to ascertain if all possible measures had been taken to identify the possible points of infection control breach; and remedy any weak points in the overall workflow, particularly with regard to infection control.  

3. In the past two months, my Committee investigated the cause of the outbreak and assessed that a combination of multiple overlapping factors was the most likely explanation for the outbreak. With regard to the overall system response to the outbreak, it was found that the current system which works well for surveillance of both community outbreaks and healthcare-associated infections is not able to detect unusual infections with unique characteristics like hepatitis C. Based on our findings, we have made various recommendations to improve the current system, which we hope will serve as a useful reference in the Ministry's efforts to strengthen patient safety and care processes throughout our healthcare system.  

4. My committee and I would like to thank the management and staff of the Ministry of Health, for your assistance and strong cooperation throughout our investigations. We also benefitted from the full cooperation from colleagues at the Singapore General Hospital, which enabled us to complete the review smoothly.  

Yours sincerely,  

[Signature]  

Prof Leo Yee Sin  
Chairman  
Independent Review Committee
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Executive Summary

This report sets out the findings and recommendations of the Independent Review Committee (IRC) appointed by the Ministry of Health (MOH) to provide an objective and critical review of Singapore General Hospital (SGH)’s investigation and actions following an outbreak of Hepatitis C Virus (HCV) infections at the hospital, and to reasonably investigate any activity within its terms of reference.

Background Information on Hepatitis C Virus

2 HCV is primarily a blood-borne virus and the most common modes of infection are through unsafe injection practices, inadequate sterilisation of medical equipment, and transfusion of unscreened blood and blood products.

3 The incubation period for HCV is 2 weeks to 6 months. Acute HCV infection can be asymptomatic, resulting in significant challenges to its surveillance. Approximately 55-85% of those infected develop chronic HCV infection, of which 15-30% of these chronic carriers develop a chronic liver illness known as cirrhosis, while a small proportion may develop liver cancer. HCV infection in immune suppressed patients such as post-transplant patients can cause more profound illnesses.

4 Internationally, many HCV outbreaks have been reported both within and outside hospital settings. Due to the challenges in surveillance of HCV as outlined above, it took some time to discover and identify these documented outbreaks. The virus is resilient and stable in the environment, and such transmission of HCV from environmental contamination has been reported in literature. Viral infectivity on inanimate surfaces has been shown to be detectable from between five days to six weeks.

SGH Hepatitis C Virus Cluster

5 Between April and September 2015, a cluster of 22 cases of acute HCV infection was identified amongst patients admitted to Ward 64A or Ward 67 at SGH. Subsequently, extensive screening of those who had been admitted to these wards from January to September 2015 identified three more cases, giving a total of 25 cases. Of these, 20 were renal transplant cases. There were eight deaths within the cluster.

6 SGH had conducted its own investigation into the cluster and taken actions to tighten infection control in the affected wards. It presented its investigation findings to the Minister for Health on 25 September 2015. On 28 September, MOH appointed an IRC to provide an independent, objective and critical review of SGH’s investigation and actions. The IRC was to ascertain if all possible measures had been taken to identify the possible points where there may have been infection control breaches and to remedy any weak points in the overall workflow, particularly with regard to infection control.
The IRC set out to investigate the incident via two parallel tracks. In the first, the IRC looked into probable causes of the cluster, while in the second, the IRC looked into the system response and communications between SGH, SingHealth and MOH relating to the cluster.

For the first track, the IRC appointed two teams of international experts from the United States’ Centers for Disease Control (US CDC) and Prevention and Johns Hopkins University to strengthen its capabilities and to provide additional technical and scientific input to the committee’s review.

For the second track, the IRC appointed three Resource Persons – Professor Tan Chorh Chuan, President of NUS, Professor Chee Yam Cheng, Senior Advisor to National Healthcare Group, and Mr Ong Pang Thye, Deputy Managing Partner, KPMG. Their role was to provide guidance and work with the IRC to evaluate the various parties’ responses to the incident. As the review included reviewing MOH’s role in the outbreak, IRC member Dr Jeffrey Cutter (Director, Communicable Diseases Division, Ministry of Health) recused himself from this part of the IRC’s work.

Investigations into the Outbreak

The IRC investigated the outbreak based on the principles set forth in outbreak investigations, which focus on confirming and assessing the extent of the outbreak, creating a case definition and actively searching for cases, epidemiological investigation to develop and test hypotheses and communicating findings to relevant authorities for prevention and control measures.

Based on SGH’s investigations that were presented to MOH, SGH had by end August identified a cluster of 21 cases (later updated to 22 cases in late September) that were linked epidemiologically in time and place. From their investigations, the cluster of infections had taken place from early April to June 2015. The location at which the infection took place was the Renal Ward that was originally operating in Ward 64A, which subsequently moved to Ward 67 on 6 April 2015 when Ward 64A was under renovation, and back to Ward 64A on 28 August 2015. Laboratory analysis by SGH (and subsequently confirmed by A*STAR) noted the presence of a strain of HCV, of genotype 1b, among cases. Thus an outbreak involving a common strain of HCV was established.

To ascertain the extent of spread beyond Wards 64A and 67, the IRC reviewed SGH’s data on HCV RNA (a genetic test for HCV) and liver function tests, new HCV cases among major dialysis centres in Singapore and the national notification system. The IRC concluded that there was no evidence that the outbreak had spread beyond the two wards in SGH.

Case finding began by extensive screening of patients who passed through Ward 64A and/or Ward 67. This started with the screening of 621 patients, who had been admitted in the two wards from 1 January to 30 June 2015. This period was chosen by SGH on the basis that the vast majority of infected patients would present with positive results within 10 to 12 weeks of infection. Of these patients screened, three additional cases of HCV infection related to the cluster were identified.
14 As the latest HCV infected case could have been infected in late July, the screening period was extended to September. This would also cover the period after migration from Ward 67 back to Ward 64A. An additional 304 patients were screened and no further cases were identified.

15 In all, the HCV cluster comprised 25 patients, 20 of whom had received a kidney transplant before and were more susceptible to infections. The IRC assessed that out of the eight deaths, HCV was a likely contributory factor to the death of seven cases.

16 The earliest infected case was one who was likely to have been admitted to Ward 64A in early March 2015. Residual blood sampling showed that the case was already infected by mid-March, although there were no earlier blood samples available to be more definite regarding the date of infection. The IRC conducted extensive screening for preceding cases, but there was no definitive evidence of other HCV cases during the earliest infected case’s stay in SGH and it is uncertain as to where the case had acquired the infection from.

17 A critical review of the literature was done and taking into consideration the circumstances of this outbreak, four specific hypotheses were tested. These were drug diversion; intentional harm; product contamination; and breaches in infection control.

   a. Drug diversion was concluded to be unlikely as there were no missing narcotics and other drugs with potential for abuse in the affected wards.

   b. Extensive search and interview of staff did not yield any evidence supporting intentional harm. 319 staff including 11 of those who had since left SGH all tested negative for HCV. The findings pointed towards a low probability of foul play. This was corroborated by police investigations.

   c. Contaminated medical products were an unlikely source. 0.9% Saline solution was the only product common to all patients in the cluster. 10 randomly selected bottles of 0.9% Saline solution taken from Ward 67 tested negative for HCV.

   d. While there were established processes for the handling of procedures such as blood taking, administering of intravenous medication, environmental cleaning and waste disposal, some staff were observed to have deviated from the established standards. These practices could have led to cross-contamination of equipment (e.g. computerised medical carts and trolleys) and contamination of contact surfaces. Findings pointed towards gaps in infection prevention and control practices that likely contributed to the outbreak.

18 The IRC concluded that a combination of multiple overlapping factors was the most likely explanation for the HCV outbreak, which was found to be contained within Wards 64A and 67 of SGH.
a. Firstly, susceptible cases comprising mainly immunocompromised kidney transplant patients and the introduction of HCV (probably by the patient identified as the earliest infected case) led to acute infections with extremely high quantities of virus in these patients.

b. All affected patients had many exposures to intravenous medications and/or laboratory tests that required blood taking, exacerbating the risks of HCV spread through gaps in infection control practices.

c. There were gaps with regard to infection control practices (in particular processes involving intravenous procedures), environmental cleaning, and prevention of environmental contamination. These potentially facilitated HCV transmission in the two affected wards.

d. Finally, these could have been accentuated by the shift to another ward where the layout was different from the ward that staff were familiar with.

19 During the course of investigations, the IRC observed several commendable practices by SGH staff. For example, consistent efforts were made to maintain patient privacy and confidentiality, as well as to minimise human errors by consistently verifying the patient’s identity prior to performing procedures. SGH was also effective in upskilling their nursing workforce, with nurses trained to take on a significant share of tasks normally performed by junior doctors.

20 The IRC recommends that SGH undertake the following to minimise the risk of infection transmission:

a. Review standard operating procedures and practices on infection control, with a view to reduce risk of environmental contamination, and to ensure adequate environmental cleaning and disinfection.

b. Adhere to standard precautions for infection control, as laid out in US CDC guidelines.

c. Strengthen the framework for supervision and monitoring of staff to ensure compliance with standard operating procedures.

System Response and Communications Relating to the Outbreak

21 In this track of work, the IRC interviewed the relevant parties in MOH, SingHealth and SGH involved in the outbreak, requested documentation on their key

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actions, and reviewed correspondences among the different parties. A thematic framework was adopted in assessing key actions and responses, according to five categories: (a) recognition of an infectious disease outbreak; (b) notifications to MOH; (c) outbreak management and containment; (d) communications and escalation and, (e) roles and responsibilities of key players during the outbreak.

While the current surveillance system works well for community outbreaks of known infectious diseases and hospitals have robust frameworks to handle common Healthcare-Associated Infections (HAIs), the HCV outbreak highlighted a gap. Specific findings of the system response to the outbreak were:

a. **Recognition**: The SGH Renal Unit did not recognise the outbreak in a timely manner and there was a delay in reporting to SGH Infection Control for help in containment.

b. **Notifications**: MOH was not notified by doctors and laboratories of all the cases in the cluster. In addition, MOH-CDD did not classify the initial communicable diseases notifications as acute HCV infections despite some cases having abnormal liver function tests, as the cases were assessed not to meet the case definition of an acute infection at the time.

c. **Outbreak management and containment**: While SGH commenced investigations into the HCV cluster from mid-May 2015, and enhanced infection control measures from early-June, investigations performed by SGH were incomplete. Several elements of outbreak investigation such as assessing the severity and extent of the outbreak were done by SGH only after meeting with the Director of Medical Services (DMS) on 3 September, such as appointing an external party to chair SGH’s Medical Review Committee to determine if there were related deaths due to the HCV infection and setting up a Quality Assurance Committee to do a root cause analysis.

d. **Communications and escalation**: Within SGH, communication with senior management took place early. However, in the absence of an established framework for the unusual and unfamiliar event of the HCV outbreak, there was a delay in escalation from SGH to SingHealth, and SGH to MOH. In addition, within MOH, there was no single division with clear responsibility and capability to deal with the issue, resulting in a gap in ownership, until the matter was escalated to the DMS.

e. **Roles and responsibilities**: Within SGH, there did not appear to be clear roles and responsibilities for the management of unusual hospital outbreaks. SingHealth did not play a part in the incident. Within MOH, the DMS assessed on 3 September 2015 that more information was needed to determine the severity and extent of the outbreak, and requested SGH to complete key pieces of work within two weeks. The Minister was therefore only informed of the issue on 18 September, and briefed on 25 September, after SGH submitted their investigation report on 24 September.
In summary, there was a delay in recognising the outbreak as HCV is not easily picked up through regular surveillance due to its unique characteristics. With HCV being an unusual HAI, SGH did not recognise the outbreak in a timely manner. While SGH commenced investigations into the HCV cluster from mid-May, and implemented enhanced infection control measures from early June 2015 onwards which were instrumental in slowing the spread of infection, the IRC is of the view that the outbreak was not investigated and managed optimally. Within MOH, unlike community outbreaks, no one division has clear responsibility to deal with outbreaks of unusual HAIs. This hindered MOH’s ability to respond in a timely way to the unexpected event. In addition, the absence of an established framework for unusual and unfamiliar events resulted in delays in escalating the matter from SGH to SingHealth, from SGH to MOH, and within MOH.

The IRC noted that DMS was only briefed by SGH on 3 September. His key considerations then were to make his professional evaluation of the severity and extent of the outbreak, to ascertain that adequate infection control measures had indeed been instituted, and to ensure that new transplant patients were not potentially exposed to HCV infection until the issues had been adequately addressed. He therefore asked for specific additional investigations and actions to be taken in relation to each of these within two weeks, and when these were largely done, reported the matter to the Minister. The IRC is of the opinion that the additional investigations and actions required by DMS are professionally valid and appropriate. Overall, while there were gaps in identification, management and reporting of the outbreak, there was no evidence to suggest that escalation to DMS and subsequent notification of the Minister had been deliberately delayed.

Beyond community outbreaks, the current surveillance and outbreak response frameworks should be enhanced to cater for unusual and unfamiliar events, with regards to outbreak detection, investigation and management, communication and escalation protocols, and the appropriate roles of MOH and the hospital.

The IRC thus recommends that the following measures are undertaken to improve the system response to cater to unusual and unfamiliar outbreaks:

a. Improve the national notification and surveillance system for acute HCV, taking reference from international best practices and adapting them to the local context. Regardless of the systems in place, healthcare professionals should always be alert to unusual events.

b. Designate a single team within MOH to carry out surveillance, identify and investigate potential outbreaks, and ensure adequate expertise nationally to facilitate outbreak investigation. Hospitals should continue to take responsibility and develop structures, frameworks and capabilities for HAI outbreaks within their institutions. Capabilities can be supplemented by other public healthcare institutions and MOH where required.

c. Strengthen the escalation processes for HAIs, especially unusual and unfamiliar ones, within hospitals, public healthcare clusters and MOH, and between them through clearer guidelines on the assessment of the significance and severity of an HAI, and need for escalation.
Conclusion

27 The IRC concluded that this unusual outbreak of a blood-borne infection with low prevalence rates in Singapore was likely due to a combination of multiple overlapping factors concentrated during the period of April to June 2015 in the Renal Wards of SGH. In particular, the concentration of very ill patients and gaps in infection control practices provided an environment for the infection to spread.

28 While existing surveillance and response systems lend themselves well to known community outbreaks and HAIs, the system response to the incident, which is considered an unusual one, revealed some gaps in the system. The IRC thus recommends improving the notification and surveillance system for acute HCV; designating a single team within MOH to oversee surveillance, investigation and management of outbreaks and ensure adequate expertise nationally to facilitate outbreak investigation; and strengthening escalation processes for HAIs and unusual risks.
## Glossary

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<tr>
<td>Analytic epidemiology</td>
<td>Tests hypotheses about causal relationships by quantifying the association between exposures and outcomes using a comparison group as baseline.</td>
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<td>Alanine Aminotransferase</td>
<td>A type of liver protein/ enzyme that also forms a component of liver function tests.</td>
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<td>Case</td>
<td>A diseased individual who fulfils the case definition (see case definition).</td>
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<td>Case definition</td>
<td>A set of standard criteria specifying clinical conditions and limitations on time, place, and person, to determine whether a diseased individual is included as a case of the outbreak.</td>
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<td>Case finding</td>
<td>The act of surveying a population to find individuals with a disease.</td>
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<td>Cluster</td>
<td>An aggregation of two or more cases of a disease closely linked in time and place.</td>
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<td>Descriptive epidemiology</td>
<td>Identifies patterns among cases by organising data according to time, place and person to generate hypotheses.</td>
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<td>Epidemic chart</td>
<td>A chart or graph that shows the time course of a disease outbreak in which the number of new cases of a disease is plotted over time.</td>
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<td>Epidemiology</td>
<td>The distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems.</td>
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<td>Genetic material</td>
<td>Material that forms the genome.</td>
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<td>Genotype</td>
<td>Genetic makeup of an organism, or of different strains of viruses.</td>
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<td>Glucometer</td>
<td>A medical device for determining the approximate concentration of glucose in the blood.</td>
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<td>Hand hygiene</td>
<td>A general term that applies to handwashing, antiseptic handwash, antiseptic hand rub, or surgical hand antisepsis.</td>
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<td>Haemodialysis</td>
<td>A process of cleansing the blood of a person whose kidneys are not working normally.</td>
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<td>Term</td>
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<td>HCV</td>
<td>Hepatitis C virus (HCV) is a RNV virus that is blood-borne and causes liver infection.</td>
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<td>HCV RNA test</td>
<td>The detection of the HCV RNA, the genetic material of HCV, from a PCR test (see PCR).</td>
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<td>Healthcare-associated infection (HAI)</td>
<td>Infections acquired in a healthcare setting.</td>
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<td>Hepatitis</td>
<td>Inflammation of the liver.</td>
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<td>Hepatitis C</td>
<td>Infection of the liver that results from the Hepatitis C virus.</td>
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<tr>
<td>Immune System / Immune Response</td>
<td>Biological structures and processes that protects against disease and illness.</td>
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<td>Immunocompromised</td>
<td>Having an impaired immune system.</td>
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<td>Infectivity</td>
<td>The proportion of individuals exposed to an infectious agent and become infected by it.</td>
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<td>Incubation period</td>
<td>The period between exposure to an infection and the appearance of the first symptoms.</td>
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<td>Molecular clock</td>
<td>A method used to deduce time periods based on the rate of change of genetic material.</td>
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<td>Outbreak</td>
<td>Two or more cases where the onset of disease is closely linked in time and place, where there is suspicion of, or evidence of, a common source of infection.</td>
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<td>PCR</td>
<td>Polymerase Chain Reaction (PCR) is a technique for <em>in vitro</em> amplification of specific DNA or RNA.</td>
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<td>Phylogenetic study</td>
<td>The study of natural evolutionary relationship through classification of genetic sequences.</td>
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<td>Reservoir</td>
<td>Any person, animal, plant, soil or substance in which an infectious agent normally lives and multiplies.</td>
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<td>RNA</td>
<td>Ribonucleic acid (RNA) is a genetic material present in all living cells and controls cellular protein synthesis</td>
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<td>Spot map</td>
<td>Map showing geographical location of individuals with a specific attribute e.g. cases of a cluster.</td>
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<td>Transmission</td>
<td>Any mode or mechanism by which an infectious agent is spread through the environment or to another person.</td>
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<td>Venepuncture</td>
<td>Collection of blood from a vein, usually for testing</td>
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<td>Viral load</td>
<td>Quantity of virus in a given volume.</td>
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<td>Window of infection</td>
<td>Period indicating earliest possible start of infection to end of infection.</td>
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CHAPTER 1

Introduction

1.1 The Renal Unit in the Singapore General Hospital (SGH) first noticed an increase in Hepatitis C cases between April and May 2015. On 31 August 2015, the SGH team presented to the Ministry of Health (MOH) a cluster of 21 cases of acute Hepatitis C Virus (HCV) infections amongst patients with kidney disease who had been admitted to Ward 64A or Ward 67 at SGH during the period of April to June 2015.

