MEASLES VACCINATION PROGRAMME IN SARAWAK – AN EVALUATION OF SERVICE PROVISION AND UPTAKE

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FACULTY OF MEDICINE
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ABSTRACT

Since 2009, Malaysia has maintained 95% coverage of its national measles vaccination programme as recommended by the World Health Organization, and is now moving towards measles elimination. However, in 2011, Malaysia suffered a nationwide outbreak of measles. This study explored the underlying causes of the 2011 measles outbreak by looking into both user and provider perspectives of the vaccination service. This was a mixed mode study which comprised secondary data analysis, in-depth interviews and operations research. It examined the association between immunization received at inappropriate age and occurrence of measles outbreak, in addition to current evidence to determine the relevance of current age recommendation for measles vaccine. The Malaysian World Health Survey 2002 dataset was examined to determine the performance of the national immunisation programme and proposed new indicators for age-appropriate vaccination. This was followed by an operations research on the management of the immunization service, cold chain integrity, as well as providers' knowledge and practices. Lastly the experience, needs and barriers faced by non-vaccinating parents in accessing measles vaccination service were explored using qualitative in-depth interview. Delays in obtaining measles vaccine among infants increase both risk and magnitude of measles outbreak. In Malaysia, age-appropriate measles vaccine coverage was 50%, hitherto undetected due to lack of monitoring, and could have contributed to the 2004 and 2011 outbreaks. Serosurveys conducted over the past decade showed waning of maternal antibody during infancy as early as three months old, especially among children born to vaccinated mothers and premature infants. Intervention studies suggested that infants responded well to early vaccination at six months old. Twelve non-vaccinating parents from Sarawak were successfully traced and interviewed. Parents revealed they faced multiple challenges in immunizing their children. Decision on vaccination was found to be the interaction between a parent's experience with illnesses, relationship with health workers, social network, personal belief system, material circumstances and structural barriers. During the operations research 102 clinics in Sarawak were surveyed. Knowledge and practice of vaccine storage and management by health providers were found to be inadequate, further reducing the accessibility and efficacy of vaccination service. Age-recommendation for measles vaccine should be lowered to protect higher proportion of young infants. Age-appropriate vaccination indicators more accurately reflect the population susceptibility to measles and should be routinely reported. A central infant vaccination database is indicated to facilitate tracing of defaulters, and to monitor performance of vaccination service. Improving health providers' responsiveness to parents and transforming the socio-economic landscape will remove barriers to quality vaccination service for poor parents. Designing locally relevant strategies to promote vaccine acceptability would improve uptake among the hesitant parents.

ABSTRAK

Pencapaian liputan imunisasi campak di Malaysia adalah melebihi 95% semenjak tahun 2009. Ini merupakan sasaran yang ditetapkan oleh World Health Organization (WHO) untuk negeri-negeri yang ingin membasmi jangkitan campak. Namun, Malaysia mengalami wabak campak dari tahun 2011 sehingga 2013. Thesis ini mengkaji sebab-sebab terjadinya wabak campak di Malaysia pada tahun 2011. Thesis ini menggunakan metodologi campuran, yang terdiri daripada tinjauan literatur, analisa sekunder, temubual mendalam, dan kajian operasi. Tinjauan literatur mengkaji perhubungan antara kelewatan imunisasi dan kejadian wabak campak. Bukti saintifik terkini tentang umur optima untuk dos MMR pertama turut ditinjau. Dataset dari World Health Survey (WHS) 2002 dianalisa untuk menentukan pencapaian program imunisasi di Malaysia dari segi ketepatan masa imunisasi, dan mengemukakan indikator baru untuk memantau kepatuhan kepada jadual imunisasi. Ini disusuli oleh kajian operasi yang melibatkan klinik-klinik dari segi pengurusan perkhidmatan imunisasi, fungsi rangkaian sejuk, dan pengetahuan vaksin serta imunisasi kakitangan kesihatan. Keperluan ibu bapa dan cabaran yang dihadapi oleh mereka dalam mencapai perkhidmatan imunisasi turut dikaji. Kelewatan mendapat vaksin campak menyebabkan peningkatan risiko dan saiz wabak campak. Di Malaysia, kepatuhan kepada jadual imunisasi campak ialah 50% pada tahun 2002. Ini mungkin menyumbang kepada wabak campak tahun 2004 dan 2011. Sorotan literatur mengenai seroprevalens menunjukkan bayi, terutamanya anak kepada ibu yang menerima vaksin campak dan anak pramatang, kehilangan antibodi pasif terhadap campak seawal umur tiga bulan. Dalam populasi yang menerima vaksin campak, kajian menunjukkan bayi mampu menghasilkan antibodi terhadap vaksin campak seawal enam bulan. Dua belas (12) ibubapa yang tidak mendapatkan vaksin campak untuk anak mereka telah ditemubual secara mendalam. Mereka menghadapi pelbagai factor penghalang dalam mencapai perkhidmatan imunisasi dari klinik. Faktor-faktor penghalang ini termasuk

sejarah penyakit, pengalaman lepas dengan pekerja kesihatan, pengaruh dari keluarga dan kenalan, kepercayaan tentang kesihatan, kemampuan kewangan dan pengalang geografi. Dalam kajian operasi, survei telah dijalankan di 102 klinik di Sarawak. Hasil kajian telah mengenall pasti bahawa petugas perubatan yang memberikan perkhidmatan imunisasi mempunyai kurang pengetahuan tentang rangkaian sejuk, dan cara betul untuk pengendalian vaksin. Ini mungkin menjejaskan kualiti vaksin campak yang diberikan kepada bayi, dan menyebabkan kegagalan primer vaksin. Masa untuk dos pertama vaksin campak boleh diawalkan bagi tujuan melindungi lebih ramai bayi. Indikator untuk memantau kepatuhan kepada jadual imunisasi perlu dilaporkan supaya pencapaian program imunisasi boleh dipantau secara teliti. Dari segi perkhidmatan imunisasi, pengetahuan dan layanan mesra-pelanggan oleh kakitangan klinik perlu dipertingkatkan. Bagi ibubapa yang mengalami kekangan kewangan, mengadakan perkhidmatan outreach mungkin dapat meningkatkan liputan imunisasi. Perancangan polisi kesihatan secara keseluruhan, transformasi ekonomi dan strategi yang meyakinkan masyarakat tempatan tentang kepentingan imunisasi adalah mustahak untuk meningkatkan pencapaian perkhidmatan imunisasi.

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LIST OF SYMBOLS AND ABBREVIATIONS

AEFI	:	Adverse Event Following Immunisation
CDC	:	Centers for Disease Control and Prevention
EIA	:	Enzyme Immunoassay
MDG	:	Millennium Development Goals
MMR	:	Measles-Mumps-Rubella
MOH	:	Ministry of Health
SDG	:	Sustainable Development Goals
SIA	:	Supplementary Immunization Activities
UN	:	United Nations
VPD	:	Vaccine Preventable Disease
WHO	:	World Health Organization
WHS	:	World Health Survey
WPR	:	Western Pacific Region

CHAPTER 1: INTRODUCTION

1.1 Introduction

Vaccines have contributed greatly to global health. Successful examples of vaccination programmes include elimination[1] of polio and eradication[2] of small pox – both of which are deadly diseases. In the case of measles, a classic example of vaccine-preventable disease, vaccination alone has accounted for the aversion of approximately 1.6 million deaths among children annually (World Health Organization, UNICEF, & Centers for Disease Control, 2010). Out of the averted deaths, two thirds were prevented by routine infant vaccination and one third by supplementary vaccination campaigns[3] .

Notwithstanding the many young lives saved since the advent of vaccination, measles still remains a leading cause of childhood deaths. It is responsible for the occurrence of approximately 400 deaths daily worldwide, especially amongst children below the age of five (World Health Organization, Feb 2015). Measles can cause death directly and indirectly, especially amongst malnourished children living in poverty (Chen, Chowdhury, & Huffman, 1980; Morley, 1983). This is so because measles is associated with complications such as vitamin A deficiency, failure-to-thrive and

[1] Elimination: Reduction to zero of the incidence of a specified disease in a defined geographical area for at least twelve months as a result of deliberate efforts. Continued intervention measures are required (Molyneux, Hopkins, & Zagaria, 2004; Sniadack et al., 2011).

[2] Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts. Intervention measures are no longer needed (Molyneux et al., 2004).

[3] This is also known as supplementary immunisation activities (SIA), which are regular mass measles vaccination campaigns typically targeting all children aged between 6 months and 14 years regardless of their vaccination status (Lessler et al., 2011; World Health Organization Regional Office for Africa, 2010).

immunosuppression, each of which can independently lead to death in young children (Koster et al., 1981).

In reported cases, 18% of measles patients required hospitalization, whereas 8%, 6% and 0.1% of them suffered diarrhoea, pneumonia and encephalitis respectively (Centers for Disease Control and Prevention, 2012). Historically, case fatality rate of measles range between 0.1% in the developed world to 30% in situations of conflict. The estimates for measles case fatality has improved in recent years to range between 0.05% to 6% (Cairns, Nandy, & Grais, 2010). Even so, survivors of measles are not without long-term complications, as one in 10000 may eventually develop subacute sclerosing panencephalitis (SSPE) within 10 to 20 years. SSPE is characterized by seizure, memory loss, abnormal behaviour, unsteady gait, and death in late adolescence (Moss & Griffin, 2012). To date, there is no effective medical treatment for debilitating complications like encephalitis and SSPE; therefore measles vaccination remains the one and only way to completely avert measles-related deaths and disabilities in young children.

In view of the fact that vaccination is the sole measure of preventing health complications related to and deaths caused by measles, the United Nations (UN) has listed measles vaccination coverage as a key indicator for the fifth Millennium Development Goal (MDG) of reducing childhood mortality (United Nations). In conjunction with the pledge to reduce childhood mortality worldwide, the World Health Organization (WHO) had initially set a regional target for the Western Pacific region (WPR)[4] to eliminate

[4] The WPR stretches from China in the north and west, to New Zealand in the south, and French Polynesia in the east. Its member states are China, New Zealand, Australia, Philippines, Republic of Korea, Cambodia, Lao People's Democratic Republic, Viet Nam, Japan, Malaysia, Mongolia, Samoa, Singapore, Fiji, Tonga, Papua New Guinea, Vanuatu, Solomon Islands, Cook Islands, Kiribati, Brunei Darussalam, Tokelau, Marshall Islands, Federated States of Micronesia, Tuvalu, Niue, Nauru, and Palau.

measles by year 2012 (Sniadack et al., 2011; World Health Organization, 2005). Given measles is highly contagious and that there are limited means of disease containment, the success of this goal clearly hinges on the effectiveness of national measles immunisation programmes.

Being a member state of the Western Pacific Region (WPR), Malaysia needed to achieve zero incidence of measles by 2011, and maintain as such into 2012, in order to meet the regional target of measles elimination by 2012. However, this effort has not been successful, as evidenced by the nationwide measles outbreak that occurred in year 2011. This outbreak was unanticipated because as early as 2009, Malaysia had achieved a measles vaccination coverage of 95%, the population immunity threshold required to prevent further outbreaks (Anderson, 1992; Fine, 1993).

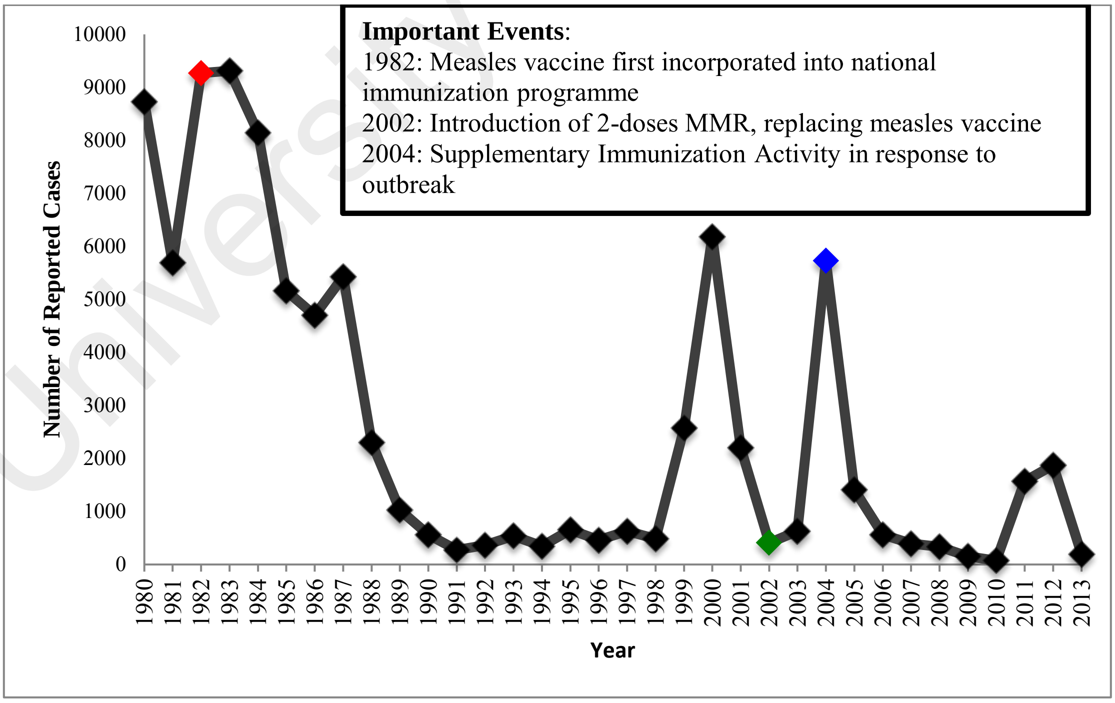


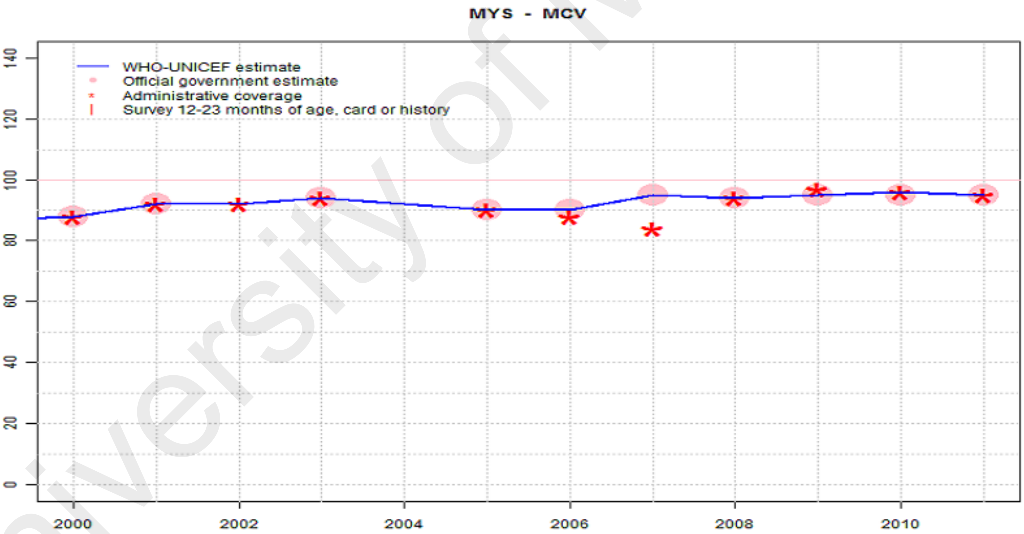
Figure 1.1: Measles cases reported in Malaysia from 1980 to 2013 (World Health Organization, 2013).

In Malaysia, whilst measles vaccination programme has a relatively short history, much has been achieved in terms of increased vaccination against measles infection and reduction in disease incidence. Measles vaccine was first included into the Malaysian national immunisation programme in 1982. Prior to the incorporation of measles vaccination, Malaysia had been reporting approximately 6000 to 9000 cases annually. As shown in Figure 1.1, starting 1992, ten years after the initiation of mass measles vaccination, less than 500 cases were reported yearly. This was a 90% reduction of incidence compared to pre-vaccination years. For two decades after 1990, Malaysia continued to make good progress towards universal measles vaccination, case reduction and elimination, save for two outbreaks in 2000 and 2004 respectively. These outbreaks were most likely due to inadequate national measles vaccination coverage then, as evidenced by the World Health Survey 2002 result that showed an actual coverage of 70% in year 2003, falling short of the 95% coverage required to ensure a herd immunity level to prevent measles epidemics during that period (Gay, 2004; Poland & Jacobson, 2012).

With heightened public health sector efforts in providing universal coverage and in part contributed by a Supplementary Immunisation Activity (SIA) campaign in 2004 in response to the 2004 outbreak, the estimated national vaccination coverage for measles had eventually reached 95% by year 2009. This high coverage has remained so since then (World Health Organization, 2012c). Coupled with the steadily decreasing measles incidence, it seemed the goal of measles elimination in Malaysia was indeed feasible by 2012.

Contrary to expectation, an outbreak of measles occurred nationwide in 2011 before finally subsiding in 2013. This event suggested that whilst Malaysia had maintained the desired vaccination coverage which exceeded 95%, it had clearly fallen short of meeting the WHO's regional targets of eliminating measles by 2012.

Unlike the previous outbreaks in 2000 and 2004 respectively, the 2011 outbreak had occurred against a backdrop of high population vaccination rates and low measles incidence since 2009. The 2000 and 2004 outbreaks occurred when the national measles coverage were 88% and 92% respectively (Figure 1.2), implying a comparatively higher degree of population under-vaccination as the likely underlying cause; however the 2011 outbreak happened when Malaysia had achieved measles vaccination coverage of 95% for three consecutive years, a level at which measles outbreak is theoretically unlikely to happen (Anderson, 1992; Fine, 1993).



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Estimate	88	92	92	94	92	90	90	95	94	95	96	95
Official	88	92	NA	94	NA	90	90	95	94	95	95	95
Administrative	88	92	92	94	NA	90	88	84	94	97	96	95
Survey	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
GoC	••	•	•	•	•	•	•	••	•	•	•	•

Figure 1.2: Measles vaccine coverage for Malaysia from year 2000 to 2011 (including WHS 2002) (World Health Organization & UNICEF, 2011)**.**

An analysis of patients' vaccination status for reported cases in the 2011 outbreak suggested that the current outbreak could result from a multitude of reasons (Figure 1.3). Among the reported cases, three-fifths of the patients had not been immunized against measles. They were either children too young to be vaccinated (32%) or age-eligible but unvaccinated individuals (28%) and 25% of the cases had previous vaccination but still acquired measles infection.

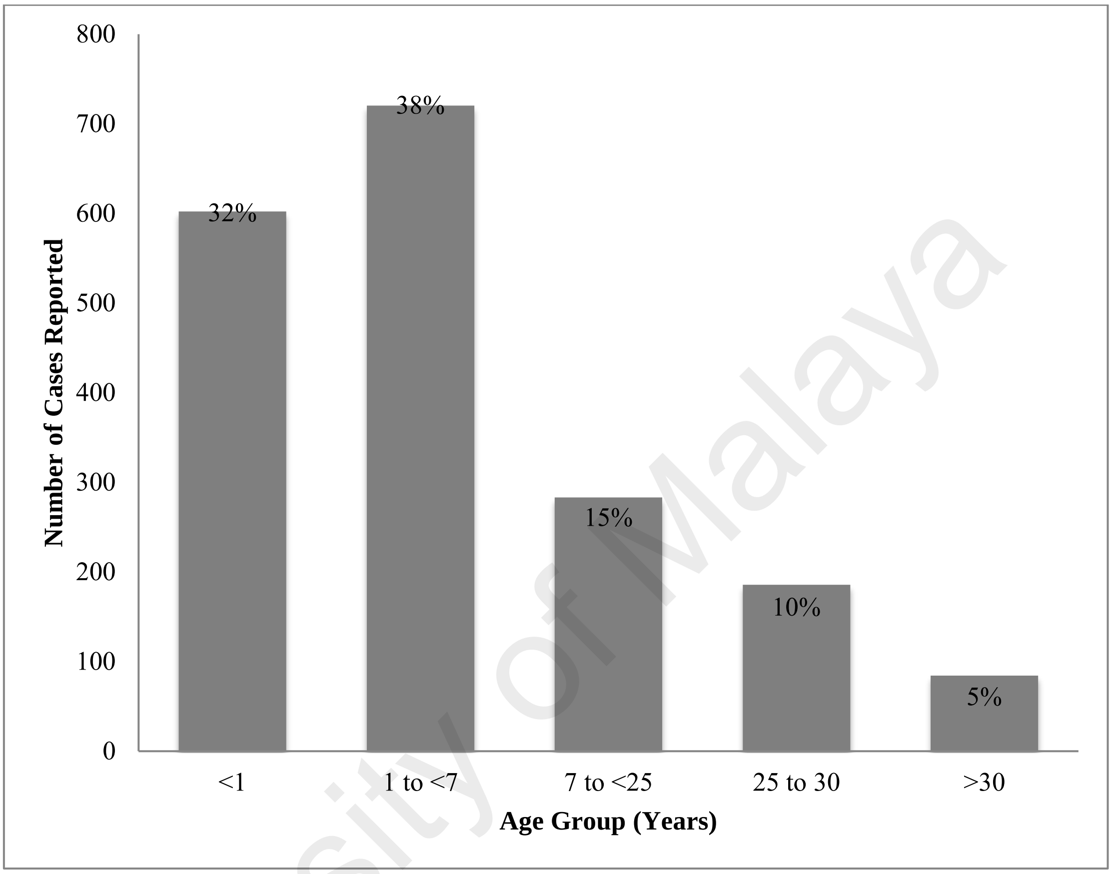


Figure 1.3: Measles cases in Malaysia by age group and vaccination status, 2011 (Ministry of Health Malaysia, 2013).

The 2011 to 2013 measles outbreak involved all 13 states in Malaysia including Sabah and Sarawak on the island of Borneo. This is an interesting case because these states are separated from the Peninsular Malaysia by the South China Sea, while at the same time, Singapore, a neighbouring country with a much closer proximity to Peninsular Malaysia, did not record any measles outbreaks. The case distribution in these Malaysian states were similar to each other and to the national distributions, suggesting that the underlying cause of the 2011 outbreak was probably systemic, or an element of the macroenvironment which exerted its influence nationwide (Ministry of Health Malaysia, 2012b). The situation in Sarawak is further described below.

Almost all cases in Sarawak were clustered in three densely populated cities of Kuching, Bintulu and Miri, which are separated by great geographical distances. Similar to the national distribution, 23% of the patients were age-eligible but unvaccinated, and another one-third had measles infection even before they reached the age of vaccination. Again, a quarter of the patients had previously been vaccinated against measles (Figure 1.4). The fact that patient vaccination profiles at state and national levels were similar implicates a common causative pathway of a systematic nature rather than due to local peculiarities.

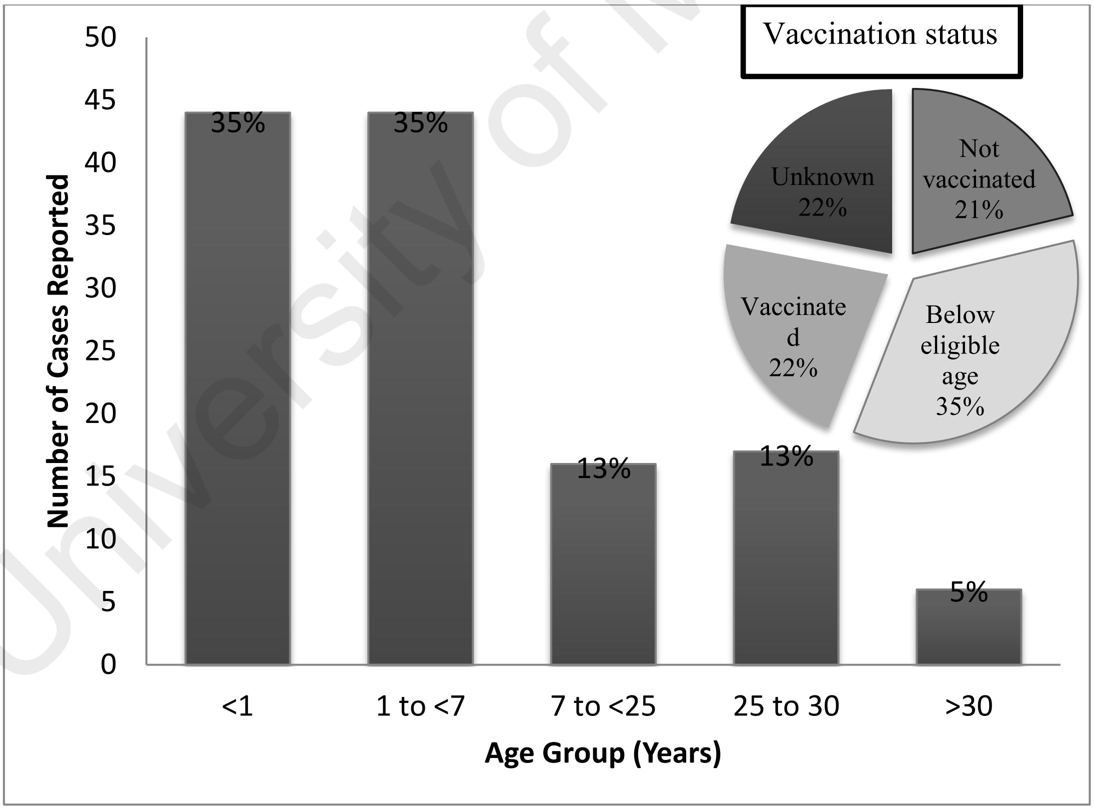


Figure 1.4: Measles cases in Sarawak by age group and vaccination status, 2011 (Abdul Kadir, 2012) .

1.2 Motivation of study

In view of the above observations pertaining to the 2011 outbreak, the mixed pattern of vaccination history among measles patients suggested a multifactorial causation pathway for the recent outbreak as compared to older outbreaks which were most likely due to population under-vaccination. Whilst failure to vaccinate susceptible populations remains a main public health concern, the presence of vaccinated patients suggested that vaccine failure could be another important cause.

Vaccine failure has been defined as “the occurrence of the specific vaccine-preventable disease in a person who has been appropriately and fully vaccinated taking into account the incubation period and the normal delay for the protection to be acquired as a result of immunisation” by Heininger et al (Heininger et al., 2012). Its underlying causes encompass a wide range of issues involving the process of delivering a vaccine from its manufacturing sites, via various storage points to its final recipient, which requires flawless logistics and strict adherence to cold-chain maintenance procedures. Furthermore, a vaccine administered in perfect condition to a child may still fail to elicit the desired immunological response.

Vaccine-related vaccine failure can be due to manufacturing defect and deficiency in vaccine efficacy caused by poor storage conditions or incomplete coverage of known pathogen strains.

Vaccinee (host)-related vaccine failure denotes lack of seroconversion caused by various health conditions like immunodeficiency, infection, malnutrition, immature immune system, interference from maternal antibody or recently administered immunoglobulins (Heininger et al., 2012). Initial inability to mount appropriate immune response to a vaccine is termed primary vaccine failure, while waning of immunity after initially successful immunisation is termed secondary vaccine failure (Mathias et al., 1989; Pannuti et al., 2004; Reyes et al., 1987).

There is evidence that vaccines provided via public health facilities were exposed to unfavourable ambient temperature, making primary vaccine failure a real possibility. This widely quoted study involving health clinics in Kelantan, a state in northern Malaysia, on cold chain integrity was done in 1996 by Hanjeet et al, and reported various weaknesses in the vaccine distribution process (Hanjeet et al., 1996).

In general, vaccine failure is more often the result of insufficiencies in the health system that prevent the delivery of a vaccine of good quality to an immuno-competent infant, thus culminating in a futile attempt to generate and maintain immunity to the disease it is supposed to prevent.

On the other hand, failure to vaccinate happens when a vaccine is not appropriately administered to the indicated population for any reason. Failure to administer a vaccine can stem from two major categories of instances, namely, usage issues such as non-compliance of the target population or administration errors; and programme-related issues like vaccine shortages and inappropriate recommendations especially those that dictate inappropriate timing and number of doses for a vaccine (Heininger et al., 2012). Though many of children who came down with measles during the 2011 measles outbreak were below the recommended vaccination age of one year, the Ministry of Health Malaysia (MOH) only changed the recommended age for MMR vaccinations from twelve months to nine months in 2016, five years after the outbreak occurred (Ministry of Health Malaysia, 2016).

There are also inherent characteristics in the national health system that could potentially reduce the performance of the health system in delivering vaccines to all children who need the service; for example, shortages in manpower and transport that are vital in ensuring adequate contact between providers and recipients.

An additional factor that may impede effective vaccination as regards the Sarawakian children population may also be attributed to its geography of mountainous terrain, extensive coastlines and porous borders. These factors expose Sarawak to irregular in-migration of citizens from neighbouring countries, especially Indonesia and Philippines. The Sarawak State Health Department measles statistics indicated that 15% of reported cases in 2012 were non-citizens. With exception of one case (Vietnamese), all were Indonesians. Their vaccination status were reported as unknown, presumably because they could not recall or had no documentation of their vaccination history.

Therefore it was not unreasonable to speculate that among the non-citizens, measles vaccination coverage was low. As people of similar sociodemographic background tend to live in the same residential area, the migrants might form a close knitted community which was susceptible to infection and conducive to the rapid spread of measles through this subpopulation.

As migrant workers and their children were not included in the Sarawakian population census, the issue of low vaccination uptake in this community might not be obvious to the health authorities. Unless they had accessed the public health system voluntarily, it was difficult for the local maternal and child health teams to detect unmet needs of the migrant population, and to offer them the much needed vaccination and other preventive services.

The existence of these vulnerable subpopulations who do not have ready access to public health services for various reasons had directly affected efforts by the local health authorities to contain the measles outbreaks, and hence defeated the purpose of the free-vaccination-to-all policy, which had been implemented by the Ministry of Health (MOH) until the fee schedule revision in 2014 that imposed vaccination charges on non-Malaysians. The fears and possible negative perceptions experienced by such vulnerable populations need to be explored and actively removed before high population measles vaccination coverage can be achieved in its truest sense.

Another possible reason for this apparent discrepancy between vaccination coverage rate and actual population immunity could be due to delayed, or untimely vaccinations undetectable through annual national statistics on vaccine coverage. Delayed vaccination creates a period of vulnerability to infection between planned and actual vaccination dates. Although the year-end statistics can indicate a good population vaccination coverage rate, it does not account for the months during which some children remain susceptible to measles infection due to vaccination delays. In the event these children come into contact with any measles patient, they would in turn become reservoirs of infection and propagate an outbreak.

In Malaysia, the indicator often used to measure the performance of measles vaccination programme is the annual vaccine coverage rate. The overall national coverage has the advantage of being a standardized indicator recognized by the World Health Organization to enable cross-country comparison and monitoring of trends. However, this annual national coverage performance may not be adequate as an assessment tool, be it to predict population immunity against measles or to measure the effectiveness of vaccination services; nor can it answer the question of whether all children are protected by a vaccine as soon as they lose their passive immunity.

The available data give only a picture of successful vaccination programme, with no indication on its quality. Little is known about how the vaccination service was organized and provided, the quality of vaccine providers and the experience of parents as the group most affected by vaccination service. Such information provides vital insights into the contextual factors that interact with parental vaccination behaviours that will influence the success or failure of a health programme, and can potentially guide policy makers in improving vaccine service delivery (Jack, 2006).

In view of the complexities of issues that potentially contributed to the occurrence of the recent measles outbreak, research that fully evaluates all aspects of vaccination service is more appropriate to answer the question why a measles outbreak occurred despite statistics showing excellent vaccination coverage. As far as is known, a comprehensive evaluation of measles vaccination programme has not been undertaken locally to look into the causes of the 2011 measles outbreak.

1.3 Study Objectives

Having realized the need of a study to gain a greater understanding than that supplied by available data, and provide a new perspective to community interaction with the vaccination service providers, this study was designed to investigate the underlying causes of the measles outbreak in Sarawak which occurred in 2011.

As with all other public health programmes, running a vaccination service requires a combination of programme planning at policy-makers' level, followed by service organization and implementation at the ground level. The proportion of population vaccinated, on the other hand, is the end product of vaccination service utilization by the community, which in turn is determined by access issues such as availability, geographic accessibility, affordability and acceptability (Jacobs et al., 2012; O'Donnell, 2007).

Certain factors that could negatively affect vaccine uptake and coverage such as setting the age eligibility and vaccine information database are determined at programme planning level. Thus the first group of study objectives are aimed at evaluating the organization of health services, mechanisms to ensure age-appropriateness and age recommendation for measles vaccination at the national level.

Actual access, uptake and delivery of vaccines occur at the ground level, and are very much influenced by local factors such as historical, social, cultural and demographic background of parents or guardians. As the largest state in Malaysia, Sarawak faces more challenges in delivering effective vaccination service to the population in the forms of limited land transport network, harsh geographical terrain, widely dispersed rural clinics compared to other states. Therefore studies on the provider-recipient interface are conducted at the state level in Sarawak because these sites are most likely to yield information on gaps in implementation of services on the ground.

Study objectives are listed as follows.

1. To develop a conceptual framework to evaluate the contributing factors leading to the measles outbreak in Malaysia in 2011
2. To review development of the national vaccination programme in Malaysia to identify changes that may have contributed to the measles outbreak in Malaysia in 2011
3. To review evidence of relationship between delayed vaccination and occurrence of measles outbreaks
4. To review evidence for optimal age for measles vaccination
5. To identify appropriate indicators of measles vaccination coverage that may be predictive of future occurrence of measles outbreaks in Malaysia
6. To evaluate maintenance of measles vaccine cold chain as a contributing factor to occurrence of the 2011 measles outbreak in Sarawak.

7. To evaluate levels of measles related knowledge and practice of measles vaccination among health staff as a contributing factor to occurrence of the 2011 measles outbreak in Sarawak
8. To explore factors that may have resulted in parents' decisions not to vaccinate their children that could have contributed to occurrence of the 2011 measles outbreak in Sarawak.
9. To identify factors that may have contributed to the measles outbreak in Malaysia in 2011, consequently policy recommendations for improvement of the national vaccination programme in Malaysia and other developing countries.

1.4 Public health significance of study

This study evaluates measles vaccination programme from the perspective of timely coverage, in contrast with the traditional annual coverage. It aims to provide a more accurate assessment of adequacy of protection to the Malaysian population as offered by the existing vaccination programme.

As mass vaccination alters the population's immunity against measles infection, the epidemiological landscape for measles and causation of outbreaks understandably differ from pre-vaccination era. By constructing a conceptual framework, this study hopefully serves as a foundation for future research in enriching knowledge on alternative pathways of measles outbreak other than purely from the viewpoint of under-vaccination.

From the policy makers' point of view, this study offers insights into parents' knowledge and experience which subsequently guide their decision to utilize vaccination service or otherwise, as well as explores the barriers that prevent parents from accessing vaccination service on time. By using qualitative methods, this study can potentially uncover unvoiced needs and concerns that may not be possible to elicit using conventional, quantitative study designs.

From a provider's point of view, this study adds to the body knowledge that addresses health providers' competency on childhood vaccination management and vaccine maintenance. It also provides baseline data on vaccination practices by private and public providers. This is especially important in Malaysia, where health care services are provided by a dichotomous system which comprises a government-led and funded public sector, and a private sector.

The results of this study will serve as evidence base for policy makers to monitor if the local vaccination programme is achieving its goal, by indirectly assessing whether the vaccination services are user-friendly and easily accessible by the local population. This can also be extrapolated to the performance of other preventive health services in general because these services are also offered in the same settings.

By highlighting gaps in the vaccination services that need strengthening, the evidence gathered can become the empirical data to serve as the basis for developing and re-testing effectiveness of any interventions to improve the national immunisation programme.

1.5 Thesis layout

Following the first chapter on Introduction, Chapter 2 is a literature review that examines evidence on various systematic, structural and societal factors that culminate in the occurrence of a measles outbreak. The findings are collated to construct a conceptual framework that serves as a road map to the study as a whole.

Chapter 3 sets out the basic features of the Malaysian health system. It is designed to provide a background and contextual information to national immunisation programme as a whole, with measles vaccine as one among the seven routine, free vaccines given to children residing in Malaysia.

Chapter 4 looks in greater detail at available evidence on the association between delayed vaccination and the occurrence of measles outbreaks that examines delayed vaccination as a valid cause of failure to eliminate measles from a geographical region.

Chapter 5 examines the evidence for policy recommendations of the optimal age for the first measles vaccination, whether it be twelve months as practised in 2011, or the current nine months after the policy change in year 2016. Evidence from the last 10 years was reviewed to determine the level of immunity against measles infection and the earliest possible age of immune response to measles vaccine in the modern-day infants.

Chapter 6 appraises the performance of vaccination programme in Malaysia by evaluating the extent of delay in measles vaccination among children aged five years and younger, with the aim of improving monitoring of childhood vaccination programme by additional performance indicators.

Chapter 7 evaluates levels of knowledge, experience and practices of health care providers who administer vaccines to children. The performance of cold chain equipment in each clinic was also appraised. These issues are of fundamental importance to successful inoculation of measles vaccine in infants, with ultimate implication on population herd immunity against measles infection.

Chapter 8 examines barriers to vaccination as experienced by parents who did not attend measles vaccination sessions, either deliberately or unintentionally.

The final chapter is an overall discussion of the challenges for immunisation programme in achieving and maintaining robust herd immunity, with conclusion and policy recommendations for the future direction of an improved programme for elimination of measles for Malaysia and other developing countries.

CHAPTER 2: A FRAMEWORK FOR EVALUATING MEASLES OUTBREAKS IN VACCINATED POPULATIONS

2.1 Introduction

Theories are important in guiding research, as they provide coherent and systematic explanations of an event, identify concepts or, explain relationships in an understandable way (Glanz & Bishop, 2010; Meleis, 2005).

This chapter reviews evidence on measles outbreaks occurring around the world in the post-vaccination era and the causes behind such outbreaks. It examines factors that may have influenced the effectiveness of immunisation against measles infection through a theoretical lens and attempts to summarize possible gaps in measles elimination programmes as presented in available literature.

The review addresses two main areas related to the current challenges in measles vaccination and elimination as faced by Malaysia, namely failure to vaccinate and vaccine failure. Section 2.2 gives an overview of measles as a disease of public health importance. Section 2.3 examines measles epidemiology especially concentrating on countries anticipating measles elimination. Sections 2.4 to 2.8 focus on studies addressing various probable causes of measles outbreaks in the modern era. Section 2.9 presents the conceptual framework which is developed from reviewed evidence on factors leading to measles immunisation failure which is applied in this thesis. The chapter then concludes with a summary in section 2.10.

2.2 Public health significance of measles

Measles is a highly contagious disease. The basic reproductive number (R_0), which is defined as the average number of people infected by one infectious person in a completely susceptible population, for measles is between 12 to 18 (Fine, 1993). One measles patient is capable of transmitting the disease to at least 12 contacts. This is high in comparison to other childhood diseases like polio and small pox, each of which has an R_0 range of 5-7 (Anderson, 1992; Fine, 1993).

Due to the infectious nature of measles, before measles vaccine was available in 1963, measles affected mainly children in the age group of five to nine years, and 99% of the population had had measles by the age of 20 years (Centers for Disease Control and Prevention, 2012). In the pre-vaccine era, measles was responsible for at least 15000 cases of blindness per year worldwide (World Health Organization, 2012a).

The development of measles vaccine and its inclusion into routine childhood immunisation programmes had greatly altered the epidemiological landscape for measles infection. In the past decade, there was a 75% reduction of measles-related deaths from 733000 in year 2000 to 146000 in year 2013. This translates to an impressive 1.6 million averted deaths per year which were attributable to measles immunisation (Perry et al., 2014).

The effectiveness of measles vaccine is due to several facts. Firstly, measles has a short period of contagiousness and illness; secondly, humans are the only reservoir to maintain virus transmission (Moss, Ota, & Griffin, 2004); lastly, both natural infection and vaccination confer long-lasting immunity against measles infection (Moss & Scott, 2009). Consequently it is logical to postulate that if enough people are immune against measles, viral transmission will stop and it will become possible to eradicate the disease from the population.

The global health significance of measles is also evident in the emphasis placed by WHO on its elimination. In 2003, the Regional Committee for the Western Pacific

(WPR) established the regional goal of measles elimination. This was followed-up in 2005 by establishment of 2012 as the target year for measles elimination. However, this goal was not met (Strategic Advisory Group of Expert, 2012.). In 2012, the World Health Assembly endorsed the Global Vaccine Action Plan with the new objective to eliminate measles in four of the six WHO regions by 2015, namely America, Europe, Eastern Mediterranean and the Western Pacific (Strategic Advisory Group of Expert, 2014).

As an integral component of disease elimination, measles vaccination also carries important public health and economic significance. It is so well-aligned to the fourth MDG of reducing under-five mortality by two-thirds between 1990 and 2015 that measles vaccination is listed as one of the milestones for monitoring individual country performance and progress towards that goal (United Nations, 2014). After 2015, the MDGs were succeeded by the Sustainable Development Goals (SDGs), among which vaccination and elimination of infectious diseases were few of the many health goals. The fourth MDG was continued as the SDG 3, under the subgoal 3 of ending preventable under-five deaths by 2030. The role of vaccination was recognised in the additional subgoal 8 of achieving universal health coverage, affordable essential medicines and vaccines for all (United Nations Development Group, 2015).

Unfortunately, despite success in reducing measles-related deaths, progress towards disease elimination has stalled since 2008. This is largely due to numerous prolonged measles outbreaks in the African, Eastern Mediterranean and European regions. Similarly, progress in WPR was set back by outbreaks in China, Philippines and Vietnam. Thus, with the exception of America, the WHO had already concluded in 2014 that regional elimination of measles would not be achieved on time (Strategic Advisory Group of Expert, 2014).

2.3 Measles Resurgence

In the past decade, there is a widespread resurgence of measles in both developing and developed world. As of the end of 2013, large outbreaks were still being reported in the Democratic Republic of the Congo (89,108 cases), India (13,822 cases), and Pakistan (8,749 cases), and new outbreaks were reported from Nigeria (52,852), and China (26,883) (Perry et al., 2014).

Similarly, European countries were also facing a series of outbreaks, especially in communities that declined vaccination for various religious or philosophical reasons. More detailed description of recent measles outbreaks is given in Table 2.1.