1.2 On 18 September 2015, the Minister for Health was informed about the cluster of HCV in SGH. SGH made a presentation to the Minister for Health on 25 September 2015, informing him of the cluster of HCV infections and that the 22nd case within the cluster had been detected. The Minister directed the appointment of an Independent Review Committee (IRC) to provide an objective and critical review of SGH’s investigation and actions. The IRC was to ascertain if all possible measures had been taken to identify the possible points where there may have been infection control breaches and to remedy any weak points in the overall workflow, particularly with regard to infection control. In addition, the committee was to review the overall timeliness and appropriateness of response mechanisms within the healthcare system as a whole.

Background

Information on Hepatitis C Infection

1.3 HCV is a blood-borne virus and the most common modes of infection are through unsafe injection practices, inadequate sterilisation of medical equipment, and the transfusion of unscreened blood. This virus can also be transmitted sexually and can be passed from an infected mother to her baby; however, these modes of transmission are much less common. HCV is not airborne and not spread by activities such as sneezing or coughing. It is also not spread by normal social contact like hugging, nor through food, water or the sharing of utensils.

1.4 Hepatitis C is a liver disease caused by HCV. The incubation period for HCV is 2 weeks to 6 months. HCV cases can be acute (i.e. recent infection, within 6 months of exposure), or chronic (i.e. beyond 6 months from infection). A person who acquires an acute HCV infection usually does not manifest any symptoms. Thus, HCV infection may go undetected for a long period of time. The asymptomatic nature of the infection, coupled with a variable and long incubation period, poses significant challenges on infectious disease surveillance systems. For instance, a scientific paper published in 2015 reported that the United States had significant under-ascertainment of acute HCV infection in their surveillance system.²

1.5 About 15 – 45% of acutely infected persons clear the virus spontaneously within 6 months of infection without any treatment. About 55% to 85% of persons with an acute HCV infection go on to develop chronic infections. In the group with chronic HCV infections, 15 – 30% of them may progress to liver cirrhosis (hardening of the liver) within 20 years, and some may also develop liver cancer within this timeframe. Immunocompromised patients (especially kidney transplant patients) can develop severe liver injury, a condition known as fibrosing cholestatic hepatitis, leading to liver failure and death. Current antiviral medicines can cure approximately 90% of HCV infections.

1.6 HCV infection is diagnosed in two steps:

a. Screening for anti-HCV antibodies with a serological test identifies people who have been infected with the virus.

b. If the test is positive for anti-HCV antibodies, a nucleic acid test for HCV RNA is needed to confirm HCV infection. About 15 – 45% of people infected with HCV spontaneously clear the infection by a strong immune response without the need for treatment. Although no longer infected, they will still test positive for anti-HCV antibodies.

1.7 Due to the weakening of their immune system, the antibody test may not be as accurate for certain groups of persons (e.g. kidney transplant patients on immunosuppressant medications), and directly using the HCV RNA test is more appropriate. Aligned with international best practices, SGH switched from using the HCV antibody test to the more sensitive HCV RNA test in 2014 for its renal patients.

1.8 However, both the HCV antibody and RNA blood tests cannot differentiate between acute and chronic HCV infections. To do so, correlation with clinical findings and other laboratory results is required. Importance is placed on the detection of acute HCV cases so as to ensure that these newly diagnosed cases are not part of an outbreak of acute HCV.

1.9 An outbreak of infectious diseases is defined by the World Health Organisation as the occurrence of cases in excess of what would normally be expected in a defined location or season. For HCV, the US Centres of Disease Control and Prevention (US CDC) used a threshold of two cases in its analysis of HCV outbreaks in healthcare facilities, explaining that outbreak-associated infections are defined as those with epidemiological evidence supporting healthcare related spread.

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1.10 In the United States, the US CDC received reports of 22 Hepatitis C outbreaks in healthcare facilities from 2008 to 2014. One outbreak involved eight cases infected in a haemodialysis facility from 2007 to 2009 but was only discovered when an audit was carried out in 2009. All eight cases did not display symptoms and there were no focal sources identified for the outbreak other than possible breaches in infection control practices. Another comprehensive review in 2015 looked at HCV outbreaks involving dialysis centres. It showed that the transmissions were commonly due to sharing of contaminated haemodialysis machines, use of multidose medicine vials, breaches in environmental cleaning and disinfection practices, and failures in medication preparation and administration practices. However, the exact mechanisms of transmission of HCV often could not be fully ascertained in the facilities where outbreaks occurred.

1.11 Another characteristic of HCV is its resilience and stability in the environment. It was demonstrated in a controlled laboratory experiment that HCV infectivity in a liquid environment was detectable for up to 5 months at lower temperatures (4°C). Viral infectivity on inanimate surfaces has been shown to be detectable from between 5 days to 6 weeks. HCV has also been detected in dried blood spots on surfaces in the environment for up to one year.

**Hepatitis C Outbreak in SGH**

1.12 From between late April to end May 2015, the Renal Unit of SGH noticed an increase in the number of positive results on HCV RNA tests. In early June, there were five cases of newly diagnosed HCV infections in the ward within the space of a few weeks, as compared to an average of two to four cases per year among SGH’s pool of renal transplant patients. Recognising this unusually high number of HCV infections, the Renal Unit conducted a check of the Dialysis Centre in mid-May. Thereafter, the Infection Control Unit of SGH was contacted on 3 June 2015 to investigate a potential outbreak. In the meantime, clinicians performed HCV tests for all patients in the Renal Ward whose liver function tests showed abnormal values. This led to the discovery of more cases.

1.13 Based on the review of the infection control team, measures including reinforced hand hygiene amongst the medical staff, use of disposable kidney dishes;
and replacing multi-dose vials of medication with single-use vials were implemented in Ward 67 and the hospital by 24 June 2015.

1.14 There are many sub-types of Hepatitis C viruses. To establish whether cases with HCV in the Renal Unit were infected by the same strain, viral genetic tests (also called phylogenetic studies) were performed by SGH in July 2015. Results from these tests showed that the HCV strains of all infected patients were closely related, further confirming the presence of an outbreak.

1.15 By 13 August 2015, a total of 21 patients who had been admitted to Ward 64A or Ward 67 from April to June 2015 were found to have had HCV infection within the same cluster. (Patients from Ward 64A were moved to Ward 67 when Ward 64A was closed for renovations between 6 April and 28 August).

1.16 SGH related the findings of this unusually large cluster of HCV patients to MOH on 31 August and presented to the Director of Medical Services (DMS) on 3 September 2015. Following discussions and instructions by the DMS, SGH convened two inquiries - (i) a Medical Review Committee (MRC) to review the seven death cases that had occurred by end-August, and (ii) a Quality Assurance Review Committee (QAC) to review the workflow processes in the areas in SGH where the infected patients had received treatment or medical procedures. The MRC was chaired by Professor Teo Eng Kiong, Chairman Medical Board of Changi General Hospital and a specialist in liver diseases, and met on 9 September. MOH appointed Dr Serena Koh, a Deputy Director in its Clinical Quality, Performance and Technology Division to be a member of the QAC, which met on 23 September.

1.17 SGH submitted their final report to MOH on 24 September and briefed the Minister for Health on 25 September 2015.

The Independent Review Committee

1.18 Following the briefing by SGH, Minister instructed that an independent review committee be convened to provide an objective and critical review of SGH’s investigations, findings and actions. This was with the intent of providing assurance that measures carried out were sufficient and to glean learning points for the wider healthcare system. In particular, the Independent Review Committee (IRC) was tasked to ascertain if all possible measures had been taken to identify possible points of infection control breaches, and to remedy any weak points in the overall workflow with regards to infection control. The IRC was to also determine if there were gaps in the process, including the timeliness of SGH’s response, the reporting of crucial information both within SGH and MOH, and whether there were areas that needed to be tightened and improved upon, such as safety protocols and escalation of information.

Appointment and Constitution of the IRC

1.19 The IRC was chaired by Professor Leo Yee Sin and was appointed on 28 September 2015. The committee comprised experienced clinicians from different disciplines, including Hepatology, Renal medicine, Infection Control, Nursing, and Quality Improvement and Process Audit. (Table 1.1)
Table 1.1: Composition of the Independent Review Committee

<table>
<thead>
<tr>
<th>Member</th>
<th>Designation</th>
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</thead>
<tbody>
<tr>
<td>Prof Leo Yee Sin (Chairman</td>
<td>Director (Institute of Infectious Diseases &amp; Epidemiology)</td>
</tr>
<tr>
<td>of Committee)</td>
<td>Clinical Director (Communicable Disease Centre)</td>
</tr>
<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
</tr>
<tr>
<td>Ms Paulin Koh</td>
<td>Chief Nurse</td>
</tr>
<tr>
<td></td>
<td>Changi General Hospital</td>
</tr>
<tr>
<td>Dr Titus Lau</td>
<td>Senior Consultant, Division of Nephrology</td>
</tr>
<tr>
<td></td>
<td>National University Hospital</td>
</tr>
<tr>
<td>Prof Lim Seng Gee</td>
<td>Senior Consultant, Division of Gastroenterology &amp; Hepatology, Department of Medicine</td>
</tr>
<tr>
<td></td>
<td>National University Hospital</td>
</tr>
<tr>
<td>A/Prof Helen Oh</td>
<td>Head, Infectious Diseases</td>
</tr>
<tr>
<td></td>
<td>Changi General Hospital</td>
</tr>
<tr>
<td>A/Prof Quek Swee Chye</td>
<td>Deputy Chairman of Medical Board</td>
</tr>
<tr>
<td></td>
<td>National University Hospital</td>
</tr>
<tr>
<td>Dr Jeffery Cutter</td>
<td>Director, Communicable Diseases Division</td>
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<td></td>
<td>Ministry of Health</td>
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</tbody>
</table>

Terms of Reference

1.20 The IRC’s Terms of Reference were as follows:

a. To provide an independent, objective and critical review of SGH’s report, and seek to ascertain if all possible measures had been taken to:

   (i) Identify the possible points of infection control breach;

   (ii) Remedy any weak points in the overall workflow particularly with regard to infection control;

b. To reasonably investigate any activity within its Terms of Reference, which will include but is not limited to the following:

   (i) Review the work and findings of the two Committees convened by SGH to investigate this Cluster (i.e. the Medical Review Committee and Quality Assurance Review Committee);

   (ii) Interview any staff member to clarify issues; and

   (iii) Perform site inspections at SGH.

Methodology and Approach of Investigation

1.21 The IRC took to the task of investigating the outbreak along basic principles of an outbreak investigation (Annex A). The scope and activities included the formation
of an investigation team and resources, establishing the existence and extent of an outbreak, verifying the diagnosis, constructing case definitions, finding cases systematically, performing descriptive epidemiology and developing hypotheses, evaluating those hypotheses, communicating findings to recommend and implement control measures, and recommending forward surveillance planning. As timeliness of response is critical in disease outbreaks, the IRC also reviewed the timeliness and overall responses of the outbreak within the healthcare system. As this involved reviewing MOH’s actions and decisions in response to the outbreak, IRC member - Dr Jeffery Cutter (who is the Director of Communicable Diseases Division in MOH) - recused himself from this series of reviews undertaken by the committee.

**Formation of Investigation Teams within the Committee**

1.22 To conduct the investigations, the Chairman of the IRC organised the committee into three functional teams:

   a. **Epidemiology Team** – This team was to primarily focus on epidemiological investigations, determining the extent of outbreak, conducting case finding, as well as formulating and testing hypotheses. This team was supported by an assigned group of researchers specialising in the field of genetic evolution and bioinformatics. The researchers’ role was to study the relatedness of cases through phylogenetic mapping and the direction of transmission within the cluster.

   b. **Case Review Team** – This team was to comprehensively review all HCV cases identified during the outbreak to determine if they were acute in nature; review the report by the SGH Medical Review Committee on fatal cases that had been infected with HCV during the outbreak, as well as other deaths among patients who were admitted to the affected wards during the outbreak period to supplement case-finding efforts.

   c. **Quality Assurance Team** – The team was to review clinical processes and practices that might have led to gaps in infection control practices, and to recommend infection control practices.

1.23 Concurrently, the IRC conducted an assessment of the healthcare system’s response to the outbreak. This involved interviewing relevant parties in MOH, SingHealth and SGH involved in the outbreak, requesting documentation on their key actions, and reviewing correspondences between the different parties.

**Appointment of Resource Persons and Experts**

1.24 The Chairman of the IRC appointed a team of resource persons to assist the committee in their investigative work and review. These persons had expertise in the areas of clinical epidemiology, data analysis, biostatistics, infection control, risk management, and organisational leadership. These resource persons, together with their areas of expertise, are listed in Table 1.2.
<table>
<thead>
<tr>
<th>Resource Person</th>
<th>Designation</th>
<th>Area of Expertise</th>
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<tbody>
<tr>
<td>A/Prof Angela Chow</td>
<td>Head, Department of Clinical Epidemiology</td>
<td>Clinical Epidemiology</td>
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<td></td>
<td>Institute of Infectious Disease and Epidemiology</td>
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<td></td>
<td>Tan Tock Seng Hospital</td>
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<tr>
<td>Asst Professor Mark Chen</td>
<td>Assistant Professor, Saw Swee Hock School of Public Health</td>
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<tr>
<td></td>
<td>National University of Singapore</td>
<td></td>
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<tr>
<td>Asst Prof Wong Chia Siong</td>
<td>Consultant, Department of Clinical Epidemiology</td>
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<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
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<tr>
<td>Dr Win Mar Kyaw</td>
<td>Senior Epidemiologist, Department of Clinical Epidemiology</td>
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<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
<td></td>
</tr>
<tr>
<td>Ms Adriana Tan</td>
<td>Data Analyst, Department of Clinical Epidemiology</td>
<td>Data analyst supporting epidemiology investigation</td>
</tr>
<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
<td></td>
</tr>
<tr>
<td>Mr Joshua Wong</td>
<td>Biostatistician, Department of Clinical Epidemiology</td>
<td>Biostatistician supporting case control study</td>
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<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
<td></td>
</tr>
<tr>
<td>Dr Tan Hui Ling</td>
<td>Assistant Chairman Medical Board, (Clinical Quality and Audit)</td>
<td>Quality Assurance Audit</td>
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<tr>
<td></td>
<td>Tan Tock Seng Hospital</td>
<td></td>
</tr>
<tr>
<td>Ms Sharon Salmon</td>
<td>Assistant Director of Nursing Administration</td>
<td>Infection Control Expert to assist in Quality Assurance Audit</td>
</tr>
<tr>
<td></td>
<td>National University Hospital</td>
<td></td>
</tr>
<tr>
<td>Dr Richard Guan</td>
<td>Hepatologist, Medical Clinic One Mount Elizabeth Medical Centre</td>
<td>To assist in clinical case reviews</td>
</tr>
<tr>
<td>A/Prof Dan Yock Young</td>
<td>Senior Consultant, Division of Gastroenterology &amp; Hepatology</td>
<td></td>
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<tr>
<td></td>
<td>National University Hospital</td>
<td></td>
</tr>
<tr>
<td>Dr Chong Chern Hao</td>
<td>Senior Resident</td>
<td></td>
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<tr>
<td></td>
<td>National University Hospital</td>
<td></td>
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<tr>
<td>Dr Mark Muthiah</td>
<td>Senior Resident</td>
<td></td>
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<tr>
<td></td>
<td>National University Hospital</td>
<td></td>
</tr>
<tr>
<td>Prof Tan Chorh Chuan</td>
<td>President, National University of Singapore</td>
<td>To advise the committee on matters pertaining to reporting, surveillance and response workflows and structures</td>
</tr>
<tr>
<td>Prof Chee Yam Cheng</td>
<td>President, National Healthcare Group College</td>
<td></td>
</tr>
<tr>
<td>Mr Ong Pang Thye</td>
<td>Deputy Managing Partner, KPMG</td>
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</table>
1.25 The IRC also appointed two teams of international experts to strengthen its capabilities and to provide additional technical and scientific input to the committee’s review. The two teams were from the US CDC and Johns Hopkins University. The international experts worked closely with the Review Committee, including attending committee meetings, as well as conducting site visits and interviews with the local team. (Please see Table 1.3 for details of the international experts and Annex B for their curriculum vitae)

Table 1.3: International Experts

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Name</th>
<th>Designation</th>
</tr>
</thead>
</table>
| Centers for Disease Control and Prevention | Dr Scott Dewey Holmberg  
(Team Lead)          | Chief, Epidemiology and Surveillance Branch, Division of Viral Hepatitis, National Center for HIV, Hepatitis, STD, and TB Prevention |
|                                    | Dr Amanda Beaudoin          | Veterinary Medical Officer, International Health Quality Team, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention |
| Johns Hopkins University           | Prof Trish Perl  
(Team Lead)          | Professor of Medicine and Pathology, School of Medicine, Johns Hopkins University |
|                                    | Ms JoEllen Harris           | Director, Epidemiology and Infection Prevention Program, Johns Hopkins Health System |
CHAPTER 2
Investigation of the Outbreak

2.1 The Independent Review Committee’s investigative work into the HCV cluster was based on the basic principles of outbreak investigation as detailed in paragraph 1.21 above.

Confirming the Cluster and Determining the Extent of Transmission

2.2 At the onset of investigative work by the IRC on 5 October 2015, SGH had already identified a cluster of 22 cases that were linked epidemiologically in time and place. As such, the presence of an outbreak of common source was quickly established. The time period appeared to be from early April to early August 2015. The location was the Renal Ward that originally operated in Ward 64A, which subsequently moved to Ward 67 for renovation on 6 April 2015, and back to Ward 64A on 28 August 2015. Laboratory findings by SGH (subsequently confirmed by A*STAR laboratory) had revealed a common strain of genotype 1b HCV.

2.3 To ascertain the extent of spread beyond the implicated wards, the IRC focused on 4 areas:

a. To determine if there was an increased rate of HCV during the period, as detected by SGH laboratory (which provides HCV RNA testing services to multiple other institutions in Singapore), 5 years’ worth of records from 2010 to 2015 were reviewed. This did not show significant increases above baseline. (Figure 2.1) Despite an increase in the number of HCV RNA tests over the years, the absolute number of HCV RNA positive cases did not increase. In addition, SGH laboratory analysed all HCV RNA positive samples from January to June 2015 and did not find any other cases belonging to the same HCV strain.

Figure 2.1: Monthly New HCV-Positive and Total HCV RNA Tests in SGH from 2010 to 2015

*Data includes only samples collected up to 15 Oct 2015
b. To determine if there was an under-diagnosis of HCV at SGH, random residual samples of 19 patients in other wards at SGH with abnormal liver function tests between May and June 2015 were tested for HCV. A total of 18 samples had sufficient amounts for testing and all were negative for HCV RNA.

c. To determine if the HCV cluster extended to other renal patients in the community, checks were done on HCV screening test results of patients attending dialysis centres. There was no detectable increase of HCV cases among major renal dialysis centres (e.g. National Kidney Foundation, Kidney Dialysis Foundation)\textsuperscript{12}. Four patients on haemodialysis who were reported by the two largest voluntary welfare organisation (VWO) dialysis providers to have had recent change in their HCV test status from negative to positive in 2015 were reviewed. These strains were not linked to the SGH cluster.

d. To determine if the HCV cluster extended beyond SGH, a check with the MOH national notification system showed no increases in the number of HCV cases outside of the SGH cluster in 2015. There were no significant deviations in national monthly baseline rates of HCV notifications from January 2013 to September 2015, and no clusters of acute HCV cases among dialysis centres when reviewing data from 2008 onwards from the National Renal Registry. However, the IRC also recognised the underlying limitations of incomplete notifications from doctors and laboratories to MOH. [See also paragraph 3.20 on MOH's notifications and surveillance]

2.4 The above findings suggested that the HCV outbreak in SGH was localised and limited to Wards 64A and 67.

The Cluster of HCV Cases

Case Finding from Affected Wards

2.5 For the purposes of searching for any earlier and later HCV cases (i.e. case finding), a case was defined as a patient who had been admitted to Ward 64A and/or Ward 67 from between January and June 2015 (and later extended to September 2015) and tested positive for HCV RNA.

2.6 At the start of IRC’s work, patients who were admitted from 1 January to 30 June 2015 were already being recalled for screening for HCV infection by SGH using HCV antibody and HCV RNA tests. This period was chosen by SGH on the basis that the vast majority of infected patients would present with positive results by 10 to 12 weeks after infection. SGH had identified a total of 678 patients for HCV testing, and picked up three additional patients with HCV, who were then referred to specialists at SGH for further management.

\textsuperscript{12} Renal patients on dialysis routinely undergo HCV testing every 6 months, usually by dialysis centres.
2.7 During the course of investigation, IRC noted that the latest HCV infected case could have acquired infection in late July in Ward 67. This finding prompted the IRC to recommend further extension of screening from 1 July to 30 September 2015.

2.8 This would also provide adequate assessment that infection control measures implemented by SGH in the month of June were effective in stemming HCV infections as well as ensuring stability in infection prevention and control measures after the migration from Ward 67 back to Ward 64A. For this period, SGH identified a further 326 patients for HCV testing. There were no new HCV cases identified during this second recall. This indicated that there was no evidence of further transmission in the month of September after the move of patients and staff from Ward 67 back to Ward 64A on 28 August 2015.

2.9 To supplement case-finding efforts, the Case Review Team examined the case records of 74 cases, admitted to Ward 64A and Ward 67 from 1 January to 30 September 2015, who had since passed away according to the National Electronic Health Records (NEHR). An additional 32 cases who had passed away were picked up by SGH during recall screening. Factors to evaluate the contribution of HCV to the death of patients were also developed. (Details can be found in Annex C). Testing of residual blood samples for HCV, if available, was conducted for cases with signs of liver dysfunction. Five samples were available for testing and there were no new cases of HCV detected in this group.

2.10 In summary, as of 20 November 2015, a total of 925 patients had been contacted by SGH (92% of the 1004 identified patients). Of these, three patients had been tested positive for HCV infection within the same cluster, and another one patient who was not in the cluster. A summary of patients screened is as shown in Table 2.1. This brought the total number of patients in the HCV cluster to 25 with HCV RNA positive tests identified between March and October 2015.

Table 2.1: Screening of Patients by SGH for HCV

<table>
<thead>
<tr>
<th>Number of patients identified by SGH for screening^</th>
<th>Jan to Jun 2015</th>
<th>Jul to Sep 2015</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Screened</td>
<td>678</td>
<td>326</td>
<td>1004</td>
</tr>
<tr>
<td>Results of Patients who have been Screened</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C negative</td>
<td>617</td>
<td>304</td>
<td>921</td>
</tr>
<tr>
<td>Hepatitis C positive</td>
<td>4^</td>
<td>0</td>
<td>4^</td>
</tr>
<tr>
<td>Patients Not Screened</td>
<td>57</td>
<td>22</td>
<td>79</td>
</tr>
<tr>
<td>Reasons for not being Screened</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passed Away (Updated during recall screening)</td>
<td>31</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td>Deferred Appointments</td>
<td>6</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Uncontactable</td>
<td>9</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Declined screening</td>
<td>11</td>
<td>3</td>
<td>14</td>
</tr>
</tbody>
</table>

^ Excludes 74 cases that had since passed away according to NEHR
^ One patient was HCV of a different strain / genotype
**Case Definition and Case Review for Acute Hepatitis C**

2.11 At the same time, the Case Review Team embarked on reviewing all 25 HCV infected cases within the outbreak cluster. This was to determine if cases were ‘acute’ (i.e. recently infected) or ‘chronic’ (i.e. infected for a long period of time) cases. If found, chronic cases may point towards a possible source for the cluster of acute cases. For the definition of an acute case of HCV, the Case Review Team adopted case definitions used by the US CDC\(^{13}\). The process included the review of clinical case notes and laboratory test results, following which cases were classified into ‘Definite’, ‘Likely’, ‘Suspected’ and ‘Uncertain’ for HCV. Further details on the classification of HCV as acute or chronic, can be found in Annex C.

2.12 To narrow the period of infection for cases, residual blood samples- if available- were tested. These samples were taken at various points in time before cases became HCV RNA positive. Results were then correlated with clinical presentations and other laboratory markers (e.g. liver function tests). The purpose was to determine if there was additional evidence for acute infections. Of the 25 cases, 22 fulfilled the strict criteria of “Likely” or “Definite” acute HCV infections\(^{14}\). For the remaining three cases, more definite conclusions regarding whether the infection was acute or chronic could not be reached due to the lack of additional information.

2.13 However, in view of the close epidemiological links (admission to the affected wards during the period of spread), as well as tight clustering of strains in the laboratory analysis [see also paragraph 2.20 on phylogenetic analysis], all 25 cases were concluded to be part of the same cluster, including the three cases that could not be classified as acute cases.

**Description of Cases from the Cluster**

2.14 The average age of the 25 cases was 51 years old, with an almost equal distribution between genders (48% male). 20 patients (80%) had received a kidney transplant in the past (ranging from as early as 1992 to 2015) and were on post-transplant medications which suppressed their immune systems. Of the 20, 17 cases (85%) had undergone kidney transplantation in Singapore. 12 cases (48%) had undergone haemodialysis during their admission - of these, nine cases (36%) were on haemodialysis outside of SGH prior to their admission. Three patients (8%) neither had a kidney transplant nor were on haemodialysis. Diabetes mellitus was the most common concomitant condition (with 40% of cases having this condition). Of the 25 cases, eight cases had passed away. These were reviewed by the Case Review Team, who concluded that HCV was a likely contributory factor to the death of seven of the cases.

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\(^{14}\) These 22 cases are not the same as the initial 22 cases picked up by SGH. A line list of patients will not be published to maintain patient confidentiality.
Summary of the Cluster

2.15 In all, the HCV cluster comprised 25 patients, most of whom had received a kidney transplant before and were more susceptible to infections. There were no cases of chronic HCV infections identified.

The Sequence of HCV Infections

Date of Diagnosis of HCV Cases by SGH

2.16 The first two HCV cases diagnosed by SGH were in late April 2015, and the highest number of cases diagnosed was in late June 2015. The line chart in Figure 2.2 provides a picture of what SGH observed on the ground in terms of the number of cases detected over time.

Figure 2.2: Number of Cases Based on Date of Diagnosis by SGH

Epidemic Chart

2.17 In October and November 2015, through further HCV RNA testing of these diagnosed cases’ residual blood samples (where available), the IRC was able to construct an epidemic curve based on the earliest available HCV RNA positive test results. This is presented as a bar chart in Figure 2.3. Owing to the inherent nature of HCV, infected persons may not show any clinical symptoms for long periods of time, leading to delayed testing and diagnosis. As a result, the date of diagnosis or detection often does not correlate well with the date of infection. The latter can be difficult to pin down unless earlier residual blood samples are available for HCV testing, to trace back the date of infection as far as possible. Two cases that were detected in October 2015 did not have residual blood samples available for testing.
Figure 2.3: Epidemic Curve based on Date of Diagnosis (Line Chart) and Earliest Available HCV RNA Positive Test Results (Bar Chart)

Possible Windows of Infection

2.18 To better ascertain when cases might have been infected, “windows” of infection in Wards 64A and 67 for each case were determined. These are time periods where the acquisition of HCV infection was deemed to be most likely. The windows were based on the following parameters:

a. Period of change in HCV RNA status (from negative to positive results) where available;

b. Period of change in liver function tests (from normal to abnormal results) where available;

c. Known incubation period of HCV based on existing literature (i.e. duration from infection to change in HCV RNA status and liver function tests); and

d. Period of exposure to Wards 64A and 67.

2.19 Possible windows of infection varied among the 25 cases, and ranged from 5 to 47 days. The start date of the first window was estimated to be 25 February 2015 and the end date of the last window was estimated to be 4 August 2015, as shown in Figure 2.4 below. Taking into account the shift from Ward 64A to Ward 67 on 6 April 2015, there were three HCV cases who were likely to have been infected in Ward 64A (including the first case), with the majority of cases infected in Ward 67.
Figure 2.4: Possible Windows of Infection for Patients in HCV Cluster\textsuperscript{15}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Possible Windows of Infection for Patients in HCV Cluster}
\end{figure}

\begin{table}
\begin{tabular}{|c|c|c|c|c|c|c|c|}
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\end{tabular}
\end{table}

\textbf{Legend:}
- Period of Infection ("Window of Infection") for a Case of HCV
- Ends of the bars represent the start and end dates of each window
- Date of Reinforced Infection Control Measures by SGH
- Dates of Shifts in Wards

\textbf{Phylogenetic Analysis}

2.20 Phylogenetic analysis was performed by the laboratories at A*STAR and Duke-NUS, showing highly similar HCV strains among all 25 patients identified. Samples were also sent to US CDC laboratories for corroboration and further testing. Both local and US CDC laboratories reported the same results - that the cluster strain in both wards were not related to strains from other known HCV patients at SGH in 2015, and only distantly related to known local strains.

2.21 The team also found that genetic material of HCV strains could be divided into three groups (Figure 2.5). Two of these groups (Groups B and C) each comprised HCV strains with highly similar genetic material. The third group (Group A) comprised HCV strains with a mix of genetic material from Groups B and C. Group A strains were also noted to be from the first infected cases in the cluster. These findings suggested that HCV genetic material from Group A may have acted as a precursor to the genetic material in Groups B and C. This corroborated with the windows of infection are of different lengths depending on the amount of information available - the more information available, the narrower the window of infection. Cases are ordered according to the earliest possible date of infection, and not by order of diagnosis or order of reporting.

\textsuperscript{15}
epidemiological findings regarding the sequence of infection among cases. Further
details on phylogenetic analysis can be found in Annex D)

**Figure 2.5**: Grouping of Genetic Material in Phylogenetic Analysis

The **Earliest Infected Case**

2.22 The IRC attempted to identify the earliest infected case based on the above
epidemiological investigations. It was identified that this was likely to have been a
case of a kidney transplant patient, not previously diagnosed with HCV, and whose
first admission to SGH in 2015 was in early March to Ward 64A. The case was
admitted again in mid-March. Residual blood samples from mid-March showed that
HCV RNA test was positive with a high viral load (6.58 log IU/mL)\(^{16}\). There were no
earlier residual blood samples available for HCV testing to be more definite
regarding the date of infection.

2.23 To search for the presence of any preceding cases, all patients admitted to
Ward 64A over the same period as the earliest infected case were extensively
screened and reviewed. There was no definitive evidence of other HCV cases during
the case’s first admission. It is uncertain as to where the earliest infected case had
acquired the infection from\(^{17}\).

\(^{16}\) Persons who are uninfected with HCV have “undetectable” viral loads. A viral load of 6.58 log
IU/mL indicates that in one milliliter of blood, the case had at least 1 million copies of the HCV virus.

\(^{17}\) The case was not the index case (i.e. first case picked up). It also cannot be conclusively attributed
to be the primary case (i.e. source of the cluster), since there was still a possibility that the case had
acquired the infection during the first admission in SGH. However, there was no definitive evidence of
other HCV cases during the earliest infected case’s stay in SGH.
2.24 In conclusion, epidemiological and phylogenetic analyses show the sequence of infection within the cluster. However, though extensive screening was conducted, the IRC could not find definitive evidence of any cases preceding the earliest infected case of the cluster.

**Layout of the Two Wards**

2.25 Ward 67 is divided into two sections, namely Section 67A and 67B. Section 67A comprised 20 single-bedded rooms, of which only 15 were in use. This section housed the most number of cases. All except one HCV case in the cluster had occupied single rooms in Ward 67 at some point in time from 6 April to 28 August 2015. Maps showing the locations where HCV patients had ever stayed (“Spot maps”) for Wards 64A and 67 are shown in Figures 2.6 and 2.7.

2.26 In summary, Ward 67 has a long layout with the preparation room at the end of the ward. In comparison, Ward 64A has a more compact layout with the preparation room in the middle of the ward. This may have influenced the workflow of staff in the wards. [See also paragraph 2.35 on Breaches in Infection Control]

**Figure 2.6:** Spot Map of HCV Cases in Ward 64A (1 March – 6 April 2015) - Showing the Bed Locations of the 8 Cases that were in the Ward over this Period

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![Spot Map of HCV Cases in Ward 64A](image-url)
Figure 2.7: Spot Map of HCV Cases in Ward 67 (6 April – 28 August 2015) - Showing the Bed Locations of the 25 Cases that were in the Ward over this Period

Hypotheses Generation and Testing

Hypotheses Generated

2.27 The IRC did a critical review of the literature, taking into consideration the circumstances of this outbreak. Four specific hypotheses were to be tested. These were:

a. Drug diversion – Illegal use of controlled medications (e.g. narcotics) originally prescribed for patients, may have been diverted by an individual in the system for personal use.

b. Intentional harm – Malicious acts intended to cause harm to patients for various personal reasons. This could be a known case of HCV deliberately contaminating injectables or injecting contaminated products to patients.

c. Batch product contamination (e.g. contamination of product batches during the production process)

d. Breaches in infection control practices – Failure or non-adherence to infection prevention and control measures.
Evaluating the Hypotheses

2.28 The hypotheses of drug diversion, intentional harm and product contamination were ruled out in the following manner:

I. Drug Diversion

2.29 SGH staff who had come into contact with patients in these two wards were screened for HCV to rule out diversion and intentional harm. All 319 nurses, doctors and renal coordinators who had patient contact in Wards 64A and 67 were accounted for, including those who had since resigned or transferred out of SGH. All allied health staff and pharmacists in SGH who had contact with patients in the two wards were also screened, and all were negative for HCV. For this group, staff who had left the hospital were invited to return for screening. Of those who did so, all were negative for HCV.

2.30 In addition to the above, the hypothesis of drug diversion was also deemed unlikely as only one case was prescribed narcotics during admissions in 2015 prior to infection with HCV. All controlled drugs in both wards were also accounted for.

II. Intentional Harm

2.31 In addition to the absence of findings from screening of staff, the hypothesis of intentional harm was further explored with the assistance of the Criminal Investigations Department (CID) of the Singapore Police Force. However, no supporting evidence for this hypothesis was found.

III. Batch Product Contamination

2.32 The likelihood of the outbreak arising from a contaminated batch product was excluded as there were no common products used by all cases with the exception of 0.9% saline solution ("normal saline"). There were no leftover batches from the period that patients were infected for HCV testing. However, saline solution is used widely throughout hospitals and a wider spread of cases across wards would be expected if these solutions were contaminated. Nevertheless, 10 bottles of normal saline were randomly selected from Ward 67, and all samples tested negative for HCV RNA.

2.33 Not all affected patients received blood products during their period of admission. For those who did, the CID had checked with the Blood Bank at HSA and verified that blood products given to these patients had been screened negative for HCV. The blood donors of these products did not test positive in HCV antibody status nor HCV RNA testing.