Table 2.1: Measles outbreaks in developed nations

Country	Year	Total Cases	Fatality	Complications	Affected group	Source
Switzerland	2006-2009	4415	0.02%	Hospitalization (7.9%) Pneumonia (4.1%) Encephalitis (0.2%)	2.6% below 1 year; 66% between 5 to 19 years (school-age); 19% 20 years and older.	(Richard & Masserey Spicher, 2009)
Austria	2008	394	0	Otitis media (3%) Pneumonia (2%) Hospitalization (11%)	0.2% (1 case below 1 year); 52% between 10 to 19 years.	(Schmid et al., 2010)
Belgium	2008	137	0	Respiratory tract complications (14%) Hospitalization (7%)	12% below 1 year (9% between 6 and 12 months); 81% below 10 years	(Lernout et al., 2009)
Germany	2008	217	0	Hospitalization (11%) Otitis media (9%) Encephalopathy (12%) Pneumonia (4%)	Highest incidence below 14 years old.	(Wadl et al., 2011)
Spain	2008	155	0	(information not available)	19% under 2 years; 51% between 21 to 40 years.	(Nieto Vera et al., 2010)

Table 2.1: Continued

Country	Year	Total Cases	Fatality	Complications	Affected group	Source
United Kingdom	2008	276	0	(information not available)	9% below 15 months; 62% between 5 to 19 years (school-age).	Kumar V, 2008 (Kumar, 2008)
France	2008-2010	4753	0.06%	Hospitalization (29.7%) Encephalitis (0.06%) Pneumonia (5.3%)	9% below 1 year (56% younger than 9 months). 38% 20 years and older. Highest age-specific incidence rate for age < 2 years.	(Parent du Châtelet et al., 2010)
Austria	2009	37	0	Otitis media (5%) Hospitalization (5%)	2.7% (1 case) below 1 year; 43% between 5 to 9 years.	(Kasper et al., 2009)
Bulgaria	2009	957	0	Hospitalization (69.7%) Pneumonia (31.3%) Diarrhoea (11.5%)	13% below 1 year; 20% between 1 to 4 years; 13% older than 20 years.	(Marinova et al., 2009)
Ireland	2009-2010	320	0	Hospitalization (36%) Pneumonia (5%) Gastrointestinal upset + dehydration (0.9%) Pneumothorax (0.3%) Convulsion (0.3%)	18% below 1 year (incidence rate 52.4 per 100000); 10% above 20 years old	(Gee, Cotter, & O'Flanagan, 2010)
Poland	2009	41	0	Hospitalization (53.7%) Pneumonia (9.8%) Myocarditis+encephalitis (2.4%)	12% below 1 year; 33% older than 20 years.	(Orlikova et al., 2010)

Table 2.1: Continued

Country	Year	Total Cases	Fatality	Complications	Affected group	Source
France	2010	384	0	Hospitalization (32%) Encephalitis (0.2%) Pneumonia (6%)	10% below 1 year; 25% between 20 and 29 years; Highest incidence in children under 2 years.	(Six et al., 2010)
Germany	2010	71	0	Hospitalization (5%)	6% below 1 year; 27% below 5 years 25% between 6 to 10 years;	(Roggendorf et al., 2010)
Greece	2010	126	0	Hospitalization (66,4%) Pneumonia (14.4%) Meningitis (0.8%)	8% below 1 year; 27% between 1 to 4 years; 33% older than 20 years.	(Pervanidou et al., 2010)
Belgium	2011	155	0	Hospitalization (12%) Pulmonary complication (4%) Septic shock (0.6%) Encephalitis (0.6%)	8% below 1 year; One-third 15 years and older	(Sabbe et al., 2011)
Canada	2011	750	NA	NA		(De Serres et al., 2012)
Romania	2011	2072	0	Pneumonia (72.8%) Diarrhoea (25.4%) Convulsion (0.62%) Encephalitis (0.25%)	15% below 1 year; 43% between 1 to 4 years; 7% older than 20 years	(Stanescu et al., 2011)

Table 2.1: Continued

Country	Year	Total Cases	Fatality	Complications	Affected group	Source
England	2012	359	0	Hospitalization (17.5%)	23% below 1 year, ineligible for vaccine (19% between 6 and 12 months); 30% older than 15 years old.	(Vivancos et al., 2012)
Spain	2012	109	0	Hospitalization (10.1%) Pneumonia (1.8%)	16% below 15 months; 38% above 20 years old.	(Delgado de Los Reyes et al., 2012)
United States	2011	118	0	Hospitalization (39.8%) Pneumonia (7.6%)	15% below 1 year; 19% between 5 and 19 years; 45% above 20 years.	(Centers for Disease Control and Prevention, 2011)

Measles resurgence in these developed countries was a phenomenon which contradicted previous understanding on measles outbreaks: that outbreaks occur mainly in populations with low socioeconomic status and who have limited access to healthcare (Kaler, 2008; Muscat, 2011; Simons et al., 2012). Most of the developed countries mentioned in Table 2.1 were not those with documented major issues of access to health infrastructure or preventive health services.

Data from the country reports showed that reported measles cases were a mix of patients who were previously unvaccinated, those too young for vaccination and those with documented complete measles vaccination. These data indicate that measles resurgence in recent years is the result of persistent circulation of measles virus among pockets of susceptible persons. Susceptibility can be attributed to factors like primary vaccine failure in the vaccinated children, waning of immunity after initial success at generating antibody response, low vaccine coverage, and loss of maternal antibody (Leuridan, Sabbe, & Van Damme, 2012).

In the subsequent sections, factors leading to measles outbreaks will be discussed in detail. These are failure to vaccinate, vaccine failure due to poor vaccine quality, waning immunity years after vaccination, and susceptible infants due to policy recommendations of inappropriate timing of first measles vaccination.

2.4 Outbreak due to low vaccination coverage

EUVAC.NET, a surveillance network for vaccine-preventable diseases in Europe reported that major measles epidemics still occur annually. Among the countries affected were United Kingdom (Gee et al., 2010), France (Botelho-Nevers, Chevereau, & Brouqui, 2010; Parent du Châtelet et al., 2010), Germany (Batzing-Feigenbaum et al., 2010), Italy (D'Agaro et al., 2011), Austria (Schmid et al., 2010), Bulgaria (Marinova et al., 2009), and Romania (Stanescu et al., 2011). These outbreaks were associated with several deaths and severe complications (Carrillo-Santisteve & Lopalco, 2012; D'Agaro et al., 2011). According to an epidemiological review, countries where measles vaccination coverage rates were consistently lower than 90% since 2000 were more likely to have higher measles incidence(Cottrell & Roberts, 2011).

The publication of a study that suggested association between autism, inflammatory bowel disease and the MMR vaccine by Dr Wakefield in year 1998 caused a marked decline in MMR uptake (Godlee, Smith, & Marcovitch, 2011). In England, the vaccine uptake rate fell from 92% in year 1995 to 82% in 2005 (Asaria & MacMahon, 2006). Although the article was subsequently retracted, the impact of the article and ensuing media coverage was seen globally in the form of Measles-Mumps-Rubella (MMR) vaccine refusal. In London itself, the United Kingdom Health Protection Agency reported the MMR uptake to be just 77% during year 2007 (Ashmore et al., 2007). Subsequently in year 2008, for the first time after 14 years of no local transmission, the Health Protection Agency declared measles to be endemic in United Kingdom due to poor vaccination coverage (Editorial team, 2008).

Likewise in Ukraine, measles vaccination coverage had fallen from 98% in 2006 to 56% in year 2010, a result of on-going vaccine shortage combined with reported adverse events associated with MMR vaccination (European Centre for Disease Prevention and Control, 2012). As a result, Ukraine experienced an outbreak in 2012. Within the first 6 months of 2012, a total of 10 386 measles cases were reported (ProMED-mail, 2012), prompting the European Centre for Disease Prevention and Control to issue a health warning to potential travellers to Ukraine.

Another example was seen in the Republic of the Marshall Islands in year 2003, where a large outbreak involving 857 measles cases were reported in a population of merely 51 000 people. This outbreak occurred after 14 years of zero incidence in the country. It had also coincided with a decline in measles vaccination coverage from 93% in 1998 to just 80% in 2001 (Marin et al., 2006). However, the author did not provide further insights as to the cause of decline in the vaccination coverage.

Therefore, a logical temporal relationship could be drawn between declining vaccination coverage and subsequent measles outbreaks. An outbreak can thus be seen as a sensitive indicator of declining or inadequate vaccination uptake in the population.

2.4.1 Determinants of low utilisation of vaccination services

Various models have been developed to explain the interrelationship between people attributes and health system characteristics, and their association with vaccination.

2.4.1.1 Population determinants

(a) Socio-economic and demographic background of family

Generally, studies worldwide found that higher socioeconomic status and increased contact with the health services are indicative of better vaccination uptake.

A community survey in Belgium involving 1476 families found that factors that predicted a complete and valid vaccination status in children were: vaccination by paediatricians or in dedicated well baby clinics, mothers who were employed full-time and families with higher incomes (Theeten et al., 2007).

A smaller community survey (n=668) in Mozambique found significant importance in socioeconomic background in influencing the vaccination status of a child (Jani, De Schacht, et al., 2008). Risk factors for incomplete vaccination were: born outside

Mozambique (migrants), child delivered at home, mother had no formal education and poor accessibility of vaccination facilities (travelling time in excess of 60 minutes).

Looking at developed countries, a household survey conducted in four underserved communities in United States found that vaccination uptake was negatively associated with private health provider, and parents who did not keep vaccination cards (Rosenthal et al., 2004).

(b) ***Maternal Characteristics and Knowledge***

Maternal characteristics are the best-known determinants of the child's vaccination status.

Rahman analysed the data of 3530 children from a large-scale health survey in Bangladesh, (Rahman & Obaida-Nasrin, 2010). Higher rates of full-vaccination were associated with increase in previous birth interval, mother who was educated, mother who received anti-tetanus injection, mother in the highest wealth index group, parents who were exposed to mass media and health facility near home (shorter than one km). In short, an empowered mother was a positive predictor of the vaccination status in the child.

In Pakistan, Cockcroft et al conducted a household survey of 10423 mothers. They also found positive correlation between maternal health knowledge, in addition to socioeconomic status with the child's vaccination status (Cockcroft et al., 2009). Likelihood of receiving measles vaccination was associated with better socioeconomic status, mothers who had formal education, mothers who knew of at least one vaccine preventable disease, mothers who had not heard of bad effects of vaccination, family discussions about vaccination, living within five km of vaccination facility (for rural communities only), vaccination team who performed extended home visits (for rural communities), and mothers who received information on vaccination from home visitors.

(c) Satisfaction with health service

Factors like distance from facilities, previous unpleasant experience with vaccination, long waiting time and poor relationship with vaccination team affect parents' decision to vaccinate their children.

In Nigeria, a household survey was conducted by Abdulraheem on 685 mothers(Abdulraheem et al., 2011). He showed that the main reasons for incomplete vaccination in the children were: parental objection or concerns about vaccine safety, long distance travelling to health facilities, and long waiting time at health facilities.

A study was conducted by Friede et al in rural Philippines (Friede et al., 1985) in which 94 families were interviewed. Non-attendance of vaccination campaign was associated with bad weather on day of vaccination, inconvenient vaccination time, vaccination site more than 0.5km from home, receiving care from traditional practitioner, parents who were not members of their village councils, and perceiving pain as a deterrent. Again, socioeconomic factors did not appear to play a significant role because the study was done in a generally poor region.

In Malaysia, a cross-sectional study was conducted in 10 health clinics in Kota Kinabalu in the state of Sabah(Shamsul Azhar et al., 2012). Among the 53(16.8%) children who defaulted on vaccination schedule, identified risk factors were mothers with full time employment, older mothers and bigger family sizes. Costs, transport, perception of service quality and maternal education were not significant factors (contrary to other studies). The finding that mothers with employment tend to default vaccination appointments also differed from studies done elsewhere. However, more studies with representative samples need to be conducted in order to draw conclusive inference about the Malaysian population.

Hence, further comprehensive studies on community perception of the health service are still necessary to fill knowledge gaps on parental views in Malaysia.

2.4.1.2 Health care system determinants

In developing regions, the main problems of health care delivery are logistics and access. Some of the studies illustrating importance of access as a determinant of vaccination status in children were already discussed above.

Mitchell's research in Pakistan involved 2479 mothers from both rural and urban communities(Mitchell et al., 2009). A universal factor that determined vaccination uptake among urban and rural children was access to government facilities providing vaccination services.

Haddad et al performed a comprehensive case-series study on system-related factors that determine performance of vaccination programmes in Burkina Faso. As a minimum requirement, performance or breakdown of health service depended on having a certain amount of technical and financial resources. Beyond the minimum requirement, a strong leadership was the determinant to ensure effective mobilization of resources and good performance (Haddad et al., 2009).

In 1994, Dietz et al conducted a state-wide survey involving all 227 public health clinics in Georgia (Dietz et al., 2000). Higher performance of health clinics was associated with six factors: no waiting time, telephone reminder system, home visit for defaulter, incentive for caregiver, incentive for nurses, and nurse participating in audit process. In contrast, low clinic vaccination performance was associated with needing to conduct special community vaccination campaigns, and charging fees for vaccines.

In summary it is important to identify factors in the health system that facilitate access to quality vaccines. This is most relevant to those at risk of suffering the consequences of measles outbreaks. These are frequently the socioeconomically disadvantaged people, as they have the least means to source alternative providers if they were deterred from utilizing vaccination service in the clinic designated to serve their area.

2.5 Outbreaks despite high vaccination coverage

As documented at the beginning of the chapter, it should not be assumed that measles occurrence would be low in countries with high official vaccine coverage figures. In such regions, problems like failure to vaccinate and vaccine failure still plague the health system.

Major measles outbreaks continue to occur worldwide despite the fact that measles vaccine has been part of routine childhood immunisation programme in most countries since early 1980s.

Mathematical models predicted that 95% of a population need to be immunised to maintain a herd immunity to stop measles transmission and eliminate infection (Wright & Polack, 2006). Nevertheless, even in industrialized countries with high population vaccination coverage, measles outbreaks are seen with increasing frequency.

In pre-vaccination populations, measles epidemics occurred at 2-yearly cycles. However, high population vaccination coverage has changed the epidemiological pattern of measles to irregular outbreaks, with no spatial-temporal correlation(Rohani, Earn, & Grenfell, 1999).

Thus, it appears that in view of changing epidemiology of measles disease, high vaccination coverage does not necessarily translate into effective protection of children against measles disease. Many studies were conducted to investigate the causes of such paradoxical outbreaks of measles in apparently highly immunised populations, with resulting evidence to suggest several main reasons.

2.5.1 Importation

Measles was declared as eliminated from the United States of America in year 2000. However, a resurgence of measles incidence was seen in the late 2000s (Centers for Disease Control, 2008). In year 2011, the Centers for Disease Control (CDC) reported 222 cases of measles in the United States, the highest so far since year 1996 (Centers for Disease Control, 2011). This happened in the setting of high overall measles vaccination coverage of more than 90% since year 1996 (Centers for Disease Control, 2012).

The source of measles outbreak was attributed to importation by international travellers from other parts of the world, especially Europe and South-East Asia. However it is interesting to note that 85% of the measles patients in United States were not immunized despite being eligible for measles vaccine(Centers for Disease Control, 2012).

Similar findings were seen in Taiwan. Despite its population vaccination coverage of 96%, three measles outbreaks occurred during the period of 2008 to 2009. The source cases of the outbreaks were travellers to People's Republic of China (PRC). Unlike other countries, these outbreaks occurred in the hospitals, instead of spreading through the community (Chen, Tsou, & Liu, 2009). Thus, this observation suggested that high population immunity level did help to contain the measles outbreak within medical facilities and prevented further transmission of the virus.

2.5.2 Heterogeneity in coverage

Even in countries with high overall vaccination coverage, the distribution of immunized and susceptible people was not random or homogenous as assumed by the epidemiological and mathematical models.

The outbreaks mostly affect pockets of marginalized and minority populations where vaccination coverage was significantly lower than the general population coverage. Examples of such susceptible populations include Roma migrant population in Poland, as described by Orlikova et al (Orlikova et al., 2010). A parallel population screening at the time of a measles outbreak in 2008-2009 revealed the vaccination uptake for the migrant Roma population in Poland to be 56%, as opposed to the national average of 98% (Stefanoff et al., 2010).

This finding was echoed by an observational study in Jerusalem, where two outbreaks occurred consecutively in the years 2003 to 2004, involving Jewish ultra-orthodox neighbourhoods. Likewise, measles vaccination uptake level within the Jewish ultra-orthodox community was low (88.3% compared to the national coverage of 94%) due to religious reasons (Stein-Zamir et al., 2008).

Even in populations of single ethnic origin, the vaccination coverage for measles could differ by 26% between urban and rural communities within the same district, as found in a large community survey in Pakistan involving four districts and 14 542 children(Cockcroft et al., 2009).

Contrary to other studies where measles outbreaks occurred in a single community, a recent study of an outbreak in Canada revealed that there need not be a sizeable aggregate of susceptible individuals to facilitate spread of measles virus. The outbreak took place in Quebec, where vaccination coverage was more than 95% since 1996. Although most patients (72%) investigated were unvaccinated, the epidemiological link between confirmed cases could not be established. This suggests that measles need not occur in segregated groups of unvaccinated individuals who have close contact with one another. Instead, even a small number of unimmunized individuals scattered throughout the population was sufficient to sustain an outbreak (Dallaire et al., 2009).

2.5.3 Social/Gender Equity and vaccination coverage

The relationship between socioeconomic factors and vaccination uptake is a complex one. Correlates of vaccination uptake often differ between developed and underdeveloped countries. Past studies had yielded mixed results and they were not easily generalized to other regions of the world.

It was previously assumed that vaccine coverage rates in urban areas were higher compared to rural areas because rural people had to travel further to access health facilities. However, according to a statement by World Health Organization, urban areas might have lower than average vaccination coverage due to dense population, high in-migration that led to rapid build-up of susceptible clusters of people, and lack of compliance of immigrants to local authorities (Kearney et al., 1989).

In United Kingdom after the negative publicity surrounding the MMR vaccine in 1998, an ecological study by Atkinson in 2005 observed that measles vaccination coverage was lower in the affluent areas in London compared to the less deprived ones (Atkinson et al., 2005). However, all the subjects who were measles patients in London were assigned socioeconomic scores based on areas of residence. No individual socioeconomic data were analysed. By assuming an individual's socioeconomic standing was reflected by his area of residence, the study was subject to ecological inference fallacy.

Merely one year later, this observation was challenged by Wright et al, who found that areas in United Kingdom with low MMR vaccination coverage were more likely to have higher degree of deprivation and population density(Wright & Polack, 2006). These factors were often co-dependent and synergistically increased the size and health impact of measles outbreak. Wright's study was also an ecological study, albeit conducted on a larger scale, involving a government database for the whole of England. Detailed correlation between area measles vaccination uptake with population density, proportion of professional people was done. Therefore the result of this study was likely to be closer to the real situation.

Another ecological study in Birmingham, United Kingdom by Hawker et al seemed to reaffirm Wright's findings that socioeconomic standing influenced vaccination uptake, although the relationship was more complicated. Firstly, significant racial differences in vaccination uptake were masked by the overall vaccination coverage figure. Secondly, Caucasian children had much decreased vaccination uptake after the MMR vaccine suffered bad publicity. Thirdly, MMR vaccination uptakes among Asian children were not affected by the adverse publicity, presumably because language and communication barrier protected the parents from the unfavourable picture portrayed in the media. Fourthly, the Black-Caribbean children, who frequently resided in more deprived neighbourhood, had the lowest vaccination coverage both before and after the media crisis (Hawker et al., 2007). This suggested that the most affluent and educated members of society might reject vaccination due to presumed adverse vaccine effects, whereas failure of the poorer population to access vaccination services might be due to other reasons.

In the developing world, gender bias also played a role in non-vaccination of children. A large household-based survey done by Luquero et al in Cameroon involving 2963 children revealed that not being allowed to make family decisions was one of the reasons given by mothers for not vaccinating their children, (Luquero et al., 2011).

While women in developing countries might not be involved in decision making pertaining their children's vaccination, another ethnographic research by Dugas et al in Burkina Faso showed that even when the fathers responded favourably to childhood vaccination, the mothers did not always comply, out of reluctance to interrupt their house work (Dugas et al., 2009). Thus, efforts in health promotion and behavioural intervention need to be targeted independently at both sets of parents (Mhatre & Schryer-Roy, 2009).

In countries where district or local vaccination coverage rates varied considerably, common themes associated with socio-economic factors still emerged, as reported by Cockroft et al. These factors were mother's education, poverty and quality of local health service(Cockcroft et al., 2009). In addition, access to health facility was an equity factor common to both urban and rural regions which emerged from a large household survey in Pakistan (Mitchell et al., 2009).

2.5.4 Decreased population demand for and acceptance of childhood vaccination

In developed regions where health services were readily accessible and national vaccination coverage rates were high, reasons for low coverage in sectarian communities include religious belief, philosophical belief and fear of adverse effects.

Anis et al described the low measles vaccination rate among the ultra-orthodox Jewish community in Israel as the cause for the outbreak in year 2008 (Anis et al., 2009). The authors hypothesized from direct personal experience with the ultra-orthodox community that probable factors that contributed to non-vaccination were lack of interest in preventive health care, lack of awareness on potential dangers of measles, and disinclination to interact with public health personnel.

The hypothesis suggested by Anis was affirmed by Muhsen et al (Muhsen et al., 2012), who conducted a case-control study on 430 ultra-orthodox children in Israel to study risk factors for non-vaccination. Parental factors that were significantly associated with underutilization of vaccination service were religious belief against vaccination and believing that risk of vaccine-preventable diseases was low. However, due to the sensitive nature of this study, it suffered from low response rate (30%), which reduced the validity of its findings.

In addition to religious groups, certain communities believed that childhood illnesses were part of the growth process and refused childhood vaccination. An example of such a community was the anthroposophic[5] community, whose members were found in affluent European countries like Austria (Schmid et al., 2010), Germany (Batzing-Feigenbaum et al., 2010; Wichmann et al., 2009), and Switzerland (Richard & Masserey Spicher, 2009). These communities often practised alternative medicine in favour of modern preventive health care, and ran private anthroposophic schools, which became the foci of measles outbreaks (Richard & Masserey Spicher, 2009).

As opposed to parents in developing countries, whose main reason for not vaccinating their children was lack of knowledge and information (Bernhardt et al., 2013; Luquero et al., 2011), highly-educated parents in developed countries might refuse measles vaccination due to fear of adverse events and lack of confidence in vaccination benefits. This is evident by the marked decline in vaccination rate following negative publicity that

[5] Anthroposophy is a spiritual movement following the teachings of Austrian scientist-philosopher Rudolf Steiner founded in late 19th century. Followers advocate freedom of choice in natural remedies, preferring to let the body experience infections over the use of vaccines, antibiotics, and antipyretics (Duffell, 2001; Hanratty et al., 2000).

erroneously linked MMR vaccine and autism in United Kingdom, as discussed in previous sections (Hawker et al., 2007).