2.34 In conclusion, there was no evidence of drug diversion, intentional harm or batch product contamination as the cause for spread of HCV. The remaining hypothesis of breaches in infection control was evaluated.
IV. Breaches in Infection Control

2.35 This hypothesis was tested through the work of the Quality Assurance Team, environmental testing and the hypothesis was substantiated by detailed epidemiological analyses.

2.36 The Quality Assurance (QA) Team made a total of 18 visits to SGH from 15 October to 11 November 2015 to conduct site visits and interviews as well as to observe demonstrations of procedures by staff. The purpose of these visits was to review clinical processes and practices for areas of improvement with respect to infection control, and whether breaches in these practices could have contributed to the outbreak. The composition, objectives and methodology, including details of visits of the QA Team are shown in Annex E.

Findings Related to Infection Control

Overall Findings

2.37 The key findings related to infection control were:

a. While there were established procedures for blood taking, administering of intravenous medication, waste disposal and cleaning of equipment and contact surfaces, some staff were observed to have deviated from standards. These deviations could have led to cross-contamination of equipment (e.g. computerised medical carts and trolleys) and contamination of contact surfaces. These gaps in infection control practices potentially opened up avenues for infection transmission.

b. There were inefficiencies in workflow designs in affected wards. The workflow process issues opened up potential for modified infection control practices amongst ward staff.

Specific Findings in Affected Wards

I. Positive Findings

2.38 There were several commendable practices by the SGH staff which were observed by the QA Team. These included:

a. Consistent checking of patients’ identity (by checking two patient identifiers);

b. Verification of tasks;

c. Ensuring patient’s privacy, which was done even in simulations; and

d. A clear structure for skills development and training of nursing staff. In allocation of workload in SGH, nurses had been trained to take on a significant share of duties normally performed by junior doctors (e.g. giving first dose of IV medications, IV cannulation, venepuncture).
II. Gaps in Infection Control Practices

2.39 Hospital wards currently use computerised medical carts during procedures such as blood sampling and administration of medications. Figure 2.8 shows a picture of a computerised medical cart used for blood taking in Ward 67.

**Figure 2.8:** Computerised Medical Cart used for Blood Taking in Ward 67

2.40 Stains were found on the computerised medical carts, procedure trolleys and on the wall in the preparation room as well as some patient rooms in Wards 64A and 67. CID also confirmed that the stains they discovered on computerised medical carts, procedure trolley, glucometer, and an injection tray in preparation room during a site visit on 28 October 2015 were blood stains. Figure 2.9 shows a picture of an example of a procedure trolley used in the wards.

**Figure 2.9:** Procedure Trolley
2.41 The computerised medical carts and procedure trolleys can be possible sources of infection transmission as they are moved from patient to patient. Attention must be paid to the thorough cleaning and disinfection of these carts and trolleys.

2.42 During the demonstrations of procedures, it was observed that the computerised medical carts were not adequately cleaned after the procedures.

2.43 The computerised medical carts and procedure trolleys, after being used in procedures (and potentially contaminated), were also pushed into the preparation room, which should be an area designated as ‘clean’. This was done before the cleaning of medical carts and procedure trolleys. This practice creates opportunities for cross-contamination as medications and clean supplies required for procedures are prepared in the preparation room.

2.44 Ward staff were also observed to remove the cap of a patient’s intravenous (IV) cannula to inject medication instead of using a side port. Such a practice poses a risk of the patient’s blood flowing out through the IV cannula, leading to environmental contamination and transmission of infection, as well as exposure of the patient to contaminants entering his or her bloodstream.

2.45 There was inadequate hand hygiene observed among some staff when they were performing procedures.

III. Inefficiency of Workflows

2.46 During the ward demonstrations of procedures, it was noted that compliance with infection control practices was made more challenging due to inefficiencies in the design of work processes, which made it plausible that ward staff might have chosen to modify their practices in order to complete their tasks. This possibility was confirmed by CID’s findings during their investigation. This may explain some of the gaps in infection control practices observed.

2.47 Inefficiencies in work flow design were likely compounded by the move of the Renal Wards from Ward 64A to Ward 67 and the marked differences in the layout of the wards. For instance, the walking distances between the preparation room and patient beds were longer in Ward 67 as compared to Ward 64A.

Environmental Sampling

2.48 In order to ascertain whether the observed contamination of the computerised medical carts and inadequate environmental cleaning were related to the HCV cluster, environmental samples were collected for testing for HCV RNA in Ward 67.

2.49 On 2 November 2015, a total of 54 samples from various sites, including what appeared to be small blood stains on computerised medical carts, procedure trolleys and on the wall of the preparation room in Ward 67, were collected by NUH molecular diagnostic lab on behalf of the IRC for HCV RNA testing\(^\text{18}\). One sample,

\(^{18}\) The testing methodology used was the AmpliScreen HCV v2.0 test (Roche Diagnostics). This test is a well-established, qualitative test used for direct detection of HCV RNA in serum. This was modified for environmental testing.
taken from the wall of the preparation room in Ward 67, tested positive for HCV RNA. This was an area where a stationary trolley, which had been used for preparation of intravenous medications (a ‘clean’ procedure), had been parked. Figure 2.10 shows the layout of Ward 67 [also previously shown in Figure 2.7]. The location of the preparation room, where the HCV positive sample had been taken from, is marked with a red star.

**Figure 2.10:** Ward Layout of Ward 67 showing the HCV RNA Positive Blood Spot

2.50 In conclusion, there were gaps observed in infection prevention and control practices that likely contributed to the HCV outbreak.

**Assessing Factors Associated with Hepatitis C Infections**

2.51 To search for common factors that were associated with HCV infections amongst patients, the Epidemiology Team conducted a study comparing infected patients with non-infected patients. The study was limited to Ward 67 as the majority of the affected patients became infected in this ward, and the selected timeframe was determined based on the period that the ward was in operation (6 April to 28 August 2015). A total of 22 patients infected with HCV positive patients (HCV+) and a sample of 78 HCV negative patients (HCV-) were included in the analysis.
2.52 Key findings from the study were as follows:

a. HCV+ patients stayed in the wards longer than HCV- patients.

b. After having taken into consideration the longer stay in the wards,

   (i) HCV+ patients had received more intravenous medications than HCV- patients. In particular, they were more likely to have received intravenous medication intermittently; and

   (ii) HCV+ patients had undergone more intravenous blood-taking than HCV- patients.\(^\text{19}\).

2.53 The plausibility of multi-dose multi-patient vials contributing to the outbreak was examined closely by the IRC. For the vials in use in Wards 64A and 67, only 13 cases (52%) were exposed to at least one of these medications. Of these, three cases received exposure to two or more of such medications. Eight cases (32%) were given insulin, seven cases (28%) were given sodium bicarbonate and one case was given heparin. Multi-dose medication alone cannot fully explain the transmission of HCV to all cases in this outbreak.

2.54 Internationally, there have been many reports of glucometers being a factor associated with spread of blood-borne infections. As a result, the IRC took a close interest in glucometer use in cases. Although in the above epidemiology study, we did not find the use of glucometers to be associated the infected cases, the IRC did note that in the course of CID investigations, the blood of one HCV positive case was detected on one of the glucometers in Ward 67.

2.55 In summary, patients who had received more intravenous procedures were more likely to be infected with HCV. Further results of the study can be found in Annex F.

**Conclusion of Investigative Findings on the HCV Outbreak**

2.56 SGH commenced investigations into the HCV cluster from mid-May 2015, and strengthen infection control measures (e.g., audits on hand hygiene, ceasing use of multi-dose medication vials) from early June 2015 onwards. There was also heightened awareness among staff on the need to guard against breaches in more general infection control precautions. These measures were instrumental in slowing the spread of HCV and there were no new cases detected after the move from Ward 67 to Ward 64A on 28 August until the end of September 2015 (end of extended period of screening requested by IRC).

\(^{19}\) This was based on a surrogate measure of the frequency of laboratory tests ordered for patients.
2.57 The IRC noted that, internationally, HCV outbreaks were hard to detect and investigations into HCV outbreaks often could not establish a definitive cause. In this case, the IRC concluded that the cluster of HCV cases was an unusual outbreak that was due to a combination of multiple overlapping factors:

a. The susceptible cases comprised mainly immunocompromised kidney transplant patients and the introduction of HCV (probably by a patient identified to be the earliest infected case) led to acute infections with extremely high quantities of virus in these patients.

b. All affected patients had many exposures to intravenous medications and/or laboratory tests that required blood taking, exacerbating the risks of HCV spread through gaps in infection control practices.

c. Gaps were identified in the two affected wards with regards to infection control practices (in particular processes involving intravenous procedures), environmental cleaning, and prevention of environmental contamination. These potentially facilitated HCV transmission in the two affected wards. Furthermore, the virus is resilient and can remain infective in blood stains for several weeks, thereby increasing the risk of transmission from such gaps.

d. The spread of HCV was highest during the period when staff and patients from Ward 64A were moved to Ward 67 (i.e. from 6 April to 28 August 2015). This was likely linked to changes in workflow patterns and processes in the new environment, which had a different layout from the one the staff were familiar with, thus further increasing the likelihood of the spread of HCV in this cluster.
CHAPTER 3
Assessment of System Response and Communications Relating to Outbreak

3.1 This chapter sets out the IRC’s assessment of the system response and communications relating to the HCV outbreak in SGH.20

Approach to Reviewing System Response and Communications

3.2 In reviewing the overall response to the HCV outbreak in SGH, the key objective of the IRC is to identify insufficiencies within the existing system, and make recommendations to improve current processes in terms of timeliness and comprehensiveness of response and actions.

3.3 In approaching this piece of work, the IRC set out to examine the organisational structure, roles and responsibilities of relevant parties in MOH, SingHealth, and SGH who were involved in the outbreak, and understand the considerations behind key decisions and actions during the outbreak. As part of the information gathering process, the IRC interviewed relevant parties in MOH, SingHealth and SGH who were involved in the outbreak, requested documentation on their key actions, and reviewed correspondences among the various parties.

Overview of IRC’s Findings

3.4 Early recognition of a disease outbreak is key to ensuring a timely response to manage and contain the outbreak. The early signals of a disease outbreak are typically picked up by ground staff who may sense that something is amiss, and/or by the surveillance system at the hospital or national level. As described in Chapter 1, the suspicion of a disease outbreak would trigger a series of actions which includes establishing the existence and extent of an outbreak, verifying the diagnosis, constructing case definitions, case finding, performing descriptive epidemiology, developing hypotheses and evaluating those hypotheses. While this is in progress, there is a need to strengthen general control measures such as infection control procedures, as well as consider and implement specific control measures arising from the findings of the outbreak investigation. During a disease outbreak, timely escalation to senior decision-makers is also important, depending on the nature of the outbreak, the assessment of the extent and severity, and the rate of

20 As MOH was also subject to this review, one of the IRC members, Dr Jeffery Cutter (Director, Communicable Diseases Division, Ministry of Health), recused himself from this part of the Committee’s work. In this aspect of work, the Committee was supported by three resource persons Professor Chee Yam Cheng, Senior Advisor to National Healthcare Group; Mr Ong Pang Thye, Deputy Managing Partner, KPMG; and Professor Tan Chorh Chuan, President of NUS. In view of their wide and varied expertise in academia, medicine, corporate governance and organisational leadership, their role was to provide guidance and work with the IRC, to evaluate the various parties’ responses to the incident.
progression. Escalation will ensure that appropriate decisions can be made in a timely manner and suitable resources can be mobilised to expedite outbreak investigation and containment.

3.5 The national system of surveillance and response is a robust system that works well for community outbreaks of infectious diseases e.g. air/droplet-borne diseases like Hand Foot and Mouth Disease (HFMD), vector-borne diseases like Dengue and Malaria, etc. The system also has well-established frameworks, which are familiar to healthcare workers, particularly in hospitals, to deal with emerging infectious diseases (EIDs) like Ebola and MERS-CoV.

3.6 For infections that are acquired within hospitals, the typical practice today is for hospitals to directly investigate, manage and contain the infections, regardless of whether the infections constitute an outbreak in the hospital. Hospitals would be most familiar with their own processes and can act swiftly to localise the infection and stop the transmission chain. MOH also requires hospitals to have an Infection Control Programme with an appointed infection control committee, as well as to document infection control activities and have written policies and guidelines to deal with any infection acquired or brought into the hospital. Hospitals therefore have established frameworks to deal with common healthcare-associated infections (HAIs) like Methicillin-resistant Staphylococcus Aureus (MRSA).

3.7 The HCV outbreak in SGH has highlighted a gap in the current system with regard to outbreaks of HAIs. As HCV is an unusual HAI and has characteristics that prevent it from being picked up easily by surveillance\(^{21}\), SGH did not recognise the presence and severity of the outbreak in a timely manner, and thus did not investigate and manage it optimally. Within MOH, unlike for community outbreaks, no single division had clear responsibility to deal with outbreaks of a HAI of this nature. This hindered MOH’s ability to respond in a timely fashion to the unexpected event. In addition, the absence of an established framework for unusual and unfamiliar events, as well as the failure to recognise the potential severity, resulted in delays in escalating the matter from SGH to SingHealth, from SGH to MOH, and within MOH.

3.8 The rest of this chapter elaborates on the management of the HCV outbreak in SGH and MOH. In assessing the involved parties’ actions and responses, the IRC adopted a thematic framework according to five categories: (a) recognition of an infectious disease outbreak; (b) notifications to MOH; (c) outbreak management and containment; (d) communications and escalation; and (e) roles and responsibilities of key parties in outbreak response.

\(^{21}\) As explained in Chapter 1, a HCV infection is blood-borne and has a long and variable incubation period. In addition, the infection is often asymptomatic and can go unnoticed. These particular characteristics present significant challenges to picking it up via the current surveillance system. Compared to an airborne disease like SARS or Avian Influenza which are spread by airborne route and / or by close contact, establishing the chain of transmission is also significantly harder in the case of HCV.
Key Parties Involved

3.9 For ease of reference in the following sections, simplified organisation charts of the key parties involved from SGH and SingHealth, and from MOH are in Figures 3.1 and 3.2 respectively.

**Figure 3.1:** Simplified Organisation Chart for SGH and SingHealth
### Brief Sequence of Events

#### 3.10
Between late-April and end-May 2015, the SGH Renal Unit noticed an increase in HCV infections. The Renal Unit initiated investigation of the Dialysis Centre in mid-May. It was concluded in end-May that transmission was not related to the processes in the Dialysis Centre.

#### 3.11
As the Renal Unit could not establish a cause in the Dialysis Centre, they contacted SGH’s Infection Control Unit (IC) in early June to investigate the cluster. This led to the introduction of several infection control measures from early-June as investigations continued. The SGH Molecular Laboratory also embarked on a special laboratory test called phylogenetic test in-house, to study the genetic material of the virus and relatedness of HCV-infected cases.

#### 3.12
The National Organ Transplant Unit (NOTU), which is in charge of overseeing human organ transplants in Singapore, was also notified of HCV infections in transplant cases at SGH from late April onwards, and conveyed this information to the MOH division overseeing it – MOH-Hospital Services Division (HSD). In June, NOTU and MOH-HSD informed other relevant MOH divisions, i.e. Communicable
Diseases Division (MOH-CDD) and the Clinical Quality, Performance and Technology Division (MOH-CQPT), of the cluster. MOH-CQPT made enquiries with SGH about the cases, and was informed that investigations were in progress, and they would update MOH subsequently.

3.13 In July, SGH found the number of new HCV cases diagnosed to have reduced noticeably. This was attributed to the effectiveness of the infection control measures that had been introduced in June. Preliminary results of the phylogenetic test in early July showed close genetic links among the cases and pointed towards an outbreak caused by a common strain of HCV. SGH decided to continue with additional phylogenetic testing, which was completed in late July. On 28 August, SGH contacted MOH to arrange to share its investigation findings. The meeting took place on 31 August, after which MOH staff informed the Director of Medical Services (DMS) of the issue on 1 September.

3.14 On 3 September, SGH presented their findings to the DMS who then requested for additional information from SGH to assess the severity and extent of the outbreak. On 18 September, a summary of the incident was sent to the Minister for Health who requested for a detailed briefing by SGH. On 25 September, SGH briefed the Minister. He instructed for the matter to be made public, and for an Independent Review Committee to be appointed. On 6 October, SGH held a media briefing while MOH released a press statement on the establishment of the IRC, its members and the terms of reference.

3.15 A more detailed timeline of key events, including exchanges of information between parties, is in Annex G.

Recognition of the Outbreak

3.16 There is a range of definitions of an outbreak. By the World Health Organisation’s (WHO’s) definition, a disease outbreak is defined as the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. According to the US CDC, in the context of blood-borne infections like HCV, an outbreak is defined as two or more cases with epidemiologic evidence supporting healthcare related transmission, including patients/residents identified with acute infection, or previously undiagnosed chronic infections with epidemiologic evidence. However, the latter is not a definition widely known among professionals today.

22 WHO states that a disease outbreak is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. An outbreak may occur in a restricted geographical area, or may extend over several countries. It may last for a few days or weeks, or for several years. A single case of a communicable disease long absent from a population, or caused by an agent (e.g. bacterium or virus) not previously recognised in that community or area, or the emergence of a previously unknown disease, may also constitute an outbreak and should be reported and investigated.

23 US CDC. “Healthcare-Associated Hepatitis B and C Outbreaks Reported to the Centers for Disease Control and Prevention (CDC) 2008 -2014.”
3.17 By mid-May 2015, SGH’s Renal Unit was suspicious of an initial cluster of four HCV cases, but had thought that the increase in the number of cases could be due to the switch to a more sensitive test for HCV in 2014.

3.18 While it may not have been apparent to the Renal Unit at the time that they were in the middle of an outbreak, an investigation of the Dialysis Centre was initiated. When investigations concluded that the processes in the Dialysis Centre were not a cause for transmission, the issue was referred to Infection Control (IC) on 3 June for further investigations, after which necessary infection control measures were put into place.

3.19 The IRC noted that while HCV is an unusual HAI and has unique characteristics that prevent it from being picked up easily by surveillance, SGH did not recognise the outbreak in a timely manner. The Renal Unit had identified that something was amiss and taken actions to check the Dialysis Centre in mid-May, but referred the matter to the IC Unit after that, in early June.