2.5.4.1 Parents' decision making process regarding vaccination service

Studies have been conducted in both developed and developing countries to understand why parents refuse vaccination. A good proportion of these were qualitative research.

The social and behavioural sciences focused on the health belief model to explain lack of support for childhood vaccination among parents.

The health belief model by Rosenstock et al showed that parents based their decision to vaccinate their children on four determinants, namely perceived susceptibility of contracting disease, perceived seriousness of the disease, perceived benefits (vaccine effectiveness) when weighed against costs (safety) and lastly, cues to action (Rosenstock, 2005; Rosenstock, Strecher, & Becker, 1988).

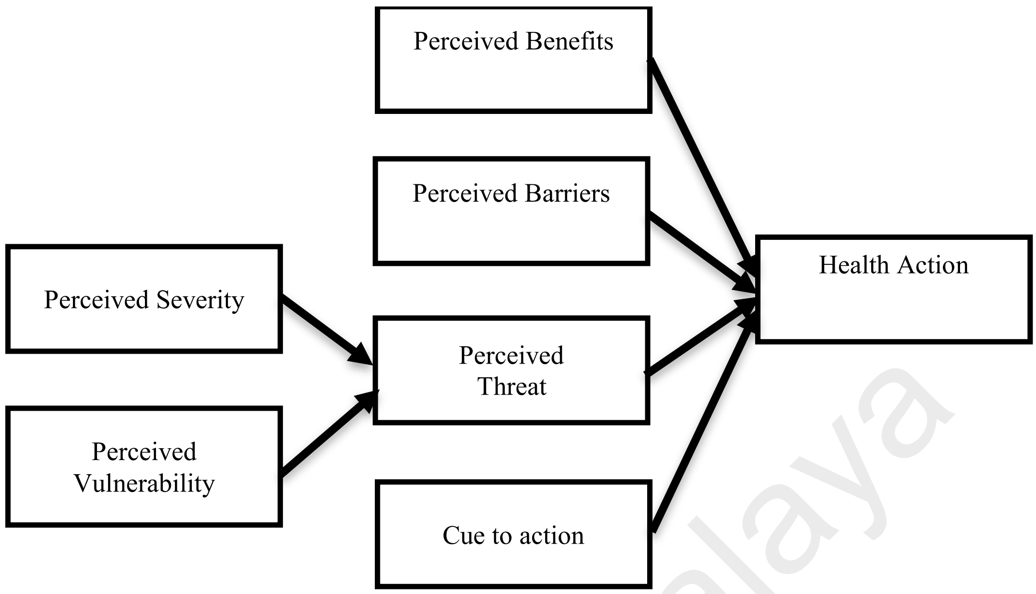


Figure 2.1: Diagrammatic presentation of the Health Belief Model (Rosenstock, 1988)

In developed countries, non-vaccination is often a conscious decision made after consideration of vaccine necessity, effectiveness and safety profile. The decision is rooted in a complex cultural and belief system, which policy makers need to understand and modify in order to effect a behavioural change.

Studies have found that parents who perceived their children as vulnerable to measles infection were more willing to bring their children for vaccination, illustrating that compliance improved when the vaccine was deemed necessary (Bond, Nolan, & Lester, 1999; Casiday et al., 2006). However, this relationship is not straight-forward. Other studies have failed to uncover similar findings (Flynn & Ogden, 2004). Thus, perception of risk alone is not enough to bring about absolute behavioural change.

In stark contrast to studies on perceived risk of measles infection and its consequences, Bond's survey in Australia found that perceived risk and benefits of MMR vaccination played an important part in deciding whether parents vaccinated their children (Bond et al., 1999). Generally, concerns about vaccine efficacy and adverse events emerged as the major factor that corroborated parental refusal of measles vaccination in studies around the world (Alfredsson et al., 2004; Bardenheier et al., 2004; Evans et al., 2001; Smith et al., 2011).

Historically in 1998, after the publication of a 12-children case series which linked the measles vaccine with development of autism and inflammatory bowel disease (Wakefield et al., 1998), both public confidence and vaccine uptake plummeted in United Kingdom, United States and other developed countries despite reassurance by public health authorities and multiple studies to disprove the findings (Hilton, Hunt, & Petticrew, 2007; Hilton, Petticrew, & Hunt, 2007). The article was subsequently retracted in 2010 but the detrimental effect to vaccine coverage remained (Godlee et al., 2011). As an aftermath, countries started to experience resurgence of measles outbreaks, which have persisted until now (Burgess, Burgess, & Leask, 2006).

The MMR controversy brought about by Dr Wakefield in 1998 can be considered as a major event in the history of public health, in which the presentation of a relatively weak piece of evidence had undermined the effort and achievement of public health authorities. It also indirectly illustrated that although the perceived risk of disease or death may not be sufficient to galvanize parents into taking preventive action, the perceived risk of any intervention acted as a powerful deterrent in parental decision-making pertaining health issues related to their children. This particular sentiment had indeed emerged as a theme in a recent qualitative study by Brown et al on British parents on their decision to vaccinate their children with MMR (Brown et al., 2012).

This unique observation, termed omission bias, had been observed previously by Ritov and colleagues in an experimental study conducted to examine vaccination behaviour by letting participants decide on vaccinating a child based on hypothetical risk scenarios based on real life situations (Ritov & Baron, 1990). Participants showed a tendency towards rejecting vaccination, albeit fully aware that it could reduce harm from disease, when it was associated with probability of harm, especially when details on a child's susceptibility to harm from either vaccination (commission) or non-vaccination (omission) was unknown. Again, this suggested that parents were averse to any risk associated with any intervention (vaccine included), preferring to omit vaccine even though they had knowledge about the potentially unfavourable outcomes of non-vaccination. Quoting a participant's words directly, "...I did not want to risk killing the child with a vaccine that is optional. It would have been my fault if the child died from the vaccine", Ritov argued that a parent's main reason for not vaccinating was "one is perceived to be more responsible for outcomes of commissions than for outcomes of omissions" (Ritov & Baron, 1990). It appears that compared to inaction, taking active measure is associated with higher degree of regret when adverse outcome occurs. Thus a person can only be persuaded to take active measure when he is given greater incentive and more reassurance of safety.

Another theme that commonly emerged from semi-structured interviews that could act as a barrier was pain experienced by the children (Marshall & Swerissen, 1999). Several studies had quoted parents' anguish at witnessing the pain inflicted on their children due to the injections (Harrington, Woodman, & Shannon, 2000; White & Thomson, 1995). Some parents went further to express their reluctance to go through the same process again (Bond et al., 1998; Wilson, 2000). This illustrated that pain experienced by children may have long-lasting impact on parents' decision for the subsequent vaccination, be it for the same child or the younger siblings.

Parental readiness for vaccination, which was founded on perception of costs and benefits of vaccine, would finally transform into action after being catalysed by social cues such as legal requirement or social norms. Parents admitted to accepting vaccination because it was required by law. Strong associations were found in Hepatitis B (Bardenheier et al., 2004) and Diphtheria-Pertussis-Tetanus (Lewis et al., 1988), but not MMR. Nonetheless, this demonstrated the power of mass media in perpetuating vaccine-related fears such as the ones associated with MMR, to the point that it overwhelms the human's natural tendency to comply with law.

Other authors had recognized that decision-making for infant vaccination usually took place in a broader socio-economic context. In fact, for parents with adequate access to both health service and health-related information, the decision to whether vaccinate a child or not could be emotionally-laden, coloured by personal and family histories, birth experiences, engagement with health providers, past issues that built or undermined their confidence in vaccination (Brown et al., 2012; Kennedy, Gray Brunton, & Hogg, 2014; Poltorak et al., 2005).

Adding to the social dimensions as described by Poltorak's ethnographic study was the issue of trust. Hilton et al noted in a focus group study in Scotland that when there were conflicting opinions between fellow parents and authorities, parents tended to lend more credibility to other parents. Health authorities, on the other hand, were seen to possess hidden agenda and thus less trustworthy as there was a possibility of conflict of interest between public health goals and children's best interest (Hilton, Petticrew, et al., 2007). Hence it appeared here that the knowledge, confidence, and stand adopted by a physician might not be a strong factor in persuading parents in accepting vaccination. Instead, encouraging physicians to be more open in addressing benefits, risks and conflicts of interest in vaccination to regain parents' trust might achieve more in terms of community acceptance towards vaccination.

As illustrated above, social support (peer, media) appeared to be another reason parents agreed to measles vaccination (Flynn & Ogden, 2004; Poltorak et al., 2005). The reverse was also true when it came to refer to a wider societal context, where non-immunizers were unwilling to take the risk of vaccine-related adverse event in order to contribute to overall population immunity (Casiday et al., 2006; Cassell et al., 2006; Gellatly, McVittie, & Tiliopoulos, 2005).

In the developing world, limitations in practical access, social and gender equity may pose additional barriers to achieving adequate population vaccination coverage (Dugas et al., 2009; Mhatre & Schryer-Roy, 2009).

Access to health care encompasses several aspects other than being geographically close to health services. They include personal convenience, affordability, willingness of the people to negotiate the health system, and cultural compatibility(Norris & Aiken, 2006).

As dual-income families become more prevalent, grandparents become heavily involved in the care of their grandchildren. In Singapore, 40% of children aged below three-years old were taken care by their grandparents. They were also the source of knowledge for cultural practices and beliefs (Thang et al., 2011). Hence, grandparents' views and opinions become important in policies involving children's health.

Rapid urbanization in Sarawak since 1990s saw the entrance of many women into the labour market. Consequently more children were taken care of by their grandparents (Sim, 2003). Sixty percent (60%) of the elderly in Sarawak lived with their children and grandchildren. Apart from assuming childcare duty, they also advised the family in various family situations (Aziz, 2007). Therefore a health programme that respects the historical experience and cultural diversity of the people is more likely to gain support and confidence from the grandparents, as they have influence over decisions pertaining to the grandchildren.

Although evidence from Malaysia is lacking, ethnographic studies conducted in developed countries showed that ethnic and linguistic minorities could feel disempowered in the mainstream health organizations. The respondents also expressed the need for more respect of their cultural identity and power of autonomy (Priest et al., 2012; Van Herk, Smith, & Tedford Gold, 2012). These studies illustrated the importance of learning the multiple dimensions of peoples' health needs, in order to build a health system that is safe and culturally responsive.

A conceptual understanding of factors that shape the parental decision-making in immunizing their children is important to devise a meaningful vaccination programme that ensures near-total coverage of the children population. It is thus important to learn about the parents' concerns regarding vaccination service so that efforts in health promotion and dissemination of health information can target the local community needs with better accuracy. For exploration of parental concerns, the qualitative approach is useful to explore the factors that influence parents' decision making process, as it removes the arbitrary boundaries on parents' flow of thought as imposed by pre-set answers and responses (Brown et al., 2010; Brown et al., 2012).

2.5.5 Providers' characteristics and their influence on vaccine coverage

Compelling evidence has shown that health workers play an important role in influencing the national vaccination coverage. They ensure the functionality and maintenance of the cold chain, administer the vaccines, as well as counsel the parents on vaccination.

In 2007, Anand et al did a cross-country econometric analysis by utilizing vaccination coverage survey information of all developing countries from the Demographic and Health Survey dataset (Anand & Barnighausen, 2007). There were 49 countries and 63 country-years in total. They found that density of nursing staff, but not doctors, was a significant predictor of measles vaccination among the population, even after controlling for other determinants like female literacy. Interestingly, gross national income (GNI) per person was not significantly associated with measles vaccination coverage.

Apart from adequacy of staff strength, the vaccinator's knowledge and attitude also exert influence on the parents' decision to immunize their children (Nikula et al., 2011).

A large community survey in Colombia by de la Hoz et al in year 2005 found that health workers with poor knowledge on vaccine contraindications predicted lower Hepatitis B vaccination coverage in the areas served by them (de la Hoz et al., 2005). Compared to Hepatitis B vaccination, which would be complete by six months of age, measles vaccination which is due at 12 months depends a lot more on parents' motivation to vaccinate their children. Thus good vaccinator knowledge becomes important in building parents' faith in the health system. In the same study, the drop-out rate for measles vaccination was high (42%) but unfortunately correlates for measles vaccination were not determined.

Another community survey in Belgium also noted that parents were of the opinion that having physicians who were pro-vaccination was important in supporting their decision to vaccinate a child (Swennen et al., 2001). Since the sample size was big (1110 children) and interviews were conducted by professional interviewers, this observation was likely to be valid.

Although health providers play a great role in determining the vaccination uptake, past studies had revealed some unsettling findings.

A cross sectional survey with good response rate from practitioners and nurses under the National Health Service, United Kingdom in 1998 found that about 25% of the vaccinators believed MMR vaccine was associated with autism. Only 20% would recommend the vaccine to a wavering parent (Petrovic, Roberts, & Ramsay, 2001).

The varied attitude among health providers towards measles vaccine was affirmed by other studies. In 2006, during an epidemiological investigation for a measles outbreak that occurred in Germany, researchers found that almost one-fifth of the parents did not immunize their children against measles because their physicians advised against it without valid contraindications (Wichmann et al., 2009).

In another study of measles outbreak in Belgium, the authors also found that almost 40% of the parents did not vaccinate their children on advice by their physicians (Lernout et al., 2009). It was not known if the physicians had legitimate reasons for offering such advice.

In Asian countries, studies on health providers' knowledge and attitudes were lacking. Likewise, association between vaccination uptake and health providers' characteristics could not be established because of paucity of evidence.

2.6 Timeliness/Age-appropriateness of vaccination

Another factor which could contribute to outbreaks of measles is untimely, or delayed vaccination. This issue is often overlooked by public health personnel in both outbreak and non-outbreak situations. In an outbreak situation, a child who had been putting off his measles vaccination but caught the infection would simply be categorized as a "non-vaccinated patient". On the other hand, in a non-outbreak situation, as long as a child ultimately receives his vaccine within the same calendar year, he would be deemed as vaccinated and protected, regardless of the length of time he spends vulnerable to measles infection due to delay in getting the vaccination.

Age-appropriate vaccination is critical in conferring maximal benefit and reducing mortality in the children. Delayed vaccination could possibly be the cause of measles outbreak despite deceptively high national coverage rate.

In an analysis of the Demographic and Health Survey from 1996 to 2005, involving 45 countries, and 217 706 children's data, it was observed that in one quarter of the countries, a quarter of the children had about 3-month delay in receiving their measles vaccination. As a result, the final vaccination coverage rates were higher compared to the real coverage at 12-months (132). Although this study included low- and middle-income countries, Malaysia was not included in the survey.

To further illustrate the case, Corsi et al had found through analysis of three consecutive national surveys from 1992 to 2006 that age-appropriate measles vaccination coverage was almost 60% in 2006 (133). Even though the age-appropriate coverage had improved markedly, it still lagged behind the overall measles vaccination rate of 70% in year 2006 (134).

The same finding was seen in Uganda. In a longitudinal study involving 765 children followed up from birth to two years, measles vaccination uptake rate was 80% as compared to the age-appropriate coverage rate of only 56%. The authors also noted that delayed vaccination was significantly related to maternal education (135).

Thus far, we have seen large number of studies illustrating the inadequacy of simple vaccine coverage in detecting delayed vaccination. By logical deduction, delayed vaccination would play a part in measles outbreak. However, direct evidence to link delayed vaccination and measles resurgence is scant and has not been reviewed in detail. In view of this, a closer examination of available evidence would be elaborated in detail in Chapter 4.

2.7 Primary Vaccine Failure

The effectiveness of vaccine in preventing disease depends on its potency and the capacity of its recipient to respond with antibody production (Orenstein et al., 1985). Malaysian data (Section 1.1) and international reports (Table 2-1), have generally showed that measles infection increasingly affected young infants below the age of one year. The high incidence of measles in infants too young to be vaccinated could suggest that the age recommendation of one year for first dose of MMR prior to year 2015 might be too late. This is supported by observations that vaccinated mothers tended to transfer less protective antibody against measles to their children (Leuridan et al., 2012; Machaira & Papaevangelou, 2012).

Other than individual vaccine recipient's ability to produce antibody to a vaccine, another vital factor which affected the success of mass immunisation is the quality or effectiveness of the vaccine. The quality of vaccine hinges on proper production, transport, storage and delivery of vaccine. Unfortunately, numerous studies from various parts of the world showed that the cold chain that was supposed to maintain vaccine quality was often broken, resulting in temperature excursions outside prescribed range and therefore reduced vaccine effectiveness (Ateudjieu et al., 2013; Hanjeet et al., 1996; Rao et al., 2012; Samant et al., 2007; Techathawat et al., 2007).

Even in the absence of documented breaks in cold chain, field studies showed that effectiveness of vaccine could fall short of the generally accepted 95%.

In the process of developing a mathematical model to calculate the benefits and costs of vaccination for a community intervention trial in Pakistan, Ledogar et al discovered that the actual effectiveness for measles vaccine was 41.5% instead of 95% as found in studies conducted in developed countries (Centers for Disease Control and Prevention, 2012). The author postulated that this low effectiveness was due to break in the cold chain or improper handling of vaccine at point of delivery (Ledogar, Fleming, & Andersson, 2009).

Studies on recent measles outbreaks from various parts of the world seemed to support Ledogar's findings. During the 2010 Malawi outbreak, Minetti et al calculated measles attack rates for 134 019 children, and the measles vaccine effectiveness was only 91% after the second dose, as opposed to the expected 99% from literature. The researcher attributed this low effectiveness to Human Immunodefiency Virus (HIV) infection, which affected about 2% of Malawi children. Other causes proposed by the researcher included cold chain failure and waning immunity (Minetti et al., 2013).

It is interesting to note that in India, epidemiological calculations for measles outbreak in Gujarat during year 2011 revealed widely varied vaccine effectiveness. For urban areas, the vaccine effectiveness was 92%, which was close to its expected performance. In the rural area, however, the effectiveness was only 73% (Mishra & Chauhan, 2012). This low vaccine effectiveness in the rural region was ascribed to recall error on measles vaccination status, but information on other important causes such as cold chain performance and logistics was not offered by the researchers.

In places where measles vaccination coverage rates are good, the quality of cold chain and vaccine potency becomes the all-important limiting factor in generating population immunity. In Tamil Naidu, Balasubramaniam described a measles outbreak which consisted of 27 cases (Roy & Balasubramaniam, 2012). All the patients were previously immunized. The cause of the outbreak seemed to lie in defective cold chain maintenance, as the health workers interviewed were not well versed with correct vaccine storage and handling techniques. This study only involved a small number of patients, and it could be argued that if the sample size was larger, a proportion of patients would be unvaccinated. However, it illustrated the importance of maintaining good quality cold chain to avoid unnecessary suffering and vaccine wastage in every child we vaccinate.

A formal evaluation of cold chain performance was conducted by Ateudjieu et al. in 2008, involving eight districts of Cameroon. In 40% of the health facilities, temperature charts were not maintained. A quarter of the refrigerators inspected had temperature excursion out of the recommended range of 2°C to 8°C, and a quarter of health facilities had never received supervisory monitoring on cold chain (Ateudjieu et al., 2013).

These findings cast serious doubts on the safety and effectiveness of vaccines that were administered from the clinics involved. Although the results were not necessarily generalizable to other health facilities, a number of recent studies in developing nations like Zimbabwe (Chadambuka et al., 2012) and Ethiopia (Woyessa et al., 2012) showed that insufficient cold chain equipment, limited transport, inadequate staff and poor supervision were real problems that prevented delivery of effective vaccines.

So far the evidence on cold chain quality came from low-income tropical countries. Apart from the widely quoted Malaysian cold-chain study conducted in 1996 (Hanjeet et al., 1996), there has been no recent literature available in other upper-middle income tropical country such as Malaysia, where resources are more plentiful but potential issues with personnel and supervision may exist.

2.8 Secondary vaccine failure

It was estimated that 4 to 8% of measles cases in outbreaks occurring in highly vaccinated communities were due to secondary vaccination failure (Pannuti et al., 2004).

A recent study conducted by Kontio et al involved four age-groups of participants to study association between methods of acquisition and persistence of immunity(Kontio et al., 2012). It was shown that antibody level and quality for measles vaccine decreased 20 years after vaccination. The level of antibody seems to persist for those who acquired immunity via natural infection. For the youngest members of the group who were entirely dependent on vaccination for immunity and deprived from boosting effect of natural infection, antibodies waned as soon as five years after second dose of MMR vaccination.

The result of Kontio's research is supported by another large-scale population study in Taiwan by Chen at al. It involved 3552 healthy volunteers with age ranging from below 1 year to above 65 years. The proportion of seropositive population dropped from 94.5% at 2 years to just 50.6% among the 21- to 25-year-olds. This was in stark contrast to the population aging 35 years and above, who were not immunized and had acquired immunity from natural infection. More than 95% still retained anti-measles antibody(Chen et al., 2012).

This phenomenon may have impact on measles elimination programme in future, as a growing proportion of the population acquired immunity from vaccination.

In fact, in a serological investigation following measles outbreak in New Jersey during year 1993, it was found that 45% of the previously vaccinated individuals had secondary vaccine failure (Erdman et al., 1993). Unfortunately the duration from last vaccination until the time of outbreak in such patients was not given, so inference could not be drawn on the duration of protection conferred by measles vaccine.

As official vaccination coverage in Malaysia is high, it is not unlikely that a proportion of the cases in the current measles outbreak would be due to secondary vaccine failure. To date, there is no local study on secondary vaccine failure or its association with the recent outbreak.

2.9 Conceptual framework for evaluating measles outbreak in vaccinated populations

Based on the literature review, Figure 2.2 below is a conceptual framework of the interplay of factors that contributed to the occurrence of measles outbreaks or measles resurgence in regions aiming for disease elimination.