**Notifications to MOH**

3.20 On MOH’s part, there are four notification systems through which it could have been alerted of the HCV outbreak in SGH (more details are at Annex H):

   a. National notification system for communicable diseases where acute HCV infections are reportable to MOH-CDD within 72 hours of diagnosis by a medical doctor or laboratory.

   b. Notifications to NOTU for post-transplant patients, to enable them to identify patients found to have HCV infection post-transplant. This would enable NOTU to follow-up with other organ recipients from the same deceased donor to ensure they did not acquire HCV infection from the transplant. Beyond this, SGH also has the routine practice of testing transplant recipients for Hepatitis B and Hepatitis C, when liver dysfunction is encountered.

   c. Reporting to MOH-CQPT, on patient safety indicators, including hospital-infection indicators\(^\text{24}\) and Serious Reportable Events (SREs). SREs in turn include patient deaths associated with the use of contaminated drugs, devices of biologics provided by the healthcare institution.

   d. Requirement to inform the DMS immediately of any HAI outbreaks.

3.21 Between May and September 2015, MOH received notifications for 15 of the initial 22 cases in the cluster via the communicable disease notification route.

3.22 Although notification is required for acute HCV infection, not all the cases in the cluster were notified by doctors and laboratories because the relevant form MD 131 does not stipulate the case definition. This creates uncertainty for doctors and

\(^{24}\) The nine HAI indicators comprise four for multidrug resistant organisms, three device-related infections, and two surgical site infections. These indicators are aligned to those tracked by the US CDC in their National Healthcare Safety Network (NHSN).
laboratories if cases should be classified as acute HCV infections. In addition, doctors and laboratories face challenges in diagnosing acute HCV infection as it is common for patients with acute infections to be asymptomatic. A person with an acute infection can go on to be chronically infected with the virus. Hence, even when there is a positive test result for HCV, it may not be easy to determine if this reflects an acute or an older, chronic infection. In addition, doctors who are in specialties outside of Infectious Diseases may not be aware of the requirements for notification. In this instance, the Renal Unit oversees a highly specialised medical discipline, and does not handle acute HCV infection frequently.

3.23 Regardless, MOH-CDD did not classify any of the 15 notifications received as acute HCV infections despite some patients’ abnormal liver function test, as the cases were assessed not to meet the case definition of an acute infection at the time.25 Hence, MOH was not aware of any acute HCV cases via this notification route.

3.24 NOTU is primarily focused on transplant patients and is not a surveillance unit. However, they received 13 notifications from SGH’s Renal Unit between April and September 2015. From late-May onwards, NOTU brought the unusually high number of notifications to MOH-HSD’s, and later MOH-CDD’s attention.

3.25 By mid-June, MOH-CDD had acted upon information from NOTU to do its own investigation, and determined that the HCV cluster was a possible HAI outbreak. As the management of outbreaks of HAIs did not strictly fall under its purview, MOH-CDD handed the matter over to MOH-CQPT in mid-June as the latter oversees clinical quality and hospital infection indicators.

3.26 As MOH-CQPT’s focus is on clinical quality improvement, it adopts a quality assurance approach26 in assessing patient safety indicators and does not have outbreak investigation and management capabilities. MOH-CQPT’s reporting formats (i.e. where hospital infection indicators are reported quarterly on a retrospective basis and SREs are reportable within two days of detection with up to 60 days thereafter to furnish a report) are therefore not designed for rapid reporting of disease outbreaks.

3.27 Although MOH-CQPT did not receive any notifications from SGH through their existing reporting channels throughout the incident, they were alerted to the increase in incidence of HCV cases by both MOH-CDD and MOH-HSD, and followed-up with SGH in mid-June, and again in end-July 2015. Although MOH-CQPT requested

25 MOH CDD has an established process to determine whether the case notified has met the case definition of an acute infection. This requires checking laboratory tests and for the presence of clinical symptoms, to see if patients meet the case definition. Despite abnormal liver function test results, the patients did not present with symptoms that met the case definition at the time, based on medical records. MOH CDD therefore did not classify them as acute cases. From 4 Oct 2015, CDD has adopted a wider surveillance case definition for acute HCV infection, aligned to the US CDC’s case definition.

26 This approach is based on the principle of open disclosure and continuous learning, where healthcare staff are encouraged to report incidents and near-misses as learning points and in doing so, improve practices.
SGH’s Office of Clinical Governance to report the incident as an SRE on 23 June (albeit as an SRE relating to transplant cases), SGH did not do so, nor explain why.

3.28 As neither SGH nor MOH staff escalated the issue to DMS during this initial period, he was only informed by MOH staff on 1 September, and subsequently briefed by SGH on the issue on 3 September. [See paragraph 3.32 on “Communication and Escalation” for more details]

Management and Containment of the Outbreak

3.29 Within SGH, after IC was activated by the Renal Unit on 3 June 2015, there was a flurry of activities to investigate the cluster of HCV cases. SGH largely undertook the investigation process within the framework for a HAI, where the hospital takes responsibility for the management and containment of the infection.

a. From early-June 2015, efforts were taken to localise the infection and cease transmission through enhanced infection control measures. This included the ceasing of multi-dose medication vials in the Renal Wards, audits on hand hygiene and injection practices in the affected wards, the use of disposable kidney dishes, and ceasing the use of multi-dose medication vials in all wards by end-June.

b. In early-June 2015, the SGH laboratory was also directed to carry out phylogenetic testing to ascertain if the infections were related. However, as this was the first time that the laboratory had to do such a test, the test could only be completed in end-July.

c. SGH wanted to complete its investigations into the HCV cluster before informing MOH of its findings. SGH staff therefore only contacted MOH staff on 28 August, to arrange to share their findings.

3.30 During this period, SGH did not seem to have a distinct structure and process to speed up and intensify the investigation and management of such an outbreak. While it carried out a careful investigation to identify possible causes of the outbreak, and undertook measures to intensify infection control, it did not take steps to fully assess the severity and extent of the outbreak. This included establishing the size of the potential exposed patient pool, conducting active case finding to ascertain the number of exposed patients who might have been infected with the virus, and determining if there were related deaths due to the HCV infection. These were held off pending the result of the phylogenetic sequencing to confirm the cluster.

3.31 These additional steps would have provided information on the severity of the outbreak. Their absence led to the DMS needing to ask SGH when he was briefed by SGH on 3 September 2015, to complete the necessary work in order for him to better assess the situation.

Communications and Escalation

3.32 There are well-established escalation protocols in place for common and known infectious diseases, and epidemic threats like MERS-CoV and Ebola, in SGH,
SingHealth and MOH. However, these did not cater for the reporting of risk events in the shortest time possible for an unusual and unfamiliar outbreak of an HAI like HCV. As a result, there was delayed event reporting between SGH and the GCEO and Board of SingHealth, between SGH and MOH, and between staff and senior management in MOH.

**Communication and Escalation within SGH**

3.33 Within SGH, communications with the Division Chair for Internal Medicine (Division Chair) and CMB took place early, by 30 May 2015. The IRC also understands that the CEO was kept informed through internal discussions with CMB and Division Chair during the period. Communications on the issue was largely informal but free-flowing.

3.34 However, the Office of Clinical Governance which oversees clinical risk, was not kept informed, although CMB (who oversees the Office of Clinical Governance) and the IC Unit (which falls within the Office) were involved by early June. Staff from the Office of Clinical Governance were only informed by MOH-CQPT on 23 June 2015.

**Escalation from SGH to SingHealth**

3.35 There was no escalation of the issue from SGH to SingHealth despite the Office of Clinical Governance’s staff’s advice to the Renal Unit on 10 July 2015 to escalate the issue to GCEO, GCRO and the Office of Risk Management. Again, this did not take place as the Renal Unit wanted investigations to be completed before further escalation took place.

3.36 Consequently, SingHealth did not realise that an outbreak was taking place. The SingHealth GCEO was only informed on 3 September while the SingHealth Board Chairman and Chairman of the Risk Oversight Committee were informed on 20 September.

**Escalation from SGH to MOH**

3.37 Escalation between SGH and MOH did not take place until the SGH team felt that investigations were completed. Although there were several regular meetings between SGH and MOH (e.g. Permanent Secretary-CEO meetings, DMS-CMB meetings), this issue did not come up. In addition, SGH senior management and some clinicians were also aware that SGH was liaising with MOH-CQPT, and thought that MOH-CQPT would inform the DMS if necessary.

**Escalation within MOH**

3.38 Within MOH, there was no single Division with clear responsibility to deal with unusual HAI outbreaks of this nature. While MOH-CDD has the capabilities to manage and contain community outbreaks, their work does not generally cover outbreaks of HAIs, unless there is a significant community element or overlap. They therefore handed over the cases to MOH-CQPT for follow-up in mid-June.
3.39 However, MOH-CQPT does not have the capability to carry out outbreak investigation and management, and thus operated within the existing paradigm where primary responsibility for investigation and management of typical hospital infections resides with the hospital concerned. Although they enquired with SGH in mid-June and later end-July about the HCV cluster, they accepted SGH’s response that they were still investigating.

3.40 After MOH-CDD had handed over the cases to MOH-CQPT, MOH CDD did not enquire about the follow-up taken, although they did request for MOH CQPT to keep them updated. Meanwhile, MOH-CQPT, which did not have the capability or capacity to investigate or respond to a potential outbreak, did not realise the potential severity of the incident.

3.41 Despite monthly meetings between the DMS and divisions in the Professional Group (including MOH’s HSD, CDD and CQPT), the issue also did not surface. Communication between NOTU and MOH’s HSD, CDD and CQPT on the HCV cluster remained at staff-level for most parts of the period. Senior staff in MOH (Group Director-level and above) were only updated in end-August to early-September, after SGH contacted MOH to share their investigation findings. Thereafter, it was escalated to the DMS on 1 September.

3.42 The IRC is of the view that earlier escalation of the matter from SGH to SingHealth, or from SGH or MOH staff to the DMS could have triggered earlier injection of additional resources and expertise to help in the outbreak investigation and management, from across the public healthcare system.

**Roles and Responsibilities of Key Parties in Relation to Outbreak Response**

3.43 As preceding sections have covered MOH and SGH staff's actions in relation to the identification and management of the outbreak comprehensively, this section reviews the roles and responsibilities of SGH and MOH senior management, as well as the role of the SingHealth cluster, in relation to the outbreak.

**SGH Senior Management**

3.44 By June 2015, SGH’s Division Chair, CMB and CEO were aware of the HCV cluster, and there were several informal discussions amongst them on this issue.

3.45 As the head of the organization, the SGH CEO is responsible for organisational and risk management, and ensuring that the GCEO, SingHealth Board, and MOH are apprised of these in a timely manner. The CMB is responsible for clinical risk and ensuring that the CEO, SingHealth Board, and MOH are apprised of these in a timely manner. There appeared to be a lack of clarity as to whether the CEO or CMB would be directly responsible for the management of clinical risks.

**Role of SingHealth and SingHealth Board**

3.46 SingHealth and its Board did not play a part in the incident because SGH did not escalate the issue to them. In addition, SGH’s IC collects and aggregates data
on hospital infection indicators\textsuperscript{27} and epidemiologically significant organisms which require reporting to MOH, and circulates to SGH senior management and presented at several SingHealth platforms. However, HCV, as an unusual HAI, is not one of the key indicators. Hence, SingHealth GCEO and Board did not receive information about the HCV cluster via this channel. Finally, although SingHealth has an Enterprise Risk Management framework\textsuperscript{28} which extends to all its institutions including SGH, it is focused on providing a strategic role in risk management, e.g. creating risk awareness and sharing best practices, rather than surveillance. The structure and process of risk identification, risk assessment, risk monitoring and reporting have not been developed to facilitate the escalation of risk events at an early stage. The HCV cluster was therefore not picked up by this framework.

\textit{MOH Senior Management}

3.47 On 3 September 2015, the DMS was presented with findings from SGH and found that based on the information available then, he was not able to make a good assessment of the overall situation, in particular with regard to the severity and extent of the outbreak. He requested the following information from SGH within two weeks, to better inform assessment and for further decision making:

a. To verify severity of outbreak:

(i) For an external party to chair SGH’s Medical Review Committee (MRC) that would review the seven deaths that had occurred then.

(ii) For SGH’s phylogenetic analysis to be verified by an A*STAR laboratory since phylogenetic analysis was a new capability for the SGH molecular laboratory and the chain of transmission had not yet been established clearly.

b. To improve containment of infection:

(i) For CMB to make arrangements to suspend transplants at SGH, and make alternative arrangements for patients, and inform MOH of these arrangements.

(ii) For a team from MOH to visit the affected wards to perform a process walkthrough with SGH’s staff, as he understood that Ward 67 might have a configuration that SGH staff were not used to.

\textsuperscript{27} The nine HAI indicators comprise four for multidrug resistant organisms, three device-related infections, and two surgical site infections. These indicators are aligned to those tracked by the US CDC in their National Healthcare Safety Network (NHSN).

\textsuperscript{28} SingHealth and SGH have an Enterprise Risk Management (ERM) framework which was put in place since 2007. The SingHealth Office of Risk Services and GCRO’s responsibility amongst others are to provide leadership on the program, its sustainability, sharing of practices, champion the risk management function, facilitate risk communication and reporting to Risk Oversight Committee at Board level and periodic reporting of risks, mitigation strategies.
(iii) For staff who were involved in the care of renal transplant patients to be screened for HCV, to ensure they were not involved in transmission.

(iv) SGH to do root cause analysis by setting up a Quality Assurance Committee (QAC) to verify the findings of the SGH Infection Control Team. In addition, an external representative from MOH should be part of the QAC.

3.48 The DMS informed the Permanent Secretary\(^{29}\) of the matter on 3 September 2015, and she took reference from the DMS’s professional judgment that there was insufficient information to allow for a fuller professional evaluation of the outbreak.

3.49 As the CMB was not present at the 3 September meeting because he was away, he subsequently met with DMS on 8 September 2015, and agreed to the key pieces of work. By 17 September night, the pieces of work in (a) – (e) had been done, while plans for (f) were in place:

a. 4 September – MOH team visited wards 64A and 67 for a process walkthrough.

b. 7 September – A*STAR laboratory completed and verified SGH’s initial findings based on phylogenetic analysis.

c. 9 September – SGH suspended renal transplant services, having made arrangements for transfer of their transplant patients to the National University Hospital (NUH).

d. 9 – 22 September – Screening for nurses and doctors from the Renal Ward and department.

e. 9 September – MRC met to review if HCV had contributed to the 7 deaths.

f. 18 September – SGH’s plans for an independent Quality Assurance review and composition of the Quality Assurance Committee (QAC) were finalised.

g. 23 September – SGH’s QAC met.

3.50 By 18 September 2015, with the further information from SGH listed in (a)-(f), DMS felt that there was sufficient information to inform the Minister for Health. Following that, Minister requested for a detailed briefing by SGH. SGH’s investigation report was submitted to MOH on 24 September, and the Minister was briefed on 25 September, after the MRC and QAC completed their investigations.

\(^{29}\) The Permanent Secretary is the Civil Service Head of MOH while the Director of Medical Services oversees all professional functions in MOH. Together, they both report to the Minister.
3.51 The IRC noted that when DMS was briefed by SGH on 3 September, his key considerations were to make a professional evaluation of the severity and extent of the outbreak, to ascertain that adequate infection control measures had indeed been instituted, and to ensure that new transplant patients were not potentially exposed to HCV infection until the issues had been adequately addressed. He therefore asked for specific additional relevant investigations and actions to be taken in relation to each of these within two weeks, and when these were largely done, reported the matter to the Minister. The IRC is of the opinion that the additional investigations and actions required by the DMS are professionally valid and appropriate. Overall, while there were gaps in identification, management and reporting of the outbreak, there was no evidence to suggest that the escalation of the matter to DMS and the subsequent notification of the Minister had been deliberately delayed.

**Briefing on 25 September 2015 to the Minister for Health**

3.52 At the briefing to the Minister on 25 September, the Minister instructed that an Independent Review Committee (IRC) should be appointed to look into the HCV cluster, since the review up to that point was largely done in-house by SGH. The IRC would be given the latitude to review the incident thoroughly, to give MOH an independent validation of SGH’s findings, and to see how the system could be improved. The Minister also instructed for the matter to be made public.

3.53 Following the briefing to the Minister, SGH prepared for the press briefing. The 8th death took place on 30 September, and the MRC was convened to determine if Hepatitis C was a cause of contributory factor to the death. The announcement of the incident was made on 6 October. MOH appointed the IRC on 28 September, which met for the first time on 5 October. The appointment of the IRC was shared with the media via MOH’s press release on 6 October 2015.

**Conclusion of Findings**

3.54 While the current surveillance system works well for community outbreaks of known infectious diseases and hospitals have robust frameworks to handle common Healthcare-Associated Infections (HAIs), the HCV outbreak highlighted a gap. Specific findings of the system response to the outbreak were:

- a. **Recognition**: The SGH Renal Unit did not recognise the outbreak in a timely manner and there was a delay in reporting to SGH Infection Control for help in containment.

- b. **Notifications**: MOH was not notified by doctors and laboratories of all the cases in the cluster. In addition, MOH-CDD did not classify the initial communicable diseases notifications as acute HCV infections despite some cases having abnormal liver function tests, as the cases were assessed not to meet the case definition of an acute infection at the time.