The causes of measles outbreak can be divided into two main themes of vaccine failure and failure to vaccinate. Vaccine failure can be divided into primary (failure to induce immunologic response) and secondary failure (waned antibody after initial successful seroconversion). Failure to vaccinate can be due to issues in uptake (pivoting on individual parental decision) and provision (determined by health organization characteristics) of vaccination service. These four main components, while also influenced to various degrees by independent factors like mass media and national health policies, interact with one another to create gaps in population immunity, which eventually culminate in a measles outbreak.

For the purpose of this thesis, investigation of factors in measles vaccination programme that had potentially contributed to the 2011 outbreak had concentrated on vaccine uptake, vaccine provision and vaccine quality component of primary vaccine failure. As the incidence of measles arising due to secondary failure is low (refer section 2.8), and the age group most affected by the 2011 outbreak was below seven years, secondary vaccine failure is unlikely to be responsible for the 2011 outbreak, and thus not studied. Similarly, primary failure of vaccine due to individual physiological factors is less common in comparison to failure due to low maternal antibody (Fine & Zell, 1994; Strebel et al., 2013). Therefore physiological disorders causing primary vaccine failure were also not part of this thesis.

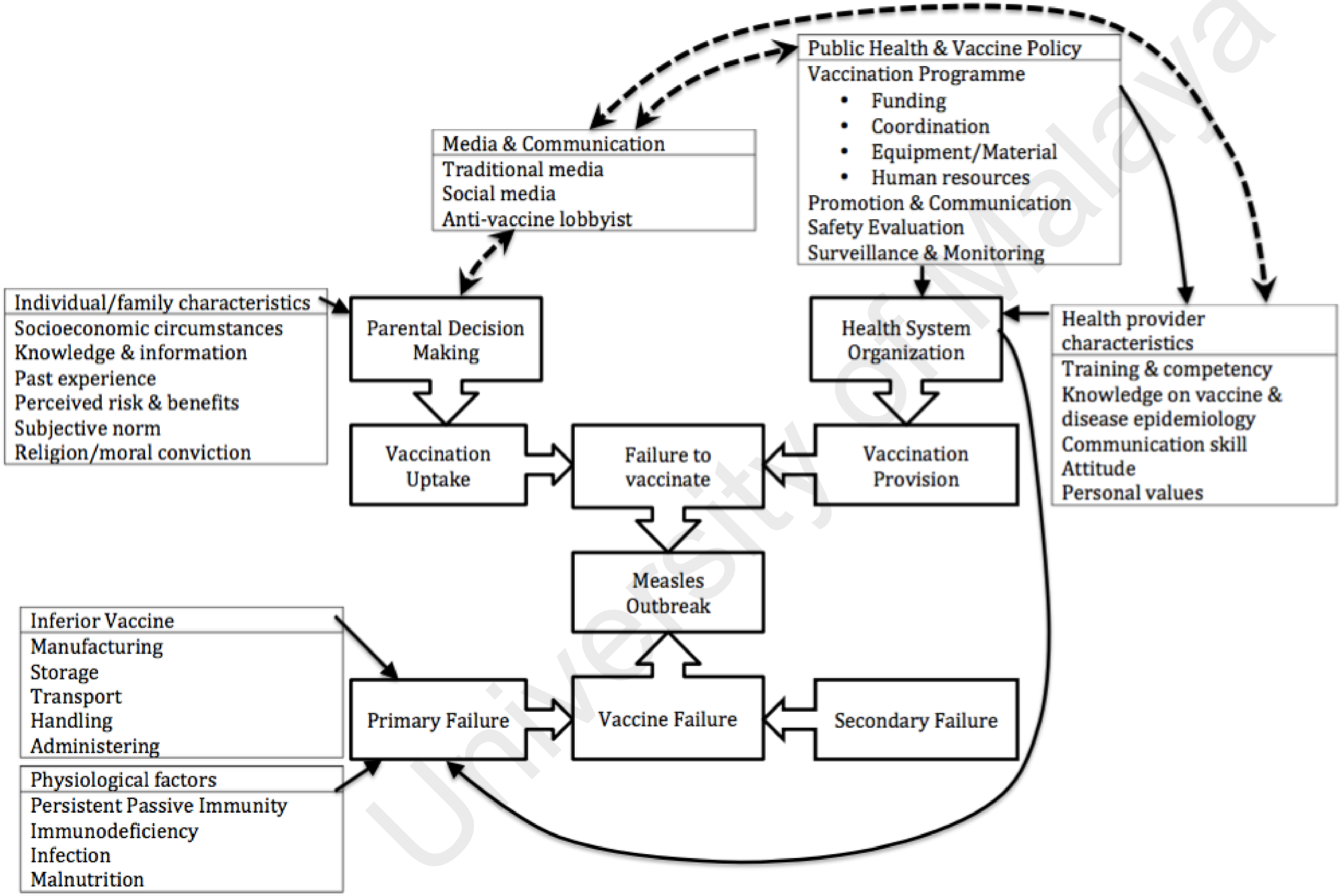


Figure 2.2: Conceptual framework for investigating measles outbreaks in post-vaccine era

2.10 Summary

Measles vaccination is one of the key indicators in Millennium Development Goal 4 (Reduce Child Mortality) because it is the only means of eliminating measles, one major killer of children below the age of five.

This literature review identified causes of measles outbreak as an indirect indicator of failure of mass vaccination in achieving desired population immunity and factors that affect utilization of vaccination service.

Overall, there is large body of published literature on measles vaccination. Current literature addresses structural barriers, parental beliefs and attitudes on measles vaccine, described through both quantitative and qualitative methods which are generally based on the risk/benefit analysis as featured in the Health Belief Model.

Although there exists significant amount of literature on the topic of measles vaccination programme, few studies are about vaccination practices in Malaysia. When available, Malaysian studies tend not to examine the perception of health care professionals and parental decision making from a socio-cultural viewpoint. Therefore, the importance of conducting such studies in Malaysia in order to bridge the knowledge gap on parental vaccination behaviour cannot be overemphasized.

Having developed the conceptual framework of events and pathways leading to measles outbreak, the next chapter will take a step further to review in-depth the development of the Expanded Programme for Immunisation (EPI) in Malaysia to identify systemic and structural changes that might have contributed to the measles outbreak in Malaysia in 2011.

CHAPTER 3: MALAYSIAN HEALTH SYSTEM AND THE NATIONAL VACCINATION PROGRAMME

3.1 Introduction

Provision of health care in Malaysia is via a multi-tiered system which consists of public and private networks of health facilities. The two systems run in parallel, and Malaysians can freely choose to use public or private health services. However, due to the higher fee schedule at private health facilities, primary and hospital care in private sector is preferentially used by the financially better-offs mainly in the urban areas, while the public health system caters to the needs of all people, especially those residing in rural regions where private facilities are often lacking. In addition, the public system also acts as the main provider for preventive health services.

The unique characteristics of the Malaysian health care system are probably rooted in its historical background. It is not the aim of this review to provide a comprehensive historical account on the development of the Malaysian health care system. This brief description of the evolution of the health care system in Malaysia will provide the context for discussion of the probable gaps in the vaccination service provision and uptake in subsequent chapters.

Section 3.2 gives an overview of the health system in Malaysia, concentrating on its historical development of health and medical care. In this section, the organization of vaccination service is also examined. Section 3.3 deals with the unique geography of Sarawak and how it subsequently shaped the cultural diversity among the people. The chapter then concludes with a summary in section 3.4.

3.2 Health care system in Malaysia

3.2.1 Historical development of the Malaysian Health System

Malaysian health system began way before Malaya gained independence in 1957. Hospitals were reported to have been built since Portuguese colonization era (1511 to 1641) in Malacca to treat government officials and the poor (Ghani & Yadav, 2008). Likewise, the Dutch government (1641 to 1825) in Malacca also set up hospitals to look after its citizens.

In 1826, the British colonial government in Malaya was first established with the formation of the Straits Settlement, which consisted of Penang, Malacca and Singapore. In early twentieth century, the colony was further expanded by formation of the Federated Malay States of Pahang, Selangor, Perak and Negeri Sembilan. By 1914, British colony in Malaya was finally completed with the acquisition of the Unfederated Malay States of Kedah, Kelantan, Perlis, Terengganu and Johore.

An important feature of the federated structure of the colonial states was the federal appointment of District Officers to enforce law and tax collection at the local districts, which were the lowest level of the British colonial administration. The formation of state and district administration system was maintained until Malayan independence in 1957, and continued as the foundation of the Malaysia, which comprised Malaya, Singapore, Sabah and Sarawak in 1963 (Tajuddin, 2012).

The primitive framework of the local public health system began before the Malayan independence in 1957, and this actually took root in the British soil. In 1842, the importance of public health was brought up by Edwin Chadwick's in his landmark report on Sanitary Conditions of the Labouring Population of Great Britain, which attributed diseases and epidemics to atmospheric impurities, damp, filth and overcrowding. Based on his observations, Chadwick recommended that such risk factors for outbreaks could be removed by “drainage, proper cleansing, better ventilation, and other means of diminishing atmospheric impurity… and where the removal of the noxious agencies appears to be complete, such disease almost entirely disappears” (Chadwick, 1842), thus leading to the enactment of the Public Health Act in 1848 (Hamlin & Sheard, 1998). Following the lead of English public authorities in improving health by better sanitation and environmental control, in 1867 the British colonial rulers set up the Straits Settlement Authority with some responsibilities for health protection. In 1880, a Sanitary Board was set up in Kuala Lumpur to ensure cleanliness of public infrastructure like streets and markets. This further evolved into a permanent Health Department in 1910, staffed by Colonial Government Medical Officers to maintain environmental sanitation in Kuala Lumpur (Ghani & Yadav, 2008).

Rubber plants were introduced into Singapore in 1877, and subsequently into Malaya. By 1920, there were about 1200 rubber estates in Malaya. Estate clinics, managed by paramedics, were set up by British companies to maintain the health of the estate work force, which comprised mainly indentured Indian labourers (Ariff & Teng, 2002).

Subsequent to opening of plantations and estates in early twentieth century, outbreaks of communicable diseases like malaria and typhoid necessitated the enactment of Malaya’s own Rump Labour Code. This covered swamp drainage, mosquito control, smallpox vaccination and quarantine regulations. Even before the Second World War, the local government was already performing the basic tasks of a modern-day local health department (Ghani & Yadav, 2008).

Between 1910 and 1940, Medical Officers of Health were appointed in each state to provide maternal and child health services, school health services, and public health services.

However, development of medical services in Malaya were approximately two decades behind public health services. It was not until 1880 that the first government hospital documented in the pre-independence Malaya, Hospital Taiping, was finally built under the British colonial administration. Subsequently, in between 1883 and 1910, government hospitals were built in all states of Malaya. These hospitals were located in state capitals, gradually expanding to cover districts. In towns with no hospitals, dispensaries were set up (Ghani & Yadav, 2008).

In post-war Malaya, services continued to run but were decentralized to the state governments, with the central government in Kuala Lumpur retaining limited scopes of functions such as quarantine and outbreak control (Ghani & Yadav, 2008). The British government had more important matters at hand - fighting the Malayan Communist Party, which rose to power during the local resistance against the Japanese invaders and conducted armed guerrilla warfare from the depth of forests. As a result, the rural Chinese populations, known to be sympathetic to the Malayan Communist Party, were relocated to urban planned settlements where they could be monitored closely to curb their support to the communists (Stubbs, 1979). Health facilities such as midwifery clinics were provided in the new settlements to gain Chinese community support. Likewise, the British colonial government also started to offer health services to the Indigenous People (Orang Asli) in rural areas in order to gain support from the community and reduce influence from the communists. The government thus started to realize the need of health service provision to the rural population, and the rural health services scheme was started in 1953 (Chee & Barraclough, 2007).

Up until this point, it is quite apparent that hospital services and public health services evolved in parallel, each being improved gradually as demanded by situation at the time. In fact, at the time of independence, the rudimentary frameworks of public health infrastructure and hospitals had already been established. The least developed component of the health system was a rural health service to take care of the majority of population who resided in rural areas of the country.

When Malaysia gained independence from Britain in 1957, the government inherited a mainly public hospital system. These hospitals were in town areas, initially built to care for the expatriates and civil servants, but later offering free or heavily subsidized medical services to the general population who were able to access such care (Chee & Barraclough, 2007).

After Independence, the federal government regained control of health-related policies by centralizing health functions previously delegated to each state. As observed by Chee & Barraclough, "Health care policy was… inseparable from the imperatives of national development, rural development, …, socio-economic equity between ethnic groups". As the ruling coalition had gained its support from the predominantly rural Malay populace, a comprehensive rural health service was well-oriented to the national development strategies (Chee & Barraclough, 2007).

Thus, public health service was further refined with the rapid expansion of the rural health system. This started as a three-tier rural health infrastructure under the First Malaya Plan in 1966, which consisted of main health centres that received referral from health sub-centres, which in turn received its referral from midwife clinics. This network of clinics provides health services to both urban and rural communities throughout the country. Health care facilities were built alongside with other infrastructural development such as roads, water and electricity supply (Ariff & Teng, 2002; Ghani & Yadav, 2008).

3.2.2 Modern provision of health care

Malaysia has a dichotomous public-private health system, in which the public sector is run by the government and funded by general taxation. In parallel, there exists a thriving private sector providing services which are paid for by individuals and medical health insurance.

As previously discussed, Malaysia inherited a health system from the British colonial government where the state, or public sector played a dominant role. After independence from British rule, this arrangement persisted until the expansion of private health system eventually caught up with the public health system.

The country's constitution provides that the federal government be responsible for all health care matters. The Ministry of Health provides a full range of health services, which cover promotive, preventive, curative and rehabilitative activities. Payment for health service is a nominal RM1 (equivalent to 0.23 USD)[6] per attendance, which covers clinical consultation, investigations and medications. Frequently this payment is waived if a patient is unable to pay.

Public sector health services are also provided by various government bodies to serve the needs of specialized populations. For example, the Ministry of Higher Education also provides secondary and tertiary medical care at various university teaching hospitals. The Ministry of Defence provides both primary and secondary level health care for officers and their families within the armed forces (Ghani & Yadav, 2008).

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[6] As of 2 December 2015, conversion done via XE Currency Converter, URL http://www.xe.com/currencyconverter/

Private provision of health care first started in the late 1970's, but the current robust private health system really began to flourish after 1983 under the initiatives of the then Prime Minister, Tun Dr Mahathir. In 1983, Dr Mahathir put forward his health privatization policy as part of 'Malaysia Incorporated', whereby the country functions as a corporate entity with the government providing an enabling environment while the private sector, supported by the public sector acts as the major mover of economic growth (Chee & Barraclough, 2007). Encouraged by the government, the private health sector expanded rapidly. As seen in Table 3.1, from 1980, private hospital beds had increased 11-fold within a span of three decades. Currently, 25% of all hospital beds belong to private sector (Ministry of Health Malaysia, 2010; Quek, 2009). Private hospitals are usually set up by entrepreneurs, while some are owned by the medical practitioners. The main focus of private hospitals is curative medical care, with increasing attention being paid to health promotive packages like screening and wellness programmes.

Table 3.1: Private health facilities in Malaysia, 1970 to 2011 (Juni, 2014).

Private facilities	**1970**	**1980**	**1990**	**2000**	**2011**
Hospitals	11	50	174	224	245
Hospital Beds	Unknown	1171	4675	9547	13673
Clinics	Unknown	Less than 1000	2000	4500	6589

Aside from private hospitals, ambulatory medical care is provided by general practitioners (GPs). They can either be owners of clinics or salaried GPs in group clinics. From 1980 onwards, the ratio of private to public doctors generally fluctuates around 45:55 depending on the economic situation and government policy on foreign practitioners (Chee, 2008). Like their counterparts in private hospitals, GPs are focused on providing curative medical care, with some providing antenatal follow-ups and on-demand vaccination. Payment for private medical services is usually on fee-for-service basis, paid out of pocket, with increasing popularity of insurance and other third party payment.

The utilization and provision of health care in private and public sectors have characteristics that separate them into two distinctive systems. Firstly, the type of service is predictable by its location, although in recent years the line of demarcation has been blurred considerably. In town areas, primary care is frequently provided by private GPs, who cater to the needs of the wealthier urban dwellers. In contrast, the health needs of the rural community were provided for by public sector doctors in the rural health network, although private clinics are increasingly being set up in rural areas (Chee & Barraclough, 2007). Secondly, utilization of service is influenced by level of care. More than 80% of outpatient or ambulatory health care are provided by private practitioners, including 2% by traditional healers. However, when hospital-level care is required, 80% of hospital admissions occur in public facilities (Syed Aljunid, 2009).

These two systems are not mutually exclusive. Crossover of services frequently occurs from public to private sector, and vice versa, according to patients' demands and expectations. Generally private practitioners provide quick and personalized care for common ailments, besides offering simple therapeutic procedures. Their care also complements the public primary care clinics which are often overcrowded with long waiting hours (Quek, 2009).

It is clear at this point that although Malaysia has a parallel public-private system of health services which has yet to be unified, with each system serving different needs of the population. The private system predominantly gives curative care for a profit, whereas the state health system gives a comprehensive range of care almost free-of-charge. As preventive and promotive health services, such as well child programme are generally not profitable (with the exception of screening and vaccination), these programmes are mainly provided by the public sector. Together, the dual system provides a high degree of access to med care for Malaysian citizens at a low level of government financing (2.2 percent of gross domestic product in 2012) (Rannan-Eliya et al., 2016).

In the following section, the role of Ministry of Health in service provision is going to be discussed in detail.

3.2.2.1 Organization of health services in the Ministry of Health

At present, the Ministry of Health (MOH) is the main health service provider in the country. MOH is responsible for formulating health policies, planning, implementing and monitoring of programmes, managing resources, enacting and enforcing health-related legislation. The range of health services given under MOH include all preventive and curative care, environmental sanitation, control of communicable disease, drugs and pharmaceuticals. Activities are mainly carried out under various departments under the Ministry, with occasional collaboration with other agencies like the local councils, Ministry of Human Resources, Department of Environment and others.

In each of the 13 states in Malaysia there is a State Health Department, led by the State Health Director who is usually a public health doctor. The State Director answers to the Director General of Health in all matters pertaining to provision of health services within the state. Resources needed for health programme implementation are allocated by the Ministry.

Each state is divided into districts, each of which has a District Health Office led by a District Health Officer. The District Health Officer is in charge of administering the health services within the district. The wide array of health services are designed to serve the needs of various populations in the districts. They include maternal and child health, primary health care, control of diseases, food safety and quality, occupational and environmental health, health promotion and education.

3.2.2.2 Public health programme – rural health services

For the purpose of delivering health services to the rural population, a district is divided into several rural health units, each served by a health centre and its attached sub-centres.

Prior to the 1970s, the rural health needs were well served by a three-tiered health infrastructure as discussed in section 3.2.1. However, in 1973, the three-tiered system was replaced by a two-tiered system as shown in Figure 3.1. The main health centres are called health clinics and act as referral centres at the local level. Each is managed by at least one medical officer, with the help of medical assistants and a public health team. In contrast, the rural clinics or maternal and child clinics (*klinik desa/klinik kesihaan ibu dan anak*) are run by trained community nurses and provide the most basic medical and preventive services. This nurse would take care of the maternal and child health in the community, focusing on safe pregnancy and childbirth, vaccination and child development, with home visits making up an important bulk of her daily routine. When necessary, she would also make referrals to the health clinic (Ariff & Teng, 2002).

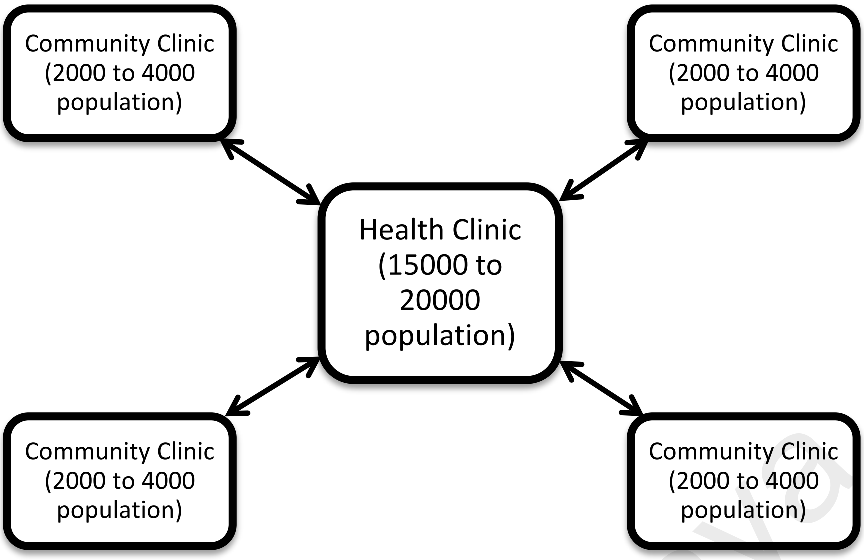

Figure 3.1: The two-tiered health public health infrastructure in Malaysia (Ghani & Yadav, 2008)

One rural health unit serves a population of 20000, with each community clinic serving up to 4000 (Ariff & Teng, 2002; Ghani & Yadav, 2008). Initially in 1960, there was one main health centre for every 638000 rural population. By 1986 after upgrading the health sub-centres, the ratio increased to one health clinic to 21697 rural inhabitants (Chee & Barraclough, 2007). In 2010, there were 813 health clinics, 1916 rural clinics, and 104 maternal and child health clinics. The health clinic to population ratio had further improved to 1:10001 (Ministry of Health Malaysia, 2010). By 2014, there were 934 health clinics, 1821 rural clinics and 105 maternal and child clinics in Malaysia, making the health clinic to population ratio 1:10390 (Ministry of Health Malaysia, 2014).

Despite improving clinic to population ratio, the workload of providers, especially nursing staff, were not necessarily lightened. As of 2012, the ratio of community nurse to population was 1:1301. Compared to the Singaporean nurse to population ratio of 1:154

in 2013 (Ong, 2013), this suggests that there might be potential limitations in services, especially the time-consuming activities such as consultation, communication and education which are vital in encouraging vaccine uptake among concerned parents (Ministry of Health Malaysia, 2012a). It is thus not unreasonable to hypothesize that currently low nurse to population ratio and possible high work burden of staff might have contributed to suboptimal vaccine coverage in the population.

In addition, the overarching concern for the welfare of rural population has resulted in the Malaysian government becoming the main provider, developer and funder of rural health network. However, such comprehensive primary care delivery system has not been replicated in the rapidly expanding urban areas. In these areas primary care is predominantly provided by private practitioners (refer Table 3.1). This leads to issues such as high medical costs which are borne by the people, and poses challenges to public health authorities in maintaining, monitoring and regulating standard operating procedures on labour-intensive services such as vaccine cold chain in the numerous private facilities.

Reliance on private practitioners to deliver primary care in densely populated cities, coupled with existing staff shortages in urban public sector could have resulted in overall compromised quality in vaccination services, which could possibly explain the concentration of measles cases in the three cities in Sarawak during the 2011 outbreak.

3.2.2.3 Public health programme – childhood immunisation

Aside from rural health, one other important component of public health programmes administered under the MOH is disease control. Childhood vaccination programme is under the purview of two units under Ministry of Health, they are the Communicable Disease Control and Family Health Development units. These two units collaborate in matters related to disease surveillance, outbreak management, as well as delivery of vaccines through various health clinics to the target population.

The expanded programme for immunisation (EPI) is an initiative launched by the WHO to combat vaccine preventable diseases (VPD) worldwide (World Health Organization & UNICEF, 2000). Subsequently, this programme was adopted by Malaysia in 1958, starting with the Diphtheria-Pertussis-Tetanus (DPT) vaccine. Other vaccines were added over the years following the inception of the programme(Ministry of Health, 2004).

Through the network of government health clinics, vaccines are available to be administered free to all children residing in Malaysia, as long as they have reached the eligible age for the vaccines.

Table 3.2 below shows the latest schedule of routine childhood vaccination practised in Sarawak (effective until 31st March 2016), in accordance to World Health Organization recommendations.

Table 3.2: Childhood vaccination schedule (until 31 March 2016) [7]

Vaccine	Age (months)										Primary school
	0	1	2	3	5	6	9	12	18	21	Year 1
BCG	■										
Hepatitis B	■	■				■					
DTaP+Hib+IPV			■	■	■				■		DT+IPV
Japanese Encephalitis							■			■	
Measles-Mumps-Rubella								■			■

Measles vaccine was officially included in the national vaccination programme in 1986. Since then, the national measles vaccination coverage for infants had grown from 70% in 1990 to 88% in 2000(Economic Planning Unit & Prime Minister's Department Malaysia, 2005).

In 2002 the measles, mumps and rubella vaccine (MMR) replaced the measles vaccine. The vaccination coverage for infants had improved further. In 2009 the national estimates from administrative data reached 95% and has sustained until 2011(World Health Organization, 2012c).

[7] Acellular Pertussis and Inactivated Polio Vaccine (IPV) replaced whole-cell Pertussis and oral Polio Vaccine (OPV) in the current DTaP-Hib-IPV vaccination programme effective from October 2008.

Table 3.3: Childhood vaccination schedule (Effective from 1st April 2016)

Vaccine	Age (months)										Primary school
	0	1	2	3	5	6	9	12	18	21	Year 1
BCG	■										
Hepatitis B	■	■				■					
DTaP+Hib+IPV			■	■	■				■		DT+IPV
Japanese Encephalitis							■			■	
Measles-Mumps-Rubella							■	■			

From 1st April 2016 onwards, the MOH has effected a change in the MMR schedule in response to the 2011 outbreak and in accordance to the WHO's recommendation for countries with high incidence of measles (World Health Organization, 2009). The first dose of MMR has been brought forward to nine months, and the second MMR to be administered at twelve months, whereas the MMR dose scheduled at first year of primary school would be discontinued in year 2022 when the current cohort affected by the change reaches school entry age.

While the MOH's effort in protecting the infants against measles infection is highly commended, it is not certain whether the recommendation is informed by the latest evidence, as national measles immunisation had produced a new generation of vaccinated mothers and thus altered the population immunity profile. Therefore there is a need to review available evidence to determine whether the current age recommendation is up-to-date and adequate to prevent measles in the infant population.

3.2.2.4 Organization of vaccination service

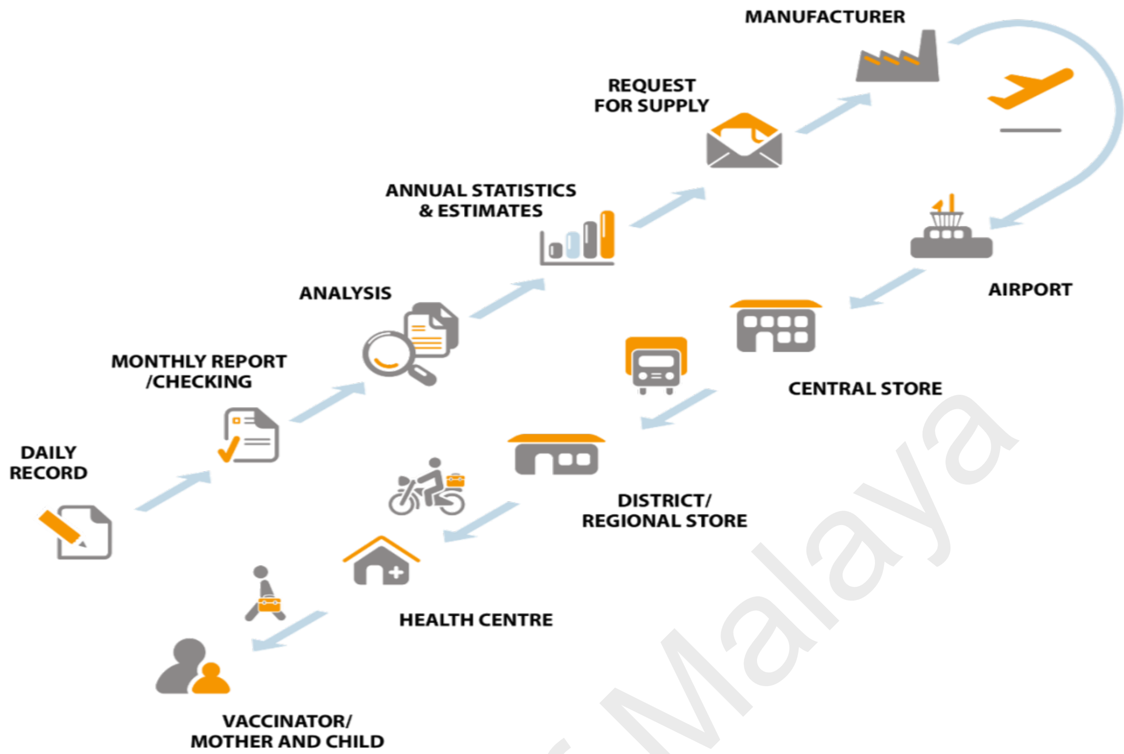

Figure 3.2: Vaccine supply chain (World Health Organization, 2014)

Vaccination service can be divided into two components: supply and maintenance of the vaccine, and administration of vaccine to children at point of care.

Vaccines are transported from the pharmaceutical distributers to the children along a complex supply chain, which links manpower, systems, equipment and relevant activities to ensure the vaccines stay in optimal condition (Kaufmann, Miller, & Cheyne, 2011).

The supply chain comprises multiple steps (refer to figure 3.2): temporary airport storage during customs clearance, central vaccine storage, regional/state storage, district storage, health centre storage, storage during clinical session (Kaufmann et al., 2011; World Health Organization, 2014).

All vaccines, being biological products, require strict storage requirements to maintain their potency. The MMR vaccine, being a live-attenuated viral vaccine, is sensitive to heat and light. Thus it has to be consistently stored at an ambient temperature between 2 to 8°C, and protected from light (Centers for Disease Control and Prevention, 2012; Kroger, Atkinson, & Pickering, 2013). Some other childhood vaccines, such as DPT vaccine and its derivatives, are damaged by freezing and thus cannot be stored at temperature lower than 2°C (Kroger et al., 2013).

It has been shown that the measles vaccine is relatively stable in its lyophilized (freeze-dried) form, with a shelf life of 24 months if kept in ambient temperature within 2 to 8°C. However, at room temperature (20 to 25°C), it can maintain its minimal potency for one month, and at ambient temperature of 37°C, its function is maintainable for one week (PATH & Working in Tandem, 2012; World Health Organization, 1998b). Hence we can see that ambient temperature plays an important part in the integrity of the cold chain and measles elimination.

Figure 3A: The cold chain

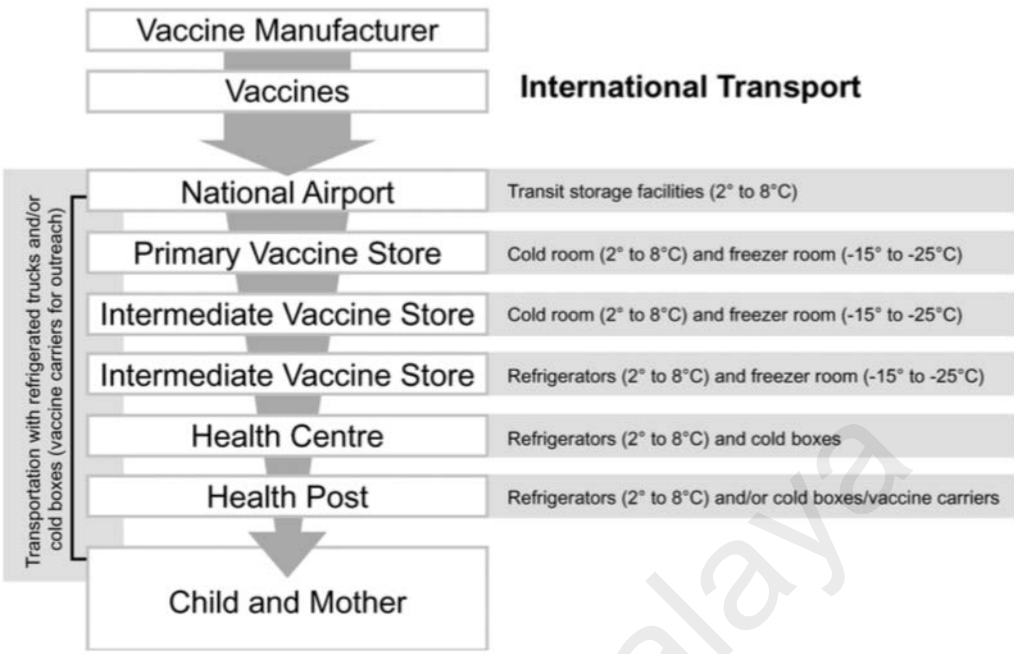

Figure 3.3: Recommended cold chain maintenance by the WHO (World Health Organization, 2004a)

Prior to 2008, vaccine vials were sent by vendors to the central/national drug store, and subsequently distributed to the state drug stores. From the state drug store, the vaccines were routinely dispatched to the peripheral clinics via the district drug stores. Vaccines can be flown from the central store to state stores, whereas distribution within the state is usually by land transport (Hanjeet et al., 1996).

Frequency of dispatching vaccine vials to the health clinics varies, ranging from weekly to monthly, according to demand by each clinic, distance of the clinic from the district store, and availability of bulk storage equipment like a top-loading refrigerator (Hanjeet et al., 1996).

However, after 2008, in order to minimize the distance of travel and increase efficiency of distribution, vendors started to send vaccines directly to regional drug stores upon request via their distribution points throughout the country[8].

In the past decade, the Vaccine Vial Monitor was used to monitor breaches in temperature, specifically exposure to heat during the transport and storage process. However, this system has been replaced by more sophisticated digital monitor enclosed within each heat-insulated cold box[9].

Monitoring and recording the temperature through the whole supply chain, up to the point of care is the key to ensuring a functioning cold chain and good, viable vaccines. However, this is not always possible. As already illustrated in the previous paragraphs, the regional stores only act as transit storage points for vaccines. There is no way to predict whether vaccines are still potent by the time they reach the regional stores from the vendors if there is flawed recording of temperature change by digital monitor during transportation. In fact, studies in Malaysia and Indonesia had documented that vaccines were subjected to extreme temperature ranges, either overheated or freezing, during transport to vaccination centres (Hanjeet et al., 1996; Nelson et al., 2004; Techathawat et al., 2007).

At health centres and vaccinators, cold chain maintenance is subject to another set of challenges. Here, vaccines would be housed in refrigerators until they are administered to children. Effectiveness of vaccine in the cold chain is largely dependent on availability

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[8] Personal communication with Mdm Normalisa, Sarawak State Pharmaceutical Laboratory And Store on 1/4/2015

[9] Personal communication with Mdm Normalisa, Sarawak State Pharmaceutical Laboratory And Store on 1/4/2015

of functioning equipment, stability of power supply, patient load and staff competence. Again, studies have shown that even government-funded health centres could experience lack of functional equipment (Rao et al., 2012), nor were cold chain maintenance standards adhered to (Ministry of Health Malaysia, 2012b). Thus, in the event that a vaccine arrives at individual health centres in optimal condition, subsequent mishandling could still affect its quality and potency.

It is now clear that the preservation of the vaccine cold chain is both labour- and resource-intensive. Gaps or omissions in following the strict procedure could result in breaches in temperature range that may reduce vaccine potency, resulting in impaired antibody production in the children, and increased risk of disease outbreak in the population. This is especially relevant in a hot and humid tropical country like Malaysia, where people rely heavily on refrigerators and air-conditioners to store biomedical items at below room temperature of 25°C. Given the limited funding and human resources in public sector clinics, it is not unlikely that gaps in cold chain maintenance exist, because cold chain and vaccine management are only part of the multitude of duties that each public health provider has to perform daily. This might have been another contributing factor to the 2011 outbreak.

At private sector clinics and hospitals, cold chain is similarly maintained for smaller volume of vaccines, to be offered to children on a pay-per-service basis. Maintenance and quality control of the cold chain in private sector is regulated by the Private Healthcare Facilities and Services Act 1998. Any non-compliance on any of these prescribed requirements constitutes an offence and could be punishable by a fine or imprisonment. Despite probabilities of being penalized for poor vaccine maintenance practices, evidence has shown that not all GPs had the capacity to store vaccines as according to recommendations (Azira, Norhayati, & Norwati, 2013). This could further compromise vaccine quality, which could be a concern in urban areas where GPs play an important role in vaccinating infants.

3.3 Health Service in Sarawak

3.3.1 Sarawak and its people

Sarawak is the biggest of the 13 states in Malaysia. Sarawak and the state of Sabah, are situated at the northern half of Borneo Island and make up what is called the East Malaysia, separated from Peninsular Malaysia (Malaya) by the South China Sea.

Borneo is home to people of several different races; the largest indigenous ethnic group being the Dayaks, followed by the Malays and Chinese. The Dayak people are divided into distinctive subgroups which include the Iban, Bidayuh, Kayan-Kenyah, Kelabit-LunBawang, Dusun-Kadazan-Murut, with high linguistic and cultural diversity (Sarawak State Government, 2016).

Archeological evidence at Niah Cave showed that the earliest settlers in Borneo probably arrived at the island around 40000 years ago. Subsequent immigration occurred in many small waves spread over several centuries, each bringing its own customs, beliefs and dialect, resulting in over 100 tribes speaking in unconnected tongues (MacDonald, 1956). However as time passed, the people gradually influenced one another, that they now commonly speak variations of Malay which is generally comprehensible to all.

According to the Sarawak State Planning Unit statistics, as of year 2010, Sarawak had 2.6 million populations, occupying a total area of 124449 km^2, with a population density of 20 people per km^2, which is the lowest in Malaysia (Department of Statistics, 2011).

To the south of Sarawak lies the East Kalimantan of Indonesia. What separates the 2 countries is the Malaysia-Indonesia border. However, limitations in border security have enabled non-citizens in making trips in-and-out of Sarawak to seek informal employment and health care, even in absence of travel documents (Eilenberg & Wadley, 2009).

Notwithstanding the ease of inter-country migration, travel within Sarawak poses a multitude of challenges to its people, largely due to thick forests and rugged mountainous terrain dissected by swift flowing rivers and rapids in the interior region,

As shown in Figure 3.4, a large part of Sarawak state land, especially the middle and southern portions, consists of rugged mountainous terrain. Only the coastline is made up of a relatively narrow stretch of plains. The same terrain also made it almost impossible to develop a comprehensive land transportation network to serve all the population in the state. At times, travel within the state is achievable only with a combination of land, riverine and air transport.

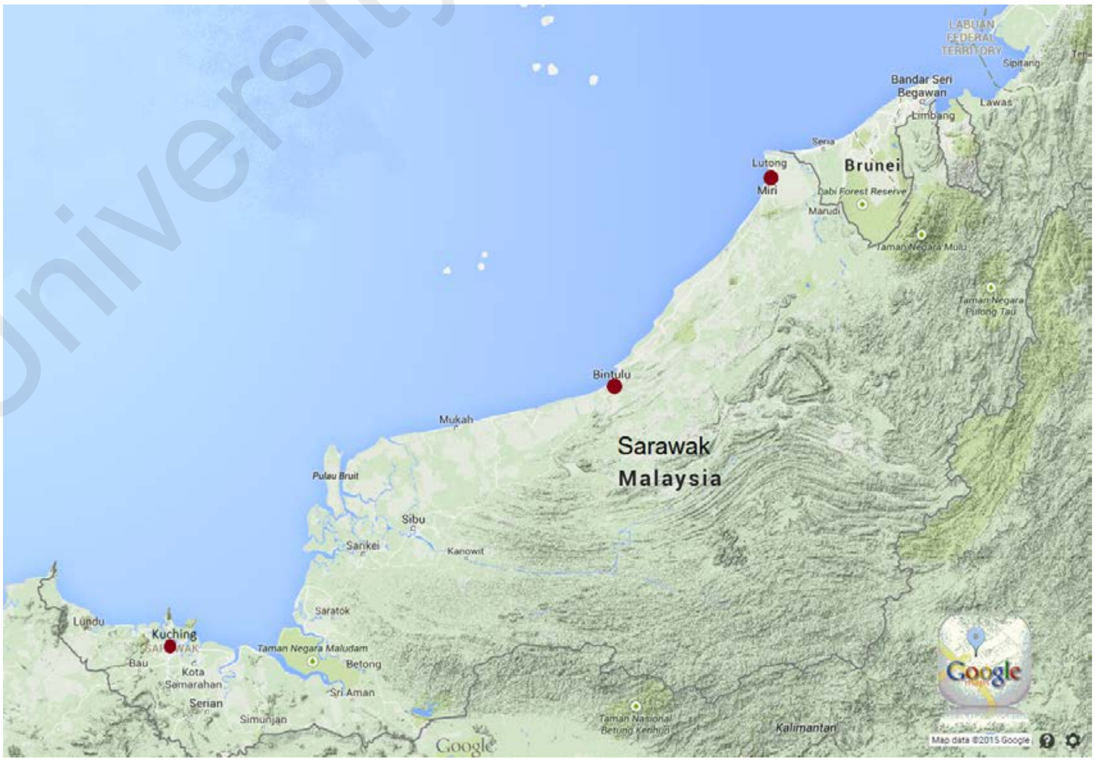

Figure 3.4: Terrain map of Sarawak by Google Maps

To overcome hurdles caused by geographical barrier, the health service delivery system in Sarawak has to adapt to the unique terrain by offering outreach services employing different modes of transportation. Static health facilities only cater to the needs of 70% of the population in Sarawak, while mobile health units offer additional 20% coverage for communities in hard-to-reach areas. Mobile health teams travel by helicopters (the Flying Doctor Service), four-wheel vehicles, boats and on-foot if necessary.

These mobile health teams visit each locality once every one or two months depending on the patient load. Health services given are primarily treatment of simple ailments, dispensing drugs for patients with chronic illnesses, routine maternal and child health services. From time to time, the Flying Doctor Service also has to help evacuate critically ill patients to the nearest hospital.

3.3.2 Vaccination practice at static health centres

At public sector clinics, the community nurses, supervised by health sisters and matrons, play a pivotal role in ensuring the smooth running of the vaccination service on the ground (Ministry of Health Malaysia, 2001). Their scope of duty includes maintaining adequate vaccine stock, storage of vaccine, handling of vaccines, assessing eligibility of children for vaccination, administering and disposal of vaccines, documentation and conducting periodic data collection and calculation.

3.3.2.1 A Typical Vaccination Session in Public Health Facility

Vaccine maintenance and vaccination procedures are standardised across all public sector clinics (Ministry of Health Malaysia, 2001). At point of contact, the community nurse will need to ascertain the purpose of visit to the maternal and child health clinic, be it for medical illnesses, vaccination or developmental monitoring.

If the child has a vaccine scheduled on the day of visit, the community nurse will screen for contraindications to vaccination, for instance intercurrent illnesses. Once she is satisfied that the child is eligible for vaccination, she will proceed to vaccinate the child using the vaccine stored in the temporary storage box.

For each vaccinated child, the community nurse needs to provide the mother with medications and home care advice on common side effects like fever and pain. She will also need to give an appointment date for the subsequent vaccination or well-baby clinic.

If a child is not sufficiently healthy for vaccination, the nurse will give a new appointment date (usually one week later). She may also refer the child for assessment by the medical officer if clinically indicated. It is a standard practice that details of the vaccination need to be documented twice: in the parent-held card as well as in the clinic record.