- c. **Outbreak management and containment**: While SGH commenced investigations into the HCV cluster from mid-May 2015, and enhanced infection control measures from early-June, investigations performed by SGH were incomplete. Several elements of outbreak investigation such as assessing the severity and extent of the outbreak were done by SGH only
after meeting with the Director of Medical Services (DMS) on 3 September, such as appointing an external party to chair SGH’s Medical Review Committee to determine if there were related deaths due to the HCV infection and setting up a Quality Assurance Committee to do a root cause analysis.

d. **Communications and escalation**: Within SGH, communication with senior management took place early. However, in the absence of an established framework for the unusual and unfamiliar event of the HCV outbreak, there was a delay in escalation from SGH to SingHealth, and SGH to MOH. In addition, within MOH, there was no single division with clear responsibility and capability to deal with the issue, resulting in a gap in ownership, until the matter was escalated to the DMS.

e. **Roles and responsibilities**: Within SGH, there did not appear to be clear roles and responsibilities for the management of unusual hospital outbreaks. SingHealth did not play a part in the incident. Within MOH, the DMS assessed on 3 September 2015 that more information was needed to determine the severity and extent of the outbreak, and requested SGH to complete key pieces of work within two weeks. The Minister was therefore only informed of the issue on 18 September, and briefed on 25 September, after SGH submitted their investigation report on 24 September.

3.55 In summary, there was a delay in recognising the outbreak as HCV is not easily picked up through regular surveillance due to its unique characteristics. With HCV being an unusual HAI, SGH did not recognise the outbreak in a timely manner. While SGH commenced investigations into the HCV cluster from mid-May, and implemented enhanced infection control measures from early June 2015 onwards which were instrumental in slowing the spread of infection, the IRC is of the view that the outbreak was not investigated and managed optimally. Within MOH, unlike community outbreaks, no one division has clear responsibility to deal with outbreaks of unusual HAIs. This hindered MOH’s ability to respond in a timely way to the unexpected event. In addition, the absence of an established framework for unusual and unfamiliar events resulted in delays in escalating the matter from SGH to SingHealth, from SGH to MOH, and within MOH.
CHAPTER 4

Conclusion and Recommendations

Introduction

4.1 The IRC has carefully considered the evidence collected during the Investigation and the written submissions that the parties have tendered.

4.2 The conclusion and recommendations of the IRC relate to the three areas of infection control, Hepatitis C Virus (HCV) surveillance, and system review of the outbreak response. The aim of these findings and recommendations is two-fold:

a. First, to provide learning lessons for all concerned in healthcare provision, so that they can work towards preventing a recurrence of this incident;

b. Second, to provide guidance on how to better handle the clinical management, investigation and information flows related to any future incidents of a similar type, to ensure timely intervention and safeguard patient safety.

4.3 To this end, the IRC sets out its findings on the probable cause of the incident and its recommendations as to how similar incidents can be prevented in future. The IRC also sets out its recommendations on how similar incidents can be managed more effectively in future.

Findings

4.4 The IRC’s investigation found that a total of 25 patients at SGH had been affected by the cluster:

a. All 25 affected patients had been admitted to Ward 64A and/ or Ward 67 (when Ward 64A was closed for renovations); and

b. Specialised genetic tests called phylogenetic studies showed that the hepatitis C strains of all the infected patients were related, identifying this as a unique cluster.

4.5 The key issue for the IRC was the identification of the cause for the cluster of infection, bearing in mind that HCV is blood-borne and would therefore need to be transmitted through blood and blood products.

4.6 During its investigation:

a. The IRC considered four specific hypotheses, i.e. (i) drug diversion; (ii) product contamination; (iii) intentional harm; and (iv) breach in infection control;
b. During the investigations, the first three hypotheses were ruled out. However, the IRC documented several gaps in infection control practices, in Wards 64A and 67, i.e. the wards which had been associated with the HCV cluster. These included inadequate hand hygiene; inadequate environmental cleaning and disinfection practices; and environmental contamination in the form of blood stains on various surfaces at Wards 67 (most notably on computerised medical cart and in the preparation room);

c. The IRC also found weaknesses in the design and practice of processes and workflows in the wards. It was noted that there were variations in practices and compliance to infection control practices was made more challenging due to inefficiencies in the design of work processes.

4.7 Following the investigation, the IRC concluded that the HCV outbreak was an unusual event and the result of a combination of multiple overlapping factors:

a. The susceptible cases comprised mainly immunocompromised kidney transplant patients and the introduction of HCV (probably by the patient identified to be the earliest infected case) led to acute infections with extremely high quantities of virus in these patients.

b. All affected patients had many exposures to intravenous medications and/or laboratory tests that required blood taking, exacerbating the risks of HCV spread through gaps in infection control practices.

c. Gaps were identified in the two affected wards with regards to infection control practices (in particular processes involving intravenous procedures), environmental cleaning, and prevention of environmental contamination. Furthermore, the virus is resilient and can remain infective in blood stains for several weeks, thereby increasing the risk of transmission from such gaps.

d. The spread of HCV was highest during the period when staff and patients from Ward 64A were moved to Ward 67 (i.e. from 6 April to 28 August 2015). This was likely linked to changes in workflow patterns and processes in the new environment, which had a different layout from the one the staff were familiar with, thus further increasing the likelihood of the spread of HCV in this cluster.

4.8 While the current surveillance system works well for community outbreaks of known infectious diseases, and hospitals have robust frameworks to deal with common healthcare-associated infections, the HCV outbreak has highlighted a gap in the current system.

4.9 In particular, there was a delay in recognising the outbreak as HCV is not easily picked up through regular surveillance due to its unique characteristics. With HCV being an unusual HAI, SGH did not recognise the outbreak in a timely manner. While SGH commenced investigations into the HCV cluster from mid-May, and implemented enhanced infection control measures from early June 2015 onwards
which were instrumental in slowing the spread of infection, the IRC is of the view that the outbreak was not investigated and managed optimally. Within MOH, unlike community outbreaks, no one division has clear responsibility to deal with outbreaks of unusual HAIs. This hindered MOH’s ability to respond in a timely way to the unexpected event. In addition, the absence of an established framework for unusual and unfamiliar events resulted in delays in escalating the matter from SGH to SingHealth, from SGH to MOH, and within MOH.

**Recommendations**

4.10 During the course of investigations, the IRC observed several commendable practices by SGH staff. For example, consistent efforts were made to maintain patient privacy and confidentiality, as well as to minimise human errors by consistently verifying patient’s identity prior to performing procedures. SGH was also effective in upskilling their nursing workforce, with nurses trained to take on a significant share of tasks normally performed by junior doctors.

4.11 The IRC recommends that SGH undertake the following to minimise the risk of infection transmission:

   a. Review standard operating procedures and practices on infection control, with a view to reduce risk of environmental contamination, and to ensure adequate environmental cleaning and disinfection.

   b. Adhere to standard precautions for infection control, as laid out in US CDC guidelines\(^{30}\).

   c. Strengthen the framework for supervision and monitoring of staff to ensure compliance with standard operating procedures.

4.12 Specific recommendations with regards to each of these areas are laid out in Annex I. The recommendations highlight relevant aspects related to the review of this HCV outbreak.

4.13 For the specific findings identified by the IRC, SGH should prepare a plan for corrective measures to be put in place. This plan should be formulated within one month and submitted to MOH for review, to ensure patient and healthcare worker safety, and maintain a high standard of patient care with particular attention to infection control.

4.14 In addition, the IRC recommends an extension of these recommendations to all healthcare institutions and a development of evidence-based guidelines on

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infection control and prevention. The Ministry of Health should have oversight over the implementation of this.

4.15 Beyond community outbreaks, the current surveillance and outbreak response frameworks should be enhanced to cater for unusual and unfamiliar events, with regards to outbreak detection, investigation and management, communication and escalation protocols, and the appropriate roles of MOH and the hospital.

4.16 The IRC thus recommends that the following measures are undertaken to improve the system response to cater to unusual and unfamiliar outbreaks:

a. Improve the national notification and surveillance system for acute HCV, taking reference from international best practices and adapting them to the local context. Regardless of the systems in place, healthcare professionals should always be alert to unusual events.

b. Designate a single team within MOH to carry out surveillance, identify and investigate potential outbreaks, and ensure adequate expertise nationally to facilitate outbreak investigation. Hospitals should continue to take responsibility and develop structures, frameworks and capabilities for HAI outbreaks within their institutions. Capabilities can be supplemented by other public healthcare institutions and MOH where required.

c. Strengthen the escalation processes for HAIs, especially unusual and unfamiliar ones, within hospitals, public healthcare clusters and MOH, and between them through clearer guidelines on the assessment of the significance and severity of an HAI, and need for escalation.

4.17 Specific recommendations with regard to each of these areas are laid out in Annex J.

Conclusion

4.18 The IRC concluded that this highly unusual outbreak of Hepatitis C in Singapore was likely due to a combination of multiple overlapping factors concentrated during the period of April to June 2015 in the Renal Wards of SGH. In particular, the concentration of very ill patients who were susceptible to infection and inefficiencies in workflow which may have led to gaps in infection control practices provided an environment for the infection to spread.

4.19 The IRC found gaps in the surveillance system for unusual HAI outbreaks, resulting in delays in detecting the outbreak. While preliminary investigations and the tightening of infection control practices by SGH served to contain the outbreak by June 2015, there was a delay in reporting the outbreak to MOH until 31 August 2015.

4.20 In addition, as the preliminary investigations by SGH were incomplete, the DMS had to request for additional work to be done when he was briefed by SGH on 3 September, which the IRC assessed to be appropriate and necessary.
4.21 The IRC recommends for (i) improvements to be made in infection control practices and compliance in all healthcare institutions; (ii) improvements to be made in how HAIs are monitored and responded to at the national level; (iii) the designation of a single team within MOH to carry out surveillance, identify and investigate potential outbreaks, ensure adequate expertise nationally to facilitate outbreak investigation; and (iv) strengthening of the escalation framework for HAIs and events of unusual risk.
ANNEX A

Epidemiologic Steps In an Outbreak Investigation

Table 6.2 Epidemiologic Steps of an Outbreak Investigation

1. Prepare for field work
2. Establish the existence of an outbreak
3. Verify the diagnosis
4. Construct a working case definition
5. Find cases systematically and record information
6. Perform descriptive epidemiology
7. Develop hypotheses
8. Evaluate hypotheses epidemiologically
9. As necessary, reconsider, refine, and re-evaluate hypotheses
10. Compare and reconcile with laboratory and/or environmental studies
11. Implement control and prevention measures
12. Initiate or maintain surveillance
13. Communicate findings

## ANNEX B

### Curriculum Vitae of International Experts

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<tr>
<th>International Expert</th>
<th>Curriculum Vitae</th>
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<tbody>
<tr>
<td>Scott Dewey Holmberg</td>
<td>Scott Dewey Holmberg is Chief, Epidemiology and Surveillance Branch, Division of Viral Hepatitis at the National Center for HIV, Hepatitis, STD, and TB Prevention (NCHHSTP) of the Centers for Disease Control and Prevention (CDC), Atlanta. Dr Holmberg’s unit in the CDC is responsible for national surveillance, outbreak investigations and research projects in viral hepatitis. Dr Holmberg’s experience includes analyses of many large public datasets, such as multiple-cause-of-death data from national death certificates.</td>
</tr>
<tr>
<td>Amanda Beaudoin</td>
<td>Amanda Beaudoin is a Veterinary Medical Officer with the International Health Quality Team, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention (CDC). Dr Beaudoin has experience with the Epidemic Intelligence Service in the US.</td>
</tr>
<tr>
<td>Trish M. Perl</td>
<td>Trish M. Perl is a professor in the departments of Medicine (Infectious Diseases) and Pathology at Johns Hopkins University School of Medicine and in Epidemiology at the Bloomberg School of Public Health. She is Senior Epidemiologist for The Johns Hopkins Health System. Prof Perl is in charge of putting in place mechanisms at her institution to measure and prevent potential healthcare-associated infections or infections that result because of medical care or problem organisms or pathogens and multidrug resistant organisms. In her role as a healthcare epidemiologist, she had been involved in the study of novel technologies and investigating outbreaks from unintended consequences of new products.</td>
</tr>
<tr>
<td>JoEllen Harris</td>
<td>JoEllen Harris is programme director of the epidemiology and infection prevention at the Johns Hopkins Health System. She is also director of the infection prevention programmes at Sibley Memorial Hospital and Johns Hopkins International; and consultant to the infection prevention programme for Johns Hopkins Community Physicians. Ms Harris has experience in providing leadership and enabling collaboration for John Hopkins’ Epidemiology and Infection Prevention Program.</td>
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ANNEX C

Findings of the Case Review Team

The Case Review Team was led by Professor Lim Seng Gee and comprised the following members.

Core Members

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<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td><strong>Prof Lim Seng Gee</strong></td>
<td>Director of Hepatology Services, National University Health System</td>
</tr>
<tr>
<td><strong>Prof Leo Yee Sin</strong></td>
<td>Director (Institute of Infectious Diseases &amp; Epidemiology) Clinical Director (Communicable Disease Centre) Tan Tock Seng Hospital</td>
</tr>
<tr>
<td><strong>A/Prof Dan Yock Young</strong></td>
<td>Chair, University Medicine Cluster, National University Hospital; Head, Department of Medicine, National University of Singapore</td>
</tr>
<tr>
<td><strong>A/Prof Helen Oh</strong></td>
<td>Head, Infectious Diseases, Changi General Hospital</td>
</tr>
<tr>
<td><strong>Dr Richard Guan</strong></td>
<td>Consultant Gastroenterologist and Hepatologist, Mount Elizabeth Medical Centre</td>
</tr>
<tr>
<td><strong>Dr Titus Lau</strong></td>
<td>Senior Consultant, Department of Nephrology, National University Hospital</td>
</tr>
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Invited International Experts

<table>
<thead>
<tr>
<th>Name</th>
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<tr>
<td><strong>Dr Scott Holmberg</strong></td>
<td>Chief, Epidemiology and Surveillance Branch, Division of Viral Hepatitis, CDC</td>
</tr>
<tr>
<td><strong>Dr Amanda Beaudoin</strong></td>
<td>Veterinary Medical Officer, Division of Healthcare Quality Promotion, International Health Quality Team, CDC</td>
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Objectives

The main objectives of the Case Review Team were to:

a) Review Hepatitis C virus (HCV) positive cases detected during the period of investigation and decide if cases were acute or chronic in nature. This was for the purposes of case-finding and the search for a chronic case.

b) Evaluate mortality cases and ascertain the contribution of Hepatitis C in the mortality of the patients; and

c) Evaluate contributions of Hepatitis C to the 106 fatal cases\(^{31}\) that SGH came to know of (through the National Electronic Health Records and

\(^{31}\) This comprises 74 deaths from the National Electronic Health Records, as well as 32 deaths updated when SGH recalled the remaining 1004 patients back for screening (See also paragraph 2.9 and Table 2.1 in Chapter 2).
recalling of patients for Hepatitis C screening) and decide if Hepatitis C contributed to the mortality of these patients. All of these 106 cases had been admitted to Wards 64A and 67 at some point from January to September 2015. This was to provide information to the epidemiology teams in their investigations on the extent of the outbreak.

Case Definitions for Acute Hepatitis C

3 Acute Hepatitis C. The case definition for an acute case of Hepatitis C used by the team was based on the 2012 case definition of Acute Hepatitis C by the US CDC, and agreed upon by members of the Case Review Team, was as follows:

a) **Definite**: Either a negative HCV RNA < 6 months prior, OR a subsequent negative HCV RNA without treatment AND Positive HCV RNA with Alanine Aminotransferase (ALT; a test of liver function) of > 400 IU/L during incident

b) **Likely**: Negative HCV RNA > 6 months before AND Positive HCV RNA with ALT elevation (not necessarily > 400 IU/L)

c) **Suspected**: No prior HCV RNA tested before AND Positive HCV RNA with ALT elevation (not necessarily > 400 IU/L)

d) **Uncertain**: No prior HCV RNA tested before Positive HCV RNA result AND Normal or absent ALT tested, OR Features of chronic liver disease.

Contribution of Hepatitis C to Death

4 Contribution to death. In the assessment of a possible contribution of Hepatitis C to mortality, the following factors were considered:

a) Was patient’s HCV RNA positive between March 2015 and October 2015, or during the patient’s admission to SGH; and

b) Was there evidence of liver dysfunction based on any of the following:

   (i) Fibrosing cholestatic hepatitis on liver biopsy;

   (ii) Development of hepatic encephalopathy or ascites during the terminal admission;

   (iii) Development of jaundice with prolonged PT (>15 seconds) during the terminal admission.

5 Based on the evaluation of these factors, the Team carefully determined the contribution of Hepatitis C to the death.

a) If both of the above conditions were met, Hepatitis C was deemed to be a likely contributory factor.
b) If there was no evidence of liver dysfunction, Hepatitis C was deemed not to have been a likely contributory factor.

c) It was not possible to determine the contribution of Hepatitis C to the death of a patient if there were no records of HCV RNA positive test results.

Findings

Acute HCV Cases

Table C-1 provides a summary of the 25 cases in the cluster. Of these, 22 cases fulfilled the criteria of either “Definitely” (13 cases) or “Likely” (9 cases) acute Hepatitis C. One case was determined to be “Likely” Hepatitis C despite not having a negative HCV RNA test result in the 6 months prior to the positive HCV RNA test result. This is because the case had multiple negative HCV Antibody (immune response) test results from 2009 to early 2015 and two positive HCV Antibody test results in late 2015. The Case Review Team agreed that there was sufficient evidence that this was likely a case of Acute Hepatitis C.

Two cases were classified as uncertain as they did not have documented changes in HCV test status from negative to positive (to prove acute HCV infection). They also did not have elevations in ALT. However, the Case Review Team also noted that based on phylogenetic analysis by the Laboratory and Epidemiology teams, these cases were from the cluster. As such, even for these two cases classified as uncertain, there was no definite evidence that any of the 25 HCV cases were chronic cases.

Table C-1: Classification of Acute Hepatitis C in the Cluster

<table>
<thead>
<tr>
<th>Classification</th>
<th>Alive</th>
<th>Passed Away</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely</td>
<td>8</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Likely</td>
<td>7</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Suspected</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Uncertain</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>8</td>
<td>25</td>
</tr>
</tbody>
</table>

Mortality Review

Of the eight death cases within the cluster, the primary causes of death were infections of the lungs (pneumonia), blood (sepsis) and transplanted kidneys (graft pyelonephritis) as well as end stage kidney failure. HCV was judged to be a likely contributory factor in seven cases. The Case Review Team met with the SGH Medical Review Committee (MRC) on 9 Nov 15 to clarify facts and to understand the rationale behind their findings and determinations for each of the eight cases.