In a busy clinic, this can potentially lead to missed vaccination opportunity[10], because a nurse needs to make a quick decision as to whether a vaccine is contraindicated in the infant. However, such a decision should not be done lightly, without carefully weighing all clinical information first. Therefore there is a real risk that a child could be deprived of a much-needed vaccine due to incorrect or hasty decision making. In fact, missed

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[10] An opportunity for vaccination is missed when a person who is eligible for vaccination and who has no contraindication to vaccination visits a health services provider and does not receive all the needed vaccines (Nujum & Varghese, 2015).

opportunity was reported in overseas studies to be the cause for 15% to 34% of non-vaccination cases (Akramuzzaman et al., 2002; Nujum & Varghese, 2015).

3.4 Summary

The health care system in Malaysia today has its root in the welfarist philosophy of the previous colonial government. However, the post-independence development of public health system has placed much emphasis on rural health service, and led to the emergence of private practitioners who fulfilled the health needs of people residing in the densely populated and rapidly developing urban areas. Private practitioners, while possessing the necessary competence in providing vaccines to the infant population, might not have the capacity to fully comply with the cold chain maintenance recommendations which are vital in ensuring vaccine viability. On the other hand, public health facilities might have suboptimal vaccine and cold chain quality despite government funding. Problems such as out-dated vaccination policy and recommendations, shortages of manpower, overcrowding of patients, bureaucratic procedures and over-documentations, could have a deleterious impact on childhood vaccination, as optimal vaccine management is labour-intensive and probably suffers compromises in quality when it clashes with a nurse's busy schedules. In conclusion, the current dichotomous public-private health services have inherent systemic problems unique to each side of the public-private divide, which could have led to suboptimal vaccination practices especially in the urban areas and subsequently contributed to the 2011 outbreak.

Having discussed the Malaysian health system as the backdrop to the 2011 outbreak, we shall next examine the importance of adherence to measles vaccination schedule in accordance to the national recommendation detailed in chapters 4 and 5, and the appropriateness of timing of first measles vaccination in a modern-day society with high population measles vaccination coverage.

CHAPTER 4: DELAYED CHILDHOOD MEASLES VACCINATION AND OCCURRENCE OF MEASLES OUTBREAKS

4.1 Introduction

Historically, it has been observed that as countries attained high population vaccination coverage, there was a concomitant reduction in measles incidence. However, it has also been recently observed that countries with high vaccination coverage still experienced bouts of measles outbreaks(Poland & Jacobson, 2012; World Health Organization, 2009), which resulted in deaths and serious complications despite the availability of good health services (Perry & Halsey, 2004).

This apparent discrepancy between population immunity and high population vaccination coverage could be explained by several factors including the existence of non-vaccinated children. However, one of the less investigated causes is the existence of pockets of susceptible persons caused by delayed vaccinations or non-compliance to vaccination schedules (Leuridan et al., 2012). Delayed vaccination could render children susceptible to measles infection during the critical period between disappearance of maternally conferred immunity and the time they developed antibody to the first dose of measles vaccine. As national reporting on vaccination coverage usually denotes the proportion of the cohort of children vaccinated which is calculated annually, it would not take into account of any delay in receipt of vaccine, as long as it occurred within the same year. This would become a risk factor for the rapid propagation of measles infection throughout a population, if there were a sufficient pool of susceptible individuals.

Whilst much research had been done to link low population vaccination coverage with measles outbreaks, the association of delayed MMR vaccination and occurrence of measles outbreak has not been systematically reviewed. This systematic review thus aims to gain insights into vaccination that occurs behind schedule, or delayed vaccination, as a possible cause of measles outbreaks.

The following sections will start with the methodology in Section 4.2, followed by results in Section 4.3, and brief discussion on study limitations in Section 4.4, before concluding with summary of findings in Section 4.5.

4.2 Method

4.2.1 Criteria for review

Studies included were primary and secondary studies that investigated the link between age-appropriateness and timeliness of first dose of measles vaccination and measles outbreaks. Studies on simple vaccination coverage, other aspects of measles vaccine (efficacy, safety, acceptability, availability) or other vaccines or theoretical papers were excluded.

Articles included were primarily in English. Articles written in languages other than English, but having abstract written in English were reviewed for relevancy of information. Relevant abstracts were also reviewed.

4.2.2 Search Strategy

Databases searched include PubMed and Embase, all literature from inception of database through to July 2013 were included. Initial search was conducted by combining Medical Subject Heading terms of “Measles Vaccine", "Measles-Mumps-Rubella Vaccine", "Immunization", “Vaccination", "Disease Outbreaks" to identify all articles with reference to vaccination and outbreaks.

Further search for articles specifically addressing delayed vaccination and outbreaks was done by combining the following key terms: measles AND (vaccin* OR immuni*) AND (delay*OR late) AND (epidemic OR outbreak).

The titles and abstracts of all articles were reviewed to decide on the full-text articles that would be retrieved and read. All references in included studies and their citation history were also reviewed to identify additional studies.

4.2.3 Additional sources

References of articles retrieved were hand-searched to find additional literature. Potentially relevant literature like government reports and guidelines were also searched.

4.2.4 Data extraction

The following data were extracted: author and date of publication, country of study; time frame of data collection; study design; sample characteristics; findings of association between delayed vaccination and measles outbreaks.

4.2.5 Quality assessment

Appraisal tool for descriptive study was used (Milton Keynes Primary Care Trust, 2002), which consisted of a 10-item checklist addressing question like focused issue, appropriate design, subject recruitment, accuracy of measurement, data collection, adequacy of sample, clarity of result, rigor of data analysis, credibility of findings, and generalizability.

Each study could receive a minimal score of 0 and maximum of 10 points, with higher score indicating better quality. Studies with score of less than 4 were discarded.

4.3 Results

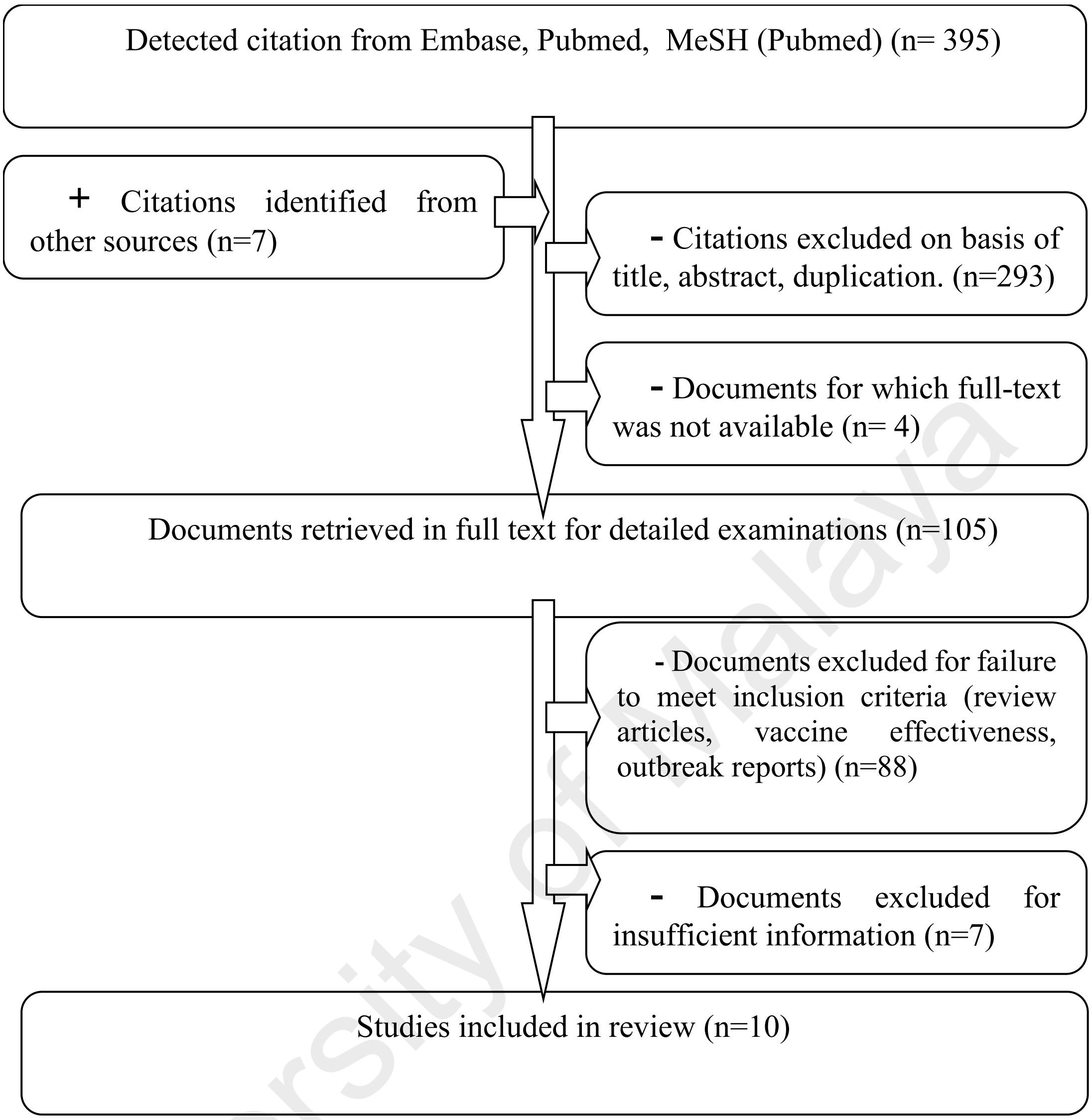

Figure 4.1: Diagram of search process

Our search produced a total of 402 titles, which consisted of 395 titles from database search and seven titles from manual search. These were imported into Endnote, which were finally reduced to 10 articles after eliminating 293 citations which consisted of duplicates and unsuitable titles, 4 articles for which full texts were not available, 88 documents which did not meet the inclusion criteria and 7 documents with insufficient information needed for analysis. The final studies consisted of: two secondary data analysis, three cohort studies, two outbreak investigations, two cross sectional surveys and one case-control study. In terms of the geographical origin of the studies, seven studies were conducted in Europe, one in North America, while the remaining two were done in Asia.

4.3.1 Summary of articles

Table 4.1: Measles outbreaks could occur despite high national vaccination coverage

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Akmatov, 2007, Kazakhstan	Secondary Data Analysis (Demographic & Health Survey 1999)	Demographic & Health Survey done in 1999. Timing of analysis unknown. Analysed after measles outbreak 2004 – 2005	4800 women of child-bearing age 815 children below 5 years Background: outbreak of measles in 2004 Overall measles coverage = 86% Age-appropriate (12 months) coverage = 66% Delay > 3 months = 6%	Political transition in Russia disrupted vaccination service. High overall coverage belied low age-appropriate coverage for measles vaccine Delayed vaccination increased time of susceptibility, may play a role in outbreaks of vaccine-preventable diseases.
Jeong, 2011, Korea	Cross-sectional survey	Sept 2007	Community survey conducted in districts facing measles outbreak. Background: reported administrative national coverage = 99% Total 394 children aged between 15 to 23 months, simple coverage for MMR from sample = 88%, timely coverage (12-15 months) = 81% of vaccinated children 20% children had early or delayed vaccination	Age-appropriate vaccination decreased risk of disease.

Table 4.2: Delayed vaccination and its impact on herd immunity

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Bielicki, 2012, Switzerland (Bielicki, Achermann, & Berger, 2012)	Dynamic cohort study	January 2006 to June 2010	Children insured with Helsana Health Insurance, Switzerland at the age of no later than 4-weeks old D.O.B. 1/1/2006 – 30/6/2008 Follow-up: 2 years Total 42950 children Findings: for children younger than 2 years, average susceptible period due to delayed MCV1 = 89.1 days. When simple coverage = 84.5% for cohort of children under 2, delay reduced the effective coverage to 48.6%	Timeliness of measles vaccination influenced the effective population immunity level.

Table 4.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Dannetun, 2004, Sweden	Cohort study	Jan – Feb 2003	Cohort of children in central Sweden born in year 1998 to 2000, registered with well-baby clinics. (MMR offered at 18 months) Total subject = 3871 children Findings: At 24 months: 80% to 88% children vaccinated At 36 months: 90% to 93% vaccinated At 48 months: 94% vaccinated Using the same model, delayed vaccination added on average 1 to 1.9 months of susceptibility to each child in the cohort.	Delayed vaccination accounted for drop in MMR coverage and increased susceptible proportion in the population.

Table 4.3: Delayed vaccination and its association with measles outbreaks

Author/Year/Location	Study Design	Time frame	Description	Conclusion
CDC, 1990, Chicago USA (Centers for Disease Control, 1990)	Epidemiological Data Analysis	Feb to Dec 1989	Age-appropriate measles vaccine coverage rate in high-incidence area = 49%, in comparison to age-appropriate coverage in low-incidence area of 79%. Measles vaccine coverage eventually became 95% by the time of enrolment for kindergarten.	Measles outbreak is associated with failure to provide vaccination at the recommended age.
Asnong, 2011, Belgium	Secondary Data Analysis (Belgium vaccine database)	Dec 2008 – Feb 2009	Measles outbreak in Orthodox Jewish community in Antwerp in 2007 to 2008. MMR coverage in outbreak region = 89% to 97%. MMR recommended at 12 months Total 949 children from nursery and primary schools included, from 8 schools of 4 different belief systems (Orthodox Jewish, Modern Jewish, anthroposophical, mainstream). Findings: Students in Orthodox Jewish schools were 3.5 times more likely to be unvaccinated for MMR, and 5 times more likely than mainstream students to have delayed MMR vaccination.	Measles outbreak was consistent with a low age-appropriate MMR vaccination coverage within a community which did not follow mainstream health practices. High regional vaccination coverage figure may mask pockets of unvaccinated population.

Table 4.3: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Qu, 2011, China	Case-control study	Jan – May 2008	Case: infants aged < 8 months with measles infection within 7 – 21 days of hospital exposure. Control: non-immunized infants, matched for residential address. Additional: secondary analysis of measles surveillance data. Findings: Hospital exposure is risk factor for infant infection. At birth, 32% had protective antibody against measles. At 7 months, only 4% had protective antibody Among 9 to 11-month- old measles patients, 73% children were not vaccinated on time.	Measles in infants were caused by loss of maternal antibody, delayed vaccination and contact with source of infection. In outbreak situation, age of vaccination needs to be lowered (to 6 months)

Table 4.3: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Barrabeig, 2011, Spain	Retrospective cohort study	Oct 2006 – Jan 2007	Outbreak 2006-2007 Study conducted 2007 Retrospective cohort in institutions attended by pre-school children. Total 15 centres, 1394 children aged between 3.5 to 70 months. (MMR age = 15 months) Vaccine coverage = 91% Vaccine effectiveness = 96% Lowering MMR to 12 months would prevent 79% of cases in children aged 12 to 15 months	Timely administration of MMR at 12 months reduces risk of measles outbreak.
Siedler, 2002, Germany	Epidemiological data analysis	1999 – 2001	Cross sectional epidemiological data analysis Combination of: Telephone survey of vaccination status in 3-year-old children Analysis of 3 surveillance databases Measles vaccine coverage at: 15 months = 22% 24 months = 77% 36 months = 87% Highest age-specific incidence of measles = in 12-24 months (36%) 500/900 (55%) reported cases could be averted if vaccinated on time.	Delayed vaccination was responsible for size of epidemic.

Table 4.3: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Van den Hof, 2002, Netherlands (van den Hof et al., 2002)	Cross sectional survey	Dutch Serological Survey 1995-1996 Timing of modelling unknown.	Mathematical modelling based on serological survey Background: measles vaccine = 14 months & 9 years. Based on current and revised vaccination schedule: Prediction of age-specific percentage of susceptible population Prediction of average percentage of lifetime spent susceptible Findings: Lowering age of MMR from 14 months to 11 months results in less reported measles cases, lower average percentage of lifetime spent susceptible to measles (not statistically significant)	Lowering age of first MMR to 11 months has relatively small impact on susceptible population or proportion of lifetime spent susceptible compared to lowering second MMR age.

4.3.2 Outbreak despite high national aggregate coverage.

Kazakhstan suffered a measles outbreak against an overall national aggregate vaccine coverage of 86%. Five years prior to the outbreak, a national household survey in Kazakhstan showed that 34% of children aged between 12- to 60 months were vaccinated against measles with a substantial delay. This suggested that the said outbreak might have been facilitated by a combination of overestimated coverage and delayed vaccination (Akmatov et al., 2008).

In Korea, despite a national coverage of 99%, a survey conducted in districts facing a measles outbreak revealed that timely MMR vaccination to be just 81%, which is much lower than the recommended 95%. The remaining 20% children who were categorized as vaccinated had received their vaccines after the recommended age (12 to 15 months), which rendered them susceptible to measles infection (Jeong et al., 2011).

Both countries had health systems similar to Malaysia, where vaccines were provided free-of-charge in primary health care facilities. Thus it was not unlikely that health system determinants associated with delayed vaccination in the two countries could play a role in the recent measles outbreak faced by Malaysia.

4.3.3 Population immunity in relation to delayed vaccination

Two studies evaluated the effect of delayed vaccination on its effect on the population's immunity. The study by Bielicki et al in Switzerland, 2012, found that while 84% of children in the cohort eventually received measles vaccine by the age of two, only 62% received it on their first birthday (as recommended). As a result, the effective population coverage in the cohort was only 48.6%. Because of delayed measles vaccination among members of the cohort, the children in the cohort spent an average 89 days unvaccinated and were susceptible to measles before their second birthday (Bielicki et al., 2012).

In a three-year cohort of close to 4000 Swedish children aged between 24 to 48 months, Dannetun et al reported that although MMR vaccine was scheduled at 18 months, only 80% to 88% of the 24-month-olds had been vaccinated (Dannetun et al., 2004). The proportion increased gradually until the overall coverage reached 94% by 48 months of age. Based on the same cohort, the total duration of vaccination delay was accountable for additional 1 to 1.9 months of vulnerability to each child.

Thus, current evidence shows that individual delay in vaccination schedule has an impact on the overall population coverage and herd immunity against measles.

4.3.4 Association between delayed vaccination and outbreak

Six studies showed evidence that delay in vaccination was associated with risk of measles outbreak.

In 1990, the Centre for Disease Control reported that from school vaccination records in Chicago, United States of America, that although 95% of children were vaccinated against measles at time of school entry, areas facing measles outbreak showed that on average, only 49% of 2-year-old children were vaccinated, compared to areas with low measles incidence, where on the average 79% of all 2-year-old children were vaccinated (Centers for Disease Control, 2011). The deficiency in population immunity became more obvious when comparing age-appropriate vaccination: 26% in areas facing measles outbreak as opposed to 50% in low-incidence areas.

Asnong et al investigated measles outbreak among the Orthodox Jewish community in Antwerp Belgium and concluded that despite high regional MMR coverage, students attending Orthodox Jewish schools were at high risk of being unvaccinated or vaccinated late compared to students from mainstream schools (Asnong et al., 2011). However, this study was limited by incomplete school vaccination database due to presence of independent private vaccinators who were not included in the database.

Qu et al reviewed outbreak reports in China, spanning the years 1953 to 2009; they noted that infant patients were most susceptible to measles infection. Although the first dose of measles-containing vaccine was scheduled at 8 months, 73% of the eligible infant patients had their vaccinations delayed (Qu, Gao, & Wan, 2011). Thus majority of the measles cases occurring during the study period of 2004 to 2009 in Tianjin, China could have been prevented by adhering to the vaccination schedule.

Barrabeig et al performed an outbreak investigation in 15 child-care centres in Spain where a measles outbreak occurred, resulting in 77 confirmed cases. As MMR was given routinely to all 15-month olds, most of the cases (93.5%) occurred in children too young to be vaccinated. Thus, although the MMR coverage in the cohort was high (91%), and calculated vaccine effectiveness was 96%, which was consistent with literature, the high number of unvaccinated children, resulted in inadequate herd immunity to curb the outbreak. Calculation based on the hypothetical age of MMR vaccination at 12 months predicted 79% of the cases among children aged between 12 to 14 months could have been averted. The author concluded that timely administration of measles vaccine at 12 months could have reduced the size of outbreak (Barrabeig et al., 2011).

Siedler demonstrated through analysis of German national surveillance database that children aged between 1- to 4 years were most susceptible to measles infection with 36% to 37% of the measles cases occurring among one-year-old children. However, the proportion of children vaccinated at 15 months as recommended by the German national schedule was only 22%, slowly rising to 77% by second birthday. This implied that despite their high susceptibility, the one-year olds were not adequately protected because of delayed vaccination. From calculation, 55% of the measles cases could have been averted if the patients were vaccinated according to schedule (Siedler et al., 2002).

Van Den Hof from Netherlands did a mathematical modelling on measures of protection (percentage of susceptible population, number of reported cases in an epidemic year, and percentage of lifetime spent susceptible) rendered by different vaccination schedules based on the Dutch Serological Survey 1995 – 1996. Lowering the age of MMR from 14 months to 11 months results in less reported measles cases, lower average percentage of lifetime spent susceptible to measles, although the benefit was not statistically significant (van den Hof et al., 2002).

In this review, all studies were observational in nature. However, a common finding was that regions facing measles outbreak had higher occurrence of delayed vaccination among infants. In addition, inferential statistics showed that a significant proportion of all measles cases could be prevented had the infants received their vaccine on time (between 55% to 79%).

4.4 Study limitations

The case definition used for a confirmed measles case was not consistent for all included studies. Some surveillance databases did not require serological confirmation, which might result in inclusion of misdiagnosed cases.

Similarly, definitions of age-appropriate and delayed vaccination varied widely in the included studies. As a result, the rates of delayed vaccination in the included studies are not comparable.

The incidence of measles was not reported consistently across the literature, ranging from attack rate, case per million to age-specific incidence rate. Not all studies gave absolute number of cases. In addition, age groups were categorized differently across studies. Therefore it was not possible to compare proportion and attack rates across countries. It was also not possible to perform meta-analysis because of the heterogeneity of data.