32 The Medical Review Committee was convened by SGH to review the seven mortalities out of the cluster of hepatitis C cases. This committee was chaired by Professor Teo Eng Kiong (Chairman Medical Board of CGH and a specialist in gastroenterology and liver disease), who was appointed by MOH as an independent expert in the panel.
9 The Case Review Team acknowledged the complexities involved in assessing contributory factors for death particularly as many of the patients had been extremely ill with concomitant infections. The Team also acknowledged that much effort had been taken by the MRC to elucidate the facts of the case, to review the cases in detail and to piece together a comprehensive chronology of events for each patient.

10 The Case Review Team agreed with the SGH MRC’s findings over the contribution of Hepatitis C to the death of five cases, as well as the finding that Hepatitis C was not contributory to the death of one case. However, for two other cases, the IRC members felt that they could not confidently exclude Hepatitis C as a contributory factor to their deaths. These two patients had developed multiple complications while in hospital (such as severe blood infection), and had underlying medical conditions (e.g. kidney failure) that could have led to their primary cause of death. However, they also had significant liver dysfunction such that the role of Hepatitis C in the patient’s overall medical condition and eventual demise could not be excluded.

Additional Review of Non-Cluster, Fatal Cases

11 Of the 106 death cases identified from recalling patients for HCV screening, Hepatitis C contributed to the death of one case. However, this was a known chronic case and hence not related to the cluster of acute Hepatitis C cases based on laboratory investigations, and had been infected years earlier. It was not a contributory cause of death in 12 cases, and unlikely to have contributed to the death of 82 cases. It was not possible to determine the contribution of Hepatitis C to the death of the remaining 11 cases. These patients had signs of liver dysfunction likely due to other known causes (e.g. cancer spreading to the liver which was previously diagnosed). However, as they had no recent HCV test to indicate their status upon demise, it is not possible to be more definitive. In short, on a balance of probabilities, the extent of the cluster was confined to the 25 cases found – 22 of them through SGH’s diagnosis and another three through extended screening.
ANNEX D

Phylogenetic Investigations

Phylogenetic investigations were led by Dr Sebastian Maurer-Stroh from the Bioinformatics Institute of A*STAR laboratories, and assisted by Assistant Professor Vijaykrishna Dhanasekaran from the Duke-NUS Graduate Medical School and Dr Cui Lin from the National Public Health Laboratories (NPHL), MOH. Work from these laboratories was to support epidemiological investigations. Inputs were also sought from staff from the molecular laboratory of SGH and the Division of Viral Hepatitis of the US Centers for Disease Control and Prevention (US CDC), led by Dr Scott Holmberg.

Objectives

2 The objectives of the Laboratory Investigative Team were to:

a. Review the laboratory method and sequence analysis carried out by SGH Lab.

b. Re-analyse the results provided by SGH Lab to establish the relatedness of outbreak cases, local non-outbreak cases and global data through phylogenetic analysis to:

(i) Determine if cases from the cluster fall into one close outbreak from a single source or multiple transmissions from different external sources;

(ii) Determine the closest related local non-outbreak or global sequences and their genetic distance from outbreak sequences;

(iii) Determine the fine-structure and sub-clustering of cases within the outbreak;

(iv) Conduct evolutionary analysis to provide a “molecular clock” of the origin of the outbreak; and

(v) Identify the utility of current sequencing efforts to elucidate the transmission chain of the outbreak.

Findings

3 The methods and approaches used by SGH lab were appropriate and the preliminary phylogenetic analysis and conclusions were correct.

4 Single or multiple source/outbreak? Consistent with the preliminary conclusion of the SGH lab, the detailed phylogenetics analysis conducted by the A*STAR and Duke-NUS converged on the finding that the 25 cases with available sequences were tightly clustered and closely linked, pointing to a single source of the outbreak.
(Figure D-1) The high genetic similarity suggests that cases were acute in nature as chronic cases would have had a higher divergence\textsuperscript{33}.

5 **Origin of the outbreak strain.** Phylogenetic analysis using HCV sequences from the outbreak and local non-outbreak cases (e.g. from other HCV samples available at SGH Lab) well as publicly available data showed that outbreak strains were most closely related to strains from Singapore, and thus likely not imported from overseas. Even so, there were still substantial differences in genetic material as compared to the closest known local strain.

**Figure D-1.** Phylogenetic Diagram showing Outbreak Strains Distinct from Other Known HCV Local Non-outbreak Strains and Other Publicly Available Sequences

6 **Sub-grouping of cases within the outbreak.** 24 outbreak cases had sufficient genetic material for deeper analysis by the local laboratories. There were two groups of HCV strains with highly similar genetic sequences, but were distinct from each other in eight marker (nucleotide) sites in a region named “E1HVR1” (“Group B”: 7 Cases; “Group C”: 7 Cases) (Figure D-2). Eight sites are unlikely to change independently by chance, thus strains within each of these groups could be linked by common events. The remaining cases can be summarised as a third group (“Group A”: 10 Cases). This group includes samples from earliest cases of the cluster and comprise a mix of genetic material from Groups B and C. These findings suggested that HCV genetic material from Group A may have acted as a precursor to strains seen in Groups B and C, and correspond with findings of the epidemiology team.

\textsuperscript{33} This is because HCV strains in chronic cases have a longer period of time in each host as compared to acute cases. This leads to more evolutionary changes in strains between cases.
7 **Timeline of transmission.** To estimate a timeline of transmission, “Bayesian molecular clock” analyses were conducted for the sequences generated from the outbreak cluster. However, HCV evolutionary rates had been previously examined in literature using a larger dataset\(^\text{34}\), and the lower and higher estimates of evolutionary rates from this study were used to infer the “time of most recent common ancestor” (TMRCA) for outbreak cases. Using the lowest and highest reported rates of $6 \times 10^{-3}$ sites/generation and $18 \times 10^{-3}$ sites/generation, the analysis showed that the earliest genetic diversity observed (albeit small) began during or before March 2015. This corroborates with the first detected case in early March 2015\(^\text{35}\).

\(^{34}\) de Oliveira T *et al.* Molecular Epidemiology: HIV-1 and HCV sequences from Libyan outbreak. Nature. 2006 Dec 14;444(7121):836-7

\(^{35}\) It was not possible to estimate any timelines within the outbreak (i.e. intra-outbreak timeline), due to the small number of genetic changes observed.
ANNEX E

Composition, Objectives and Methodology of the Quality Assurance Team

The Quality Assurance (QA) team was led by Ms Paulin Koh and comprised the following members:

Core Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ms Paulin Koh</td>
<td>Chief Nurse, Changi General Hospital</td>
</tr>
<tr>
<td>A/Prof Quek Swee Chye</td>
<td>Deputy Chairman of the Medical Board, National University Hospital</td>
</tr>
<tr>
<td>A/Prof Helen Oh</td>
<td>Head (Infectious Diseases), Changi General Hospital</td>
</tr>
<tr>
<td>Dr Titus Lau</td>
<td>Senior Consultant (Division of Nephrology), National University Hospital</td>
</tr>
</tbody>
</table>

Resource Persons

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Tan Hui Ling</td>
<td>Assistant Chairman Medical Board, Clinical Quality and Audit, Tan Tock Seng Hospital</td>
</tr>
<tr>
<td>Ms Sharon Salmon</td>
<td>Assistant Director, Nursing, Hospital Administration, National University Hospital</td>
</tr>
</tbody>
</table>

Invited International Experts

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Scott Holmberg</td>
<td>Chief, Epidemiology and Surveillance Branch, Division of Viral Hepatitis, CDC</td>
</tr>
<tr>
<td>Prof Trish Perl</td>
<td>Professor of Medicine and Pathology, School of Medicine, Johns Hopkins University</td>
</tr>
<tr>
<td>Dr Amanda Beaudoin</td>
<td>Veterinary Medical Officer, Division of Healthcare Quality Promotion, International Health Quality Team, CDC</td>
</tr>
<tr>
<td>Ms JoEllen Harris</td>
<td>Director, Epidemiology and Infection Prevention Program, Johns Hopkins Health System</td>
</tr>
</tbody>
</table>

Objectives

2 The objectives of the QA team were:

a. To determine the adequacy of existing standard operating processes for infection control;

b. To observe the actual practices in affected wards and compare these against the stated standards;
c. To assess whether there were any issues which may have impeded compliance to infection control processes.

Methodology

3 The QA team made a total of 18 visits to SGH from 15 October 2015 to 11 November 2015 to conduct site visits and interviews as well as to observe demonstrations of procedures by staff. The details of these visits are shown in Table E-1 and listed in chronological order.

4 The QA team made plans to visit clinical areas according to whether affected Hepatitis C cases had contact with that particular clinical area, with the aim of finding information on exposures that the cases could have encountered in these areas. Besides Wards 64A and 67, where all affected cases were admitted during April to June 2015, the QA team also visited other areas such as interventional radiology, diagnostic radiology, endoscopy and pharmacy. These areas were visited as they were areas with which many of the affected cases had contact, and the team wanted to review if there was anything in these areas which could have contributed to the Hepatitis C cluster. Additionally, the pharmacy and molecular laboratory were visited with the rationale that these areas handled patients’ medications and blood products, and were possible areas for a source of contamination.

5 The QA team observed work processes in:

   a. 6 clinical areas including Wards 64A, 67, 42 and 55, the Dialysis Centre and the Renal Intermediate Care Area. Ward 67 was also assessed for its design and layout.

   b. 6 procedural areas including Interventional Radiology, Diagnostic Radiology, Urology Centre, Urology OT, Endoscopy and the Interventional Nephrology Suites 1 and 2.

   c. Other areas including pharmacy and the molecular laboratory.

6 A total of 24 staff who had worked in the affected wards were interviewed to ascertain information on staffing, clinical workflow processes and training. Ten selected nursing and medical staff were asked to demonstrate specific clinical procedures either during actual clinical practice or in a mock set-up. Procedures observed or demonstrated included: venepuncture, cannulation, administration of intravenous medications, glucose monitoring and insulin administration. One housekeeper was also requested to demonstrate cleaning procedures.
<table>
<thead>
<tr>
<th>DATE</th>
<th>LOCATIONS</th>
<th>WHAT WAS DONE</th>
<th>IRC MEMBERS/ RESOURCE PERSONS PRESENT</th>
<th>INTERNATIONAL ADVISORS PRESENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 Oct 2015</td>
<td>Ward 64A, 67</td>
<td>Site visit, interviews with nurse</td>
<td>Ms Paulin Koh</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ms Sharon Salmon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dr Tan Hui Ling</td>
<td></td>
</tr>
<tr>
<td>20 Oct 2015</td>
<td>Dialysis centre</td>
<td>Site visit</td>
<td>A/Prof Helen Oh</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dr Titus Lau</td>
<td></td>
</tr>
<tr>
<td>21 Oct 2015</td>
<td>Ward 67</td>
<td>Interviews with 4 nurses</td>
<td>Ms Paulin Koh</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ms Sharon Salmon</td>
<td></td>
</tr>
<tr>
<td>22 Oct 2015</td>
<td>Ward 67</td>
<td>Interviews with 3 night shift nurses</td>
<td>Ms Paulin Koh</td>
<td></td>
</tr>
<tr>
<td>22 Oct 2015</td>
<td>Ward 42, Dialysis centre, ICA, Ward 67</td>
<td>Site visit</td>
<td>Ms Sharon Salmon</td>
<td>Dr Scott Holmberg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dr Amanda Beaudoin</td>
</tr>
<tr>
<td>23 Oct 2015</td>
<td>Ward 64A, 67, 42, Interventional Nephrology Suite</td>
<td>Site visit</td>
<td>Ms Sharon Salmon</td>
<td>Dr Scott Holmberg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>A/Prof Mark Chen</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>23 Oct 2015</td>
<td>Ward 67</td>
<td>Interviews with 3 renal doctors</td>
<td>Dr Titus Lau</td>
<td>Prof Trish Perl</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dr Amanda Beaudoin</td>
</tr>
<tr>
<td>23 Oct 2015</td>
<td>Ward 67</td>
<td>Interviews with 5 nurses and demonstration by 1 nurse</td>
<td>Ms Paulin Koh</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ms Sharon Salmon</td>
<td></td>
</tr>
<tr>
<td>24 Oct 2015</td>
<td>Laboratory</td>
<td>Site visit</td>
<td>A/Prof Helen Oh</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ms Paulin Koh</td>
<td></td>
</tr>
<tr>
<td>26 Oct 2015</td>
<td>Academia</td>
<td>Interview with 2 MOs</td>
<td>Prof Leo Yee Sin</td>
<td>Prof Trish Perl</td>
</tr>
<tr>
<td>26 Oct 2015</td>
<td>Pharmacy, Diagnostic Radiology, Ward 64A</td>
<td>Site visit and demonstration by 2 nurses at ward 64A</td>
<td>Ms Sharon Salmon</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dr Amanda Beaudoin</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Diagnostic Radiology</td>
<td>Site visit</td>
<td>Ms Paulin Koh</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Interventional Radiology</td>
<td>Site visit</td>
<td>Ms Paulin Koh</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Dialysis Centre</td>
<td>Site visit</td>
<td>Nil</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>DATE</td>
<td>LOCATIONS</td>
<td>WHAT WAS DONE</td>
<td>IRC MEMBERS/RESOURCE PERSONS PRESENT</td>
<td>INTERNATIONAL ADVISORS PRESENT</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------------------------------</td>
<td>------------------------------------</td>
<td>-------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Urology OT and Urodynamics Suite</td>
<td>Site visit</td>
<td>Nil</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Endoscopy</td>
<td>Site visit</td>
<td>Nil</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Ward 67</td>
<td>Interviews with 2 nurses</td>
<td>Ms Paulin Koh, Ms Sharon Salmon</td>
<td>Ms JoEllen Harris</td>
</tr>
<tr>
<td>27 Oct 2015</td>
<td>Ward 67</td>
<td>Site visit</td>
<td>Prof Leo Yee Sin, Ms Paulin Koh, Dr Jeffery Cutter</td>
<td>Prof Trish Perl, Ms JoEllen Harris, Dr Amanda Beaudoin</td>
</tr>
<tr>
<td>29 Oct 2015</td>
<td>Ward 67</td>
<td>Demonstrations by 2 nurses on ward 67</td>
<td>Prof Leo Yee Sin, Ms Sharon Salmon</td>
<td>Nil</td>
</tr>
<tr>
<td>2 Nov 2015</td>
<td>Ward 64A</td>
<td>Demonstration by 2 nurses and 1 housekeeper</td>
<td>A/Prof Helen Oh, Ms Paulin Koh</td>
<td>Nil</td>
</tr>
<tr>
<td>11 Nov 2015</td>
<td>Ward 42, 55 (control wards)</td>
<td>Demonstration by 3 nurses</td>
<td>Ms Paulin Koh, Ms Sharon Salmon, A/Prof Helen Oh</td>
<td>Nil</td>
</tr>
</tbody>
</table>
## ANNEX F

### Results from Investigative Study on Spread of HCV

**Table F-1:** Demographics and Comorbidities of HCV Infected (HCV+) and HCV Uninfected (HCV-) Patients

<table>
<thead>
<tr>
<th>Demographics</th>
<th>HCV+ (n=22)</th>
<th>HCV- (n=78)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years [Median (5th – 95th %)]</td>
<td>56(23-64)</td>
<td>54(30-71)</td>
<td>0.61</td>
</tr>
<tr>
<td>Male [Number (%)]</td>
<td>11(50.0)</td>
<td>34(43.6)</td>
<td>0.64</td>
</tr>
<tr>
<td>Admission through Emergency Department [6 Apr 15 - 28 Aug 15]</td>
<td>10 (45.5)</td>
<td>47 (60.3)</td>
<td>0.23</td>
</tr>
<tr>
<td>Length of stay in days [Median (5th – 95th %)]</td>
<td>11(4-36)</td>
<td>7(2-20)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Co-morbidities (Number, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2(9.1)</td>
<td>4(5.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0(0.0)</td>
<td>2(2.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>2(9.1)</td>
<td>4(5.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>0(0.0)</td>
<td>2(2.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Renal disease</td>
<td>21(95.5)</td>
<td>78(100.0)</td>
<td>0.22</td>
</tr>
<tr>
<td>Any malignancy</td>
<td>2(9.1)</td>
<td>4(5.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>Liver disease</td>
<td>3(13.6)</td>
<td>3(3.9)</td>
<td>0.12</td>
</tr>
<tr>
<td>Moderate or severe liver disease</td>
<td>2(9.1)</td>
<td>0(0.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8 (36.4)</td>
<td>25 (32.1)</td>
<td>0.8</td>
</tr>
<tr>
<td>Transplant local</td>
<td>17(77.3)</td>
<td>76(97.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Transplant (local/overseas)</td>
<td>18(81.8)</td>
<td>76(97.4)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

To ensure fair comparison between the 2 groups of patients, only 22 of the 25 HCV patients who likely acquired the infection during their stay in Ward 67 based on infection windows were included in the analysis.
### Table F-2: Effect Sizes for Exposure of Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude Odds Ratio</th>
<th>Length of Stay-Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay at W67</td>
<td>1.08 (1.03 - 1.15)</td>
<td></td>
</tr>
<tr>
<td>IV Bolus (ever had)</td>
<td>2.9 (1.09 - 7.70)</td>
<td>2.1 (0.74 – 6.00)</td>
</tr>
<tr>
<td>IV Bolus (number given)</td>
<td>1.1 (0.98 - 1.22)</td>
<td>1.05 (0.93 - 1.17)</td>
</tr>
<tr>
<td>IV Continuous (ever had)</td>
<td>2.4 (0.87 - 6.50)</td>
<td>1.5 (0.51 - 4.50)</td>
</tr>
<tr>
<td>IV Continuous (number given)</td>
<td>1.06 (0.91 - 1.23)</td>
<td>0.99 (0.84 - 1.18)</td>
</tr>
<tr>
<td>IV Intermittent (number given)</td>
<td><strong>1.04 (1.02-1.07)</strong></td>
<td><strong>1.05 (1.003-1.09)</strong></td>
</tr>
<tr>
<td>Hypocount (ever had)</td>
<td>1.03 (1.01 - 1.06)</td>
<td>1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td>Hypocount (number done)</td>
<td>1.03 (1.01 - 1.06)</td>
<td>1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td>Lab test (number done)</td>
<td><strong>1.02 (1.01 - 1.03)</strong></td>
<td><strong>1.03 (1.003- 1.06)</strong></td>
</tr>
</tbody>
</table>

Figures in red are significant findings.

### Table F-3: Assessing Effect Measure Modification of IV Continuous Fluids

<table>
<thead>
<tr>
<th></th>
<th>IV Continuous Present</th>
<th>IV Continuous Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted Odd Ratio</td>
<td>Length of Stay-Adjusted Odds Ratio</td>
</tr>
<tr>
<td>IV Bolus (number given)</td>
<td>1.02 (0.9- 1.2)</td>
<td>0.98 (0.85 – 1.12)</td>
</tr>
<tr>
<td>IV Intermittent (number given)</td>
<td><strong>1.03 (1.00 - 1.05)</strong></td>
<td><strong>1.01 (0.96- 1.06)</strong></td>
</tr>
<tr>
<td>IV Bolus (ever given)</td>
<td>2.7 (0.8 - 9.6)</td>
<td>1.95 (0.5 – 7.6)</td>
</tr>
</tbody>
</table>

Figures in red are significant findings.
### Timeline of Events

**Legend**
- Involves SGH
- Involves MOH
- Involves SGH and MOH

**14 May 2015:** SGH Renal team initiates review of SGH Dialysis Centre

**29 May 2015:** Conclusion that Hep C transmission in cluster not related to processes in centre

**27 April 2015:** SGH reports one Hep C infection case to NOTU

**Late Apr to 14 May 2015:** 3 more cases test positive for Hep C. Total positive cases from lab testing: 4 cases.

**26 May 2015:** NOTU suggests to SGH Renal that it should report to infection control physician for tracing of source of potential infection, and HSD is copied in the email correspondence. SGH Renal informs that it is already looking into the matter and it could be due to the switch to a more sensitive testing method.

**29 May 2015:** Conclusion that Hep C transmission in cluster not related to processes in centre

**3 June 2015:** Director (Infection Control) is informed.

**4 June 2015:** HSD informs CDD and CQPT, requests for CDD's follow-up

**5 - 8 June 2015:** Preliminary epidemiological investigation by SGH Infection Control and infection control measures instituted

**6 June 2015:** SGH lab generates the first phylogenetic tree based on polymerase region

**9 June 2015:** Cessation of multi-dosing in Renal Ward

**9 - 22 June 2015:** SGH lab conducts literature review and planning for gene sequencing study

**21 June 2015:** SGH Renal informs CQPT that investigation is in progress

**24 June 2015:** Cessation of multi-dosing in all wards

**24 June - 23 July 2015:** Frequent audits by Infection Control team

**3 July 2015:** SGH Renal team initiates review of SGH Dialysis Centre

**18 June 2015:** CDD notifies CQPT and asks that CQPT follow up on the Hep C cases, and informs that it is reportable as SRE

**19 June 2015:** SGH CEO is given a verbal briefing about the cluster.

**20 September 2015:** Report of incident to SingHealth Board

**23 September 2015:** Quality Assurance Committee convenes meeting

**24 September 2015:** Submission of SGH investigation report to DMS

**25 September 2015:** SGH briefs Minister (Health)

**28 September 2015:** Start of extended staff screening within SGH. MOH appoints members of Independent Review Committee.

**30 September 2015:** SGH reports 8th death

**6 October 2015:** SGH holds media briefing. MOH releases Press Statement on convening the IRC, its members and the TORs

**8 October 2015:** Medical Review Committee meets to review 8th mortality case

**11 June 2015:** NOTU notifies HSD and CDD of a new case, and asks CDD if SGH transplant activity should be suspended

**18 August 2015:** Finalise findings and reports from nursing, hepatology and infection control, in preparation for updating CEO, and briefing for GCEO and MOH. Work on treatment recommendations, patient assistance, and communications plan

**17 September 2015:** DMS is updated by CQPT on SGH's progress: Renal transplant was suspended, with arrangements made with other hospitals; Medical Review Committee had met on 9 Sept; and Quality Assurance Committee was intending to meet on 23 Sept.

**21 June 2015:** SGH Renal informs CQPT that investigation is in progress

**23 June 2015:** CQPT requests that SGH Clinical Governance follow up and report on the Hep C cases, and informs that it is reportable as SRE

**26 May 2015:** NOTU suggests to SGH Renal that it should report to infection control physician for tracing of source of potential infection, and HSD is copied in the email correspondence. SGH Renal informs that it is already looking into the matter and it could be due to the switch to a more sensitive testing method.

**29 July 2015:** Phylogenetic analysis of first 20 cases is completed, confirming cases are related.

**30 July 2015:** CQPT makes follow-up enquiry with Renal Unit

**18 August 2015:** CEO, CMB and Div Chair (Med) meet and plan for open disclosure to affected patients (awaiting completion of investigative findings), and to update GCEO and MOH – CMB decides that it is better to do a face-to-face meeting with MOH.

**August 2015:** Finalise findings and reports from nursing, hepatology and infection control, in preparation for updating CEO, and briefing for GCEO and MOH. Work on treatment recommendations, patient assistance, and communications plan

**24 August 2015:** CMB decides to add more controls and samples to increase the assay confidence for phylogenetic study

**3 September 2015:** DMS meets SGH

**10 September 2015:** SGH Clinical Governance and Renal on the 6 Hep C cases and states that it may need to be escalated to GCEO, GCRO and ORS

**27 September 2015:** CEO, CMB and Div Chair (Med) meet and plan for open disclosure to affected patients (awaiting completion of investigative findings), and to update GCEO and MOH – CMB decides that it is better to do a face-to-face meeting with MOH.

**August 2015:** Finalise findings and reports from nursing, hepatology and infection control, in preparation for updating CEO, and briefing for GCEO and MOH. Work on treatment recommendations, patient assistance, and communications plan

**24 August 2015:** CMB decides to add more controls and samples to increase the assay confidence for phylogenetic study

**31 August 2015:** Preliminary SGH findings are shared with MOH staff

**1 September 2015:** DMS is informed by MOH staff

**28 August 2015:** Div Chair (Med) proposes face-to-face meeting with MOH

**September 2015:** Preliminary A*STAR report largely concurs with SGH Lab findings

**9 September 2015:** Medical Review Committee convenes a meeting to review the 7 mortalities. Staff screening commences.

**18 September 2015:** Minister (Health) is informed

**20 September 2015:** Report of incident to SingHealth Board

**23 September 2015:** Quality Assurance Committee convenes meeting

**25 September 2015:** SGH briefs Minister (Health)

**5 October 2015:** First meeting of IRC

**30 September 2015:** SGH reports 8th death

**8 October 2015:** Medical Review Committee meets to review 8th mortality case
ANNEX H

Surveillance Systems

National Surveillance and Notification system

There are four notifications systems through which MOH could have been alerted of an outbreak by SGH.

a. National notification system for communicable diseases to MOH’s Communicable Diseases Division (MOH-CDD). This division has oversight over 42 legally notifiable diseases under the Infectious Disease Act (IDA) that range from Ebola to Hand, Foot and Mouth Disease. Under the IDA, medical doctors and laboratories must report acute HCV infection to MOH CDD within 72 hours of diagnosis. CDD also has community outbreak investigation and management capabilities.

b. Transplant-related notifications to the National Organ Transplant Unit (NOTU). NOTU is responsible for overseeing functions relating to human organ transplants in Singapore. It is a functional unit that is responsible to MOH’s Hospital Services Division (MOH HSD), which generally oversees clinical services in hospitals, including SGH’s Transplant Programme.

Patients who are transplanted with organs from deceased organ donors are screened for HCV at one month and three months post-transplant by the transplant centre. If an organ recipient screens positive for HCV, a notification is sent to NOTU, which identifies the donor from whom the HCV positive organ recipient received an organ and conducts tracing for other recipients of organs from the same deceased donor to determine their HCV status. SGH also has the routine practice of testing transplant recipients for Hepatitis B and Hepatitis C, when liver dysfunction is encountered. This is how most patients in the cluster were picked up, even though their liver dysfunction was mild at the time.

While NOTU is not a surveillance unit, it received the most warning signals from the Renal Transplant Team at SGH in the initial days of the outbreak.

c. Reporting of patient safety indicators from hospitals to MOH’s Clinical Quality, Performance and Technology Division (MOH CQPT). MOH CQPT monitors quality performance of restructured hospitals via quarterly reports on 9 key hospital infection indicators. Hepatitis C is not included within these indicators, as its incidence rate is generally very low. In addition, the quarterly reports are retrospective.

36 Apart from Hepatitis C, they are also screened for Hepatitis B and HIV.

37 The nine HAI indicators comprise four for multidrug resistant organisms, three device-related infections, and two surgical site infections.
Under the Private Hospital and Medical Clinics (PHMC) Act, hospitals are also required to report Serious Reportable Events (SREs) to MOH CQPT. This refers to events where there might be a negative consequence of care, which may or may not have been preventable. SGH did not report the HCV cluster as a SRE.

d. Reporting to DMS outbreaks under PHMC Act guidelines. It is a requirement for a hospital to inform the DMS immediately of outbreaks of hospital infection under PHMC Act guidelines.

SGH Surveillance System

2 Within SGH, the SGH Office of Clinical Governance (OCG) oversees issues relating to patient safety, and reports to the Chairman of the Medical Board (CMB). The Infection Control Department (IC) is part of OCG and is responsible for surveillance and control of infectious diseases. Regular surveillance is conducted of key pathogens like MRSA, VRE and CP-CRE. In addition, the Microbiology Laboratory will occasionally also alert OCG of unusual pathogens or pattern identified. Clinicians are also encouraged to report any unusual disease occurrences or incidence of infectious disease to IC. OCG is also alerted through the Risk Management System of infectious diseases contracted by staffs.

3 If a potential HAI outbreak is identified, ICD works with the department involved to contain its spread, and investigates to determine the root causes and if there are any other systemic issues like breaches in infection control that need to be addressed. SGH also has a Campus Disease Outbreak Task Force (DOTF) which is activated if there are major threats of emerging infectious disease like Ebola and MERS-CoV. In fact, during the May to June 2015 period, the DOTF was focusing its attention on MERS-CoV, as South Korea was experiencing a large MERS-CoV outbreak that threatened the entire Southeast Asia region.

4 In addition, ICD collects data on HAIs and epidemiologically significant organisms, including indicators required by MOH. The data is aggregated on a quarterly basis and sent to various parties, including SGH’s Senior Management, Heads of Department, and the Infection Control Committee.38

SingHealth surveillance and notification system

5 The above data on HAIs are also reported on a quarterly basis as part of SingHealth’s Board meetings. They are also reported to SingHealth’s Infection Control and Prevention Group which monitors infection control data from each SingHealth institution and is chaired by SingHealth’s CMB, who is also the CMB of SGH. Finally, it is reported at SingHealth’s twice-monthly CEO CMB meetings, which are chaired by GCEO.

38 This is a multi-disciplinary committee comprising staff from every department, which meets on a quarterly basis to discuss infection control issues, including surveillance of hospital infections rates and analysis of the cause of infections to improve patient care overall.
ANNEX I

Specific Recommendations made by the IRC on Infection Control

The IRC made specific recommendations to refresh and update standard operating procedures regarding infection control in particular, in the following areas:

Reduce risk of environmental contamination

2 A thorough end-to-end review of how procedures are carried out in the wards should be performed, with the specific aim of reducing the risk of environmental and cross-contamination.

3 A clean area (that is, an area free of any items potentially contaminated with blood or body fluids) should be designated for the preparation of IV medications. Items used during invasive procedures are considered contaminated and should not be brought into such designated clean areas.

4 Contamination of equipment and environmental surfaces should be avoided. This can be done through precautionary measures, which should be clearly communicated to staff (e.g., washable keyboard covers, not touching surfaces on computerised medical carts with contaminated or gloved hands).

5 If common medical carts are used to store clean supplies for intravenous procedures (e.g., needles and syringes), these should not be moved from patient to patient. In areas where they are used, care should be taken to avoid contamination of these carts with blood.

Thorough cleaning and disinfection of potentially contaminated surfaces

6 Current hospital standard operating procedures should be compared with best practices for cleaning.

7 Medical equipment (such as glucometers, dialysis machines and computerised medical carts) should be adequately and comprehensively cleaned in order that they do not become a vehicle for transmission of infection. Cleaning practices specific to computerised medical carts should follow guidelines which have been established and accepted for cleaning of computers used in medical setting - for example, those developed by the Association for Professionals in Infection Control and Epidemiology (APIC).

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39 ‘Potentially contaminated surfaces’ include any item or equipment or environmental surface that could have been contaminated with blood, or fluid containing blood.

8 Staff should understand and be familiar with mechanisms and prevention of cross-infection, as well as with rationale for changes made in infection control practices.

9 All aspects of environmental cleaning (e.g., equipment, room surfaces) should be adequately performed. The adequacy of cleaning should be uniformly assessed throughout the institution. Options for assessment of adequacy of cleaning should be considered, such as the use of fluorescent dye.

10 Nursing staff and housekeeping staff should be aware of their clearly designated roles and responsibilities with respect to responsibility for environmental cleaning.

**Standard Precautions**

11 There should be consistent practice of hand hygiene, achieving compliance with World Health Organisation (WHO)'s five moments for hand hygiene.

12 Appropriate use of personal protective equipment should be practised, including emphasis on performing hand hygiene before and immediately after removing gloves.

13 Proper use and handling of supplies for administering injections and infusions (e.g., syringes, needles, fingerstick devices, intravenous tubing, medication vials, and intravenous solutions) should be practiced. These practices are intended to prevent transmission of infectious diseases between one patient to another, or between a patient and healthcare personnel during preparation and administration of intravenous medications.

14 Practices of staff regarding intravenous interventions should include measures to maintain a closed intravenous (IV) system. For example, the cap of an IV cannula should not be removed to inject or infuse medications, but medication should be injected or infused through a side port.

15 The use of needleless IV devices should be considered, as this would allow the safe injection of medication without the use of needles.

16 CDC guidelines on recommendations for safe injection practices should be reviewed and followed, including the appropriate use of single-dose (or single-use) and multi-dose vials and the proper technique for accessing intravascular devices.

**Supervision and Monitoring**

17 The current framework for supervision and monitoring should be enhanced and robust to ensure staff comply to standard operating procedures.
ANNEX J

Specific Recommendations made by the IRC on Systems Response and Communications

The IRC made specific recommendations to enhance current surveillance and outbreak response systems to cater for unusual events, with regards to outbreak detection, investigation and management, communication and escalation protocols, and the role of MOH and the hospital, in the following areas:

Improve notification and surveillance system

2. The national surveillance system for acute HCV needs to be fine-tuned and re-organised, taking reference from international best practices and adapted to the local environment. The national surveillance and reporting system should be able to pick up both infections occurring in the hospital settings and in the community.

3. The IRC cautions that regardless of the surveillance system in place, alert healthcare professionals are still key to identifying that something might be amiss. All healthcare professionals should thus be alert to unusual events. Doctors, especially, are reminded of their obligation to report instances of infectious disease, as stipulated by MOH.

4. To this end, MOH should consider making access to notifications better, by including case definitions for example, so healthcare professionals can determine if their patients do indeed meet the case definition. One possibility is to build an electronic system where laboratories can automatically send notifications to MOH.

MOH to designate a single team within the Ministry to oversee outbreak detection and management

5. MOH should consider designating a team within the Ministry to adopt a broader set of responsibilities and functions across institutions and settings. This would include surveillance through the centralisation of all notifications, analysis and sense-making of data, signals and reports, with focus on identifying potential outbreaks. The team should possess outbreak investigation capabilities, which would include the ability to trigger outbreak investigations to reach a conclusion as to whether there is an outbreak, and the ability to mobilise different operational expertise as required.

6. Further to the above, MOH should also ensure that there is an overall plan to strengthen capabilities for outbreak investigation nationally, such that appropriate expertise needed to facilitate outbreak investigation can be activated when needed.

7. Hospitals should continue to take responsibility and ownership over investigation and management of HAIs as they are the most familiar with their own operations and management. To this end, they should develop clear structures and frameworks for the investigation and management of HAI outbreaks within their
institutions. For example, by enhancing the purview of an existing outbreak task force to oversee investigation and management of all kinds of outbreaks. If required, hospitals should enhance their relevant capabilities, or develop networks to do so. The capabilities that are needed include but are not limited to infectious diseases specialists, epidemiologists, infection control practitioners, specialised laboratory capability.

8 In addition, institutional clusters can facilitate better cross-institution frameworks for detection, investigation and management of outbreaks, to ensure that clinical entities under it are adequately resourced to cater for the possibility of an outbreak.

**Strengthen escalation processes for HAIs and unusual risk**

9 While hospitals continue to be the main owners of HAI risk, there should be better clarity about how to assess if a HAI or unusual event is significant or serious and escalation beyond the hospital is necessary.

10 In addition, incident reporting procedures need to be established for early risk escalation within the hospital, public healthcare cluster, and to MOH. Guidelines could include:

   a. Instances of mortality or instances where patients may be at risk due to past exposure;

   b. Instances in which there is a need for specialised laboratory or epidemiological investigation capabilities which the hospital does not have;

   c. Instances where case finding is required to identify exposed patients who could have caught the infection, and need early treatment; and

   d. Instances where there is a need for higher signature measures like calling back patients for testing and screening of staff.

11 Escalation within MOH needs to be reviewed and guidelines established, so that senior management are made aware of such risks in a timely way at appropriate junctures.

12 The IRC recognises that it may not be easy to set guidelines that can cater to all eventualities or situations. Thus, officers should be advised to be alert to and escalate any event that is unfamiliar and unusual events.