4.5 Summary of findings

Measles vaccination occurring beyond the recommended age effectively reduces the herd immunity in a population, and increases the risk and size of a measles outbreak. However, this gap in population immunity caused by delayed vaccination is easily masked by annual vaccine coverage. Therefore age-appropriate or timely vaccination coverage indicator should be routinely reported because it has implication for occurrence of measles epidemics and is sensitive in identifying gaps in vaccination service.

Having looked at evidence showing the deleterious effect of late vaccination, we will next examine the latest evidence on the optimal age of first measles vaccination for infants born in highly vaccinated populations, such as the ones in Malaysia.

CHAPTER 5: THE OPTIMAL AGE FOR FIRST MEASLES VACCINATION

5.1 Introduction

Up to this point, we have reviewed established evidence that likelihood and size of measles outbreak is influenced by the degree of population adherence to vaccination schedule, or rather, the severity of delay in vaccination in relation to the recommended age. This raises the issue of whether the official recommended age confers protection to infants as soon as they become susceptible to measles infection, and whether it independently imposes vaccination delay in addition to delay resulting from parental choices.

Historically, infants were less affected by measles infection because they were protected by anti-measles antibody transmitted from their mothers during pregnancy, which lasted until the end of their first year, when measles vaccination would induce active immunity that that protected them until adulthood. However, this may no longer be true.

High measles vaccination coverage nowadays is accompanied by a change in the epidemiological pattern, so that instead of primarily affecting toddlers (Perry & Halsey, 2004), measles outbreaks increasingly affect older children, adults (Jani, Holm-Hansen, et al., 2008) and especially infants who have not reached the recommended age for vaccination (Leuridan et al., 2012).

The disease burden among infants too young to be vaccinated was made worse by the observation that modern-day mothers who acquired anti-measles immunity by vaccination had lower titres of antibody; their antibody also persisted for shorter duration. As a direct consequence, they transferred less antibody to their foetuses compared to mothers who acquired immunity through natural infection. As women in the reproductive age-range today are likely to have received measles vaccine during their childhood, the issue of their off springs becoming susceptible to measles at a much younger age than the recommended schedule becomes pertinent (McLean, 1995; Mulholland, 1995; Muscat et al., 2009).

The optimal age for vaccination is recommended on the basis of maximal protection. In another words, a vaccine should be given as soon as an infant's passive immunity starts to wane. From the public health perspective, the optimal age for measles vaccination ought to be the age where most infants have antibody levels below the protective threshold (Leuridan & Van Damme, 2007).

In light of the changing epidemiological scenario as a direct consequence of previously successful mass immunisation programme, this literature review aims to assess the optimal age for first measles vaccination, and explore the feasibility of an alternative vaccination schedule. The following sections will start with methodology in section 5.2, followed by results in section 5.3, and brief discussion in section 5.4, before concluding with summary of findings in section 5.5.

5.2 Method

5.2.1 Criteria for review

Studies included were primary and secondary studies that investigated the link between loss of maternal antibody against measles, age for the first dose of measles vaccination, and induced seroconversion. Studies on non-human subjects, other aspects of measles vaccine (efficacy, safety, acceptability, availability) or other vaccines, or theoretical papers were excluded.

Articles included were primarily in English. Articles written in languages other than English, but having abstract written in English were reviewed for relevancy of information. Relevant abstracts were also used.

5.2.2 Search Strategy

Databases searched include PubMed and Embase, all literature from January 2004 until December 2013 were included.

Initial search was conducted by combining Medical Subject Heading terms of “Measles", "Maternal antibody", "Loss", and “Decay" to identify all articles with reference to age of vulnerability to measles.

These terms were used in various combinations using the operators “AND” and “OR” to so that maximal number of related articles were included, regardless of positive or negative findings.

Titles of all articles returned by the initial search, as well as the bibliographies of all relevant review articles were screened to identify articles of interest that would be retrieved and read in full.

5.2.2.1 Searching additional sources

Citations and references of returned articles retrieved were hand-searched to find additional literature. Potentially relevant literature like government reports and guidelines were also searched.

5.2.3 Data extraction

The following data were extracted: author and date of publication, country of study; time frame of data collection; study design; sample characteristics; findings of association between delayed vaccination and measles outbreaks.

5.2.4 Quality assessment

Appraisal tool for descriptive study was used (Milton Keynes Primary Care Trust, 2002), which consisted of a 10-item checklist addressing questions like focused issue, appropriate design, subject recruitment, accuracy of measurement, data collection, adequacy of sample, clarity of result, rigor of data analysis, credibility of findings, and generalizability.

Each study could receive a minimal score of 0 and maximum of 10 points, with higher score indicating better quality. Studies with score of less than 5 were discarded.

5.3 Results

Figure 5.1 depicted the literature search process. Searching through publications in Medline and Embase for the past ten years yielded 113 titles eligible for review. A further three titles were identified from manual search, giving a total of 116 titles. After eliminating duplicates, reviewing titles and abstracts, the final number of included articles was 22. The timing of studies spanned from early 1990s to 2012. These studies can be categorized into seroconversion trials and descriptive serological studies.

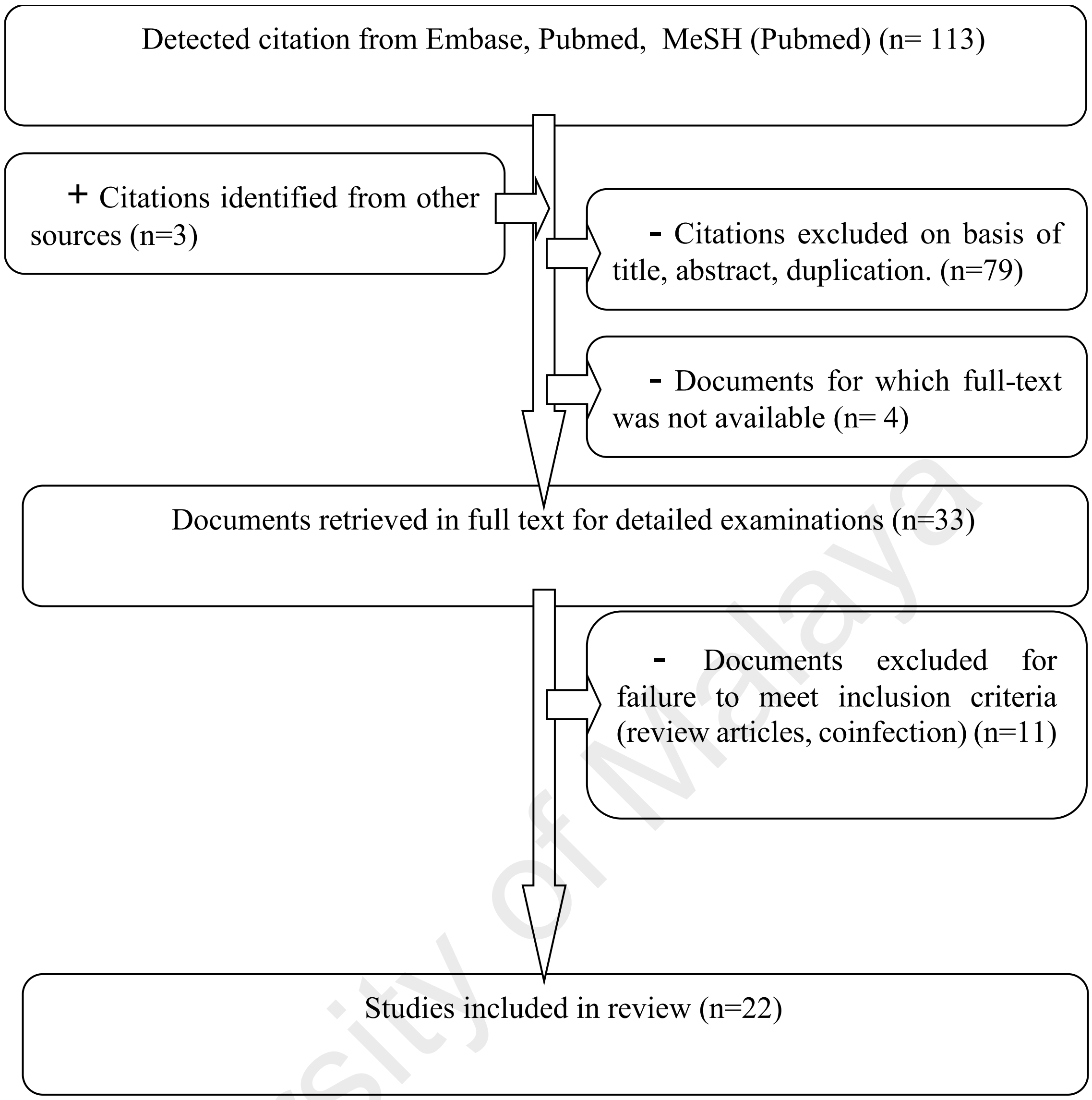

Figure 5.1: Diagram of search process

Table 5.1: Optimal age for vaccination – evidence from seroconversion studies (2004 to 2014)

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Redd, 2004, USA	Randomized Controlled Trial (Seroconversion)	1992 to 1994	Children were randomized at 7 months to receive MMR vaccine at 9 months (n=285), 12 months (n=358) and 15 months (n=347). Pre- and post-vaccination serum samples were drawn. Method: Enzyme immunoassay (EIA). Seroconversion defined as 4-fold increase in post-vaccination titre. Children vaccinated at 9 months of age were less likely to respond than were children vaccinated at 15 months of age (P<.001 for mothers born in or before 1963 and P <.03 for mothers born after 1963). Thus, children who initially had been randomized to receive MMR vaccine at 9 months of age but had not yet been vaccinated were re-randomized to be vaccinated at 12 or 15 months of age. Difference in seroconversion rate for 12-month-olds and 15-month-olds were not statistically significant. However, maternal age affected seroconversion rate. The seroconversion rate among children vaccinated at 9 months of age whose mothers were born after 1963 was 93%, compared with 83% among similarly aged children whose mothers were born in 1963 or earlier.	The current very low risk of exposure to measles in the United States does not indicate a need to lower the age for measles vaccination than the recommended 12 months.

Table 5.1: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Helfand, 2008, Malawi	Randomized controlled trial	August 2000 – September 2002	Total 1756 children completed follow-up. Infants followed up with serological samples at 6 months, 9 months and 12 months. Method: EIA, definition of positive result not available. Participants were randomized into 4 arms according to maternal HIV serostatus, infant's HIV serostatus and vaccination schedule of 6+9 months and 9 months. HIV-unexposed children randomized into receiving 1 dose at 9 months were the control group. For HIV uninfected children: the seroconversion rate at 12 months old after receiving 2 doses of vaccine at 6+9 months was 94% (HIV positive mothers), and 92% (HIV negative mothers). Children in control group (1 dose at 9 months) had seroconversion rate of only 76%.	Early first dose of vaccine at 6 months was safe and effective in HIV-negative infants. It also appeared to prime immunogenicity of 2nd dose at 9 months.

Table 5.1: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Ichikawa, 2013, Japan	Longitudinal (Seroconversion + Serological)	November 2001 – November 2005	Longitudinal study with intervention (vaccination at 6 months) for subpopulation of subjects. Preterm infants were followed up with serial serologic test up to 5 years. Method: Neutralization test. Protective level defined as 120mIU/ml. Total 152 infants tested at birth. At birth, 84% of premature infants tested positive for antimeasles antibody, between 1 to 3 months of age, 35% infants still had measles antibody. After 3 months, no infant had detectable measles antibody. Children born at lower gestational period (<28 weeks) and at lower birth weight (<1000g) had significantly lower antibody titre compared to older and heavier newborns. All 17 infants who received measles vaccine at 6 months seroconverted.	Maternally transferred immunity against the measles virus decreased to undetectable levels at by 6 months after birth in preterm infants. Early measles vaccination at 6 months after birth was effective in preterm infants and induced cell-mediated immunity.

Table 5.1: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Martins, 2008, Guinea Bissau	Randomized controlled trial (Seroconversion)	2003	Authors investigated different vaccination strategies: 2 doses at 4.5 and 9 months, 1 dose at 9 months using Edmonston-Zagreb and Schwarz strains. Method: Analysis using haemagglutination inhibition (HAI) test. Protective antibody level set at 125mIU/ml. 28% of infants aging 4.5 months were protected against measles (pre-vaccination). Among 9-month-olds, only 5% had protective antibody levels pre-vaccination. 92% of infants vaccinated at 4.5 months had measles antibody at 9 months, compared to 9% among control group. Treatment group (4.5 months) had a mortality rate ratio of 0.18 compared to control group (9 months).	In this interim analysis standard titre Edmonston-Zagreb measles vaccination at 4.5 months of age provided more than 90% protection against infection and 100% protection against admission to hospital. Early two dose strategy providing first vaccination at 4.5 months might be useful to protect infants during outbreak situation.

Table 5.1: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Kurubi, 2009, Papua New Guinea	Longitudinal study	May – December 2006	Total 141 children completed follow-up from 6 to 9 months. 1 sample each from Pre-vaccination (6 months) and Post-vaccination (7 to 9 months) session was taken per child and analysed. Method: EIA, definition of seroprotective level > 330 mIU/ml, equivocal between 150 to 330 mIU/ml, seronegative <150 mIU/ml. 42% of infants with circulating maternal antibody seroconverted after vaccination at 6 months, whereas 69% of infants with no remaining maternal antibody seroconverted. Presence of maternal antibody was significantly associated with lower rate of seroconversion (Odds Ratio = 0.41)	Antibody response to measles vaccine at 6 months was unsatisfactory, although other benefits (practical consideration, cell-mediated immune response, reduced disease severity) need to be considered
De Serres, 2012, Canada	Epidemiological data analysis (Seroconversion)	June 2011	Outbreak investigation for 1306 students in Canadian high school during outbreak in 2011. Vaccine efficacy = 97% when administered at 15 months compared to 93% at 12 months. Risk of measles is significantly higher if measles vaccine received at 12 months compared to 15 months (p=0.04)	Suggests measles vaccine be given at 15 months.

Table 5.2: Optimal age of vaccination – evidence from serological studies (2004-2014)

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Techasena, 2007, Thailand	Prospective cohort (Serological)	April 1999 to March 2001	1010 mother-infant pairs were followed up for serial serum sampling until infant was 24 months old. Method: ELISA. Protective level defined as 255mIU/ml. Total 440 infants completed follow-up. At birth, 98% infants were protected against measles. At 4 months, 36% infants had protective antibody level. The proportion dropped to 3% and 1% among 6-month-olds and 9-month-olds respectively. Low maternal antibody level and low birth weight were correlated with lower infant antibody level.	Infants became susceptible to measles infection after 4 months of age.
Karimi, 2004, Iran	Cross-sectional (Serological)	2001 to 2002	Serological study. Method: ELISA. Positive titre for measles antibody defined as optical density higher than cut-off control (0.7). Total 608 children enrolled. 132 children were between 6 to 9 months (pre-vaccination) Transplacental IgG from mothers declined from 10.0% at 6 months to 0% at 9 months of age in non-vaccinated children.	A high percentage of children at 6 months of age were susceptible to measles outbreak. However, vaccination at 9 months was associated with high primary vaccination failure (47%).

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Leineweber, 2004, Switzerland	Longitudinal (Serological)	December 1999 to December 2000	Medical blood samples taken from infants less than 12 months old were analysed for antibody against measles, mumps, rubella and varicella zoster. Method: ELISA, positive titre > 10mIU/ml 95% of term infants (n=62) had cord blood positive for antimeasles antibody. Similarly 96% of cord blood samples from preterm infants (n=73) were positive for antimeasles antibody. 62% neonates with gestational age less than 27 weeks had measles antibody, whereas all new-borns with gestational age 28 weeks and older had measurable maternal antibody. Among infants aging between 6 and 12 months, all infants born at gestational age 31 weeks and younger had lost their antibody. 19% of infants born after 32 weeks gestation still had measurable antibody. A significant number of infants born before 28 weeks of gestation lost maternal antibodies during the first 3 months of life, and between 6 and 12 months of age none of the infants born before 32 weeks of gestation still had measurable anti- bodies against measles.	Premature infants may need MMR vaccine before 12 months; however, further study on immune response to early vaccination is needed.
Kim, 2004, Korea	Cross-sectional survey (Serological)	July – Oct 2002	Seroprevalence study from 36 hospitals in Korea. Total 5826 samples for measles. Less than 10% of children had antibody against measles by 9 months old. (3.5% if exclude early vaccination)	Possible need to bring forward first measles vaccination age from 12 months old to reduce susceptible period in children.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Martins, 2009, Guinea Bissau	Randomized controlled trial (Serological)	2003-2007	Investigated different vaccination strategies: 2 doses at 4.5 and 9 months, 1 dose at 9 months using Edmonston-Zagreb and Schwarz strains. Method: Analysis using haemagglutination inhibition (HAI) test. Protective antibody level set at 125mIU/ml. In the first group, serum samples from 435 children at 4.5 months old were sampled pre-vaccination. 25% had protective level. In second group, serum samples from 343 children at 4.5 months old were sampled. 42% had protective level. Girls had less maternal antibody compared to boys.	Children were susceptible to measles before the age of vaccination (9 months). Age of measles vaccination may be reconsidered.
Gunes, 2007, Turkey	Longitudinal study (Serological)	January to June 2005	89 pairs of mothers and their infants born in Erciyes University Hospital were follow-up. Serial blood samples taken at birth, and 2 monthly until 6 months of age. Method: ELISA For babies born at term (>37 weeks), all had detectable antibody at birth. 62% still had antibody at 6 months. Proportion of infants born between 33 to 37 weeks gestation with detectable antibody was 79% at birth, and 41% at 6 months. Proportion of infants born before 33-weeks gestation with detectable antibody was 76% at birth, and 24% at 6 months.	Earlier measles vaccination schedule (compared to the recommended 9 months) might provide better protection for premature neonates whose mothers have vaccination-induced immunity.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Oyedele, 2005, Nigeria	Cross-sectional (Serological)		Method: ELISA, protective level against measles defined as 120mIU/ml Total 262 infants between 0 and 9 months of age were sampled for pre-vaccination sera. All new-borns had protective IgG level. For infants aging between 3 and 4 months, 42% were protected. 19% of infants aging between 4 and 6 months were protected. 3% of infants aging between 6 to 9 months were protected. More than half infants in Nigeria became susceptible to measles infection before 4 months.	Measles vaccination programme needed review to protect infants with early susceptibility.
Jani, 2008, Mozambique	Cross-sectional (Serological)	June to September 2005	Immunological survey for infants aging between 6- and 9-months old. Method: EIA of oral fluids (qualitative assay) Total 211 6-month-old tested, 12.3% were positive for anti-measles antibody, out of which 8% were positive for measles IgM, suggesting recent infection. Total 295 9-month-old tested, 30.5% were positive for anti-measles antibody, out of which 6.3% had evidence of recent infection.	Introduction of measles vaccine before 9-month-old with additional dose at later age might be necessary, however more supporting evidence was needed.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Gagneur, 2008, France	Cross-sectional (Serological)	October 2005 to January 2007	Hospital-based seroepidemiological study for admitted infants aging between 0 to 15 months. Method: Plaque reduction neutralization (PRN) assay. Protection threshold defined as 120mIU/ml. Total 348 infants evaluated. Proportion of infants with detectable antibody at protective level was 100% for infants up to 1 month old. Between 5th and 6th months, the antibody rapidly fell. Among 6-month-olds, only10% of infants were protected. The proportion reduced 5% at 10th month, and no infants beyond 10 months of age were protected. Mean concentration of maternal antibody fell below seroprotective threshold by 6 months.	Lowering the age of routine vaccination from 12 to 9 months of age would reduce the immunity gap between passive and active protection.
Dominguez, 2008, Spain	Epidemiological data analysis	Aug 2006 – July 2007	Descriptive study of measles outbreak in Catalonia, Spain in 2006. Significant proportion (50%) of cases occurred in infants under 15 months (age of 1st MMR) 59% of cases among children less than 4 years were unvaccinated.	Need to lower age of vaccination to 12 months old to reduce pool of susceptibles.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Waaijenborg, 2013, Netherlands	Cross-sectional (Serological)	2006-2007	Serological survey. 24147 age-stratified subjects aging <80 years donated blood sample. Out of which 1243 women and 434 children below 14 months were selected. (Susceptible antibody level determined as 0.2 IU/ml) Duration of protection for infants were 3.3 months if mothers were vaccinated, and 5.3 months if mothers were not-vaccinated against measles. Infants were vulnerable to measles before age of vaccination.	MMR vaccination has effect over maternal protection. MMR vaccination schedule therefore needs to be adapted.
Leuridan, 2010, Belgium	Longitudinal study (Serological)	May 2006 to November 2008	Serological study for pairs of mother and infants. Method: repeat serum samples from mother-infant pairs were taken. Antibody tested with ELISA method. Protective antibody level determined at 300mIU/ml. Sera from 210 infants were analysed. Infants from vaccinated women had significantly less anti-measles antibody compared to naturally immune women. At 3 months, 29% infants of vaccinated women and 60% infants of naturally immune women still had antibody. At 6 months, less than 1% infants of vaccinated women and 24% infants of naturally immune women were protected by maternal antibody. At 9 months, all infants had lost maternal antibody. The median time to loss of immunity was 2.61 months: 0.97 months for infants of vaccinated women and 3.78 months for infants of naturally immune women.	Measles vaccination could be moved forward at 9 months or early if supported by more studies.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Manirakiza, 2011, Central African Republic	Cross-sectional (Serological)	2008	Serological study with purposive sampling. Method: Measles IgG ELISA, detection level at 1.2 times Optical Density of control/index. Total 395 children aging between 1 month and 15 years were recruited. Maternally derived measles antibody was detectable in 14.8% of infants aging 3 months and younger, and none of the infants older than 3 months.	The first dose of measles vaccine was suggested to be given earlier than 9 months, with additional dose at 12 months.
Zhang,2012, China	Cross-sectional (Serological)	2009	Seroepidemiological study. Method: ELISA Protective titre against measles was defined as 1:800 or higher 433 pairs blood samples from mothers and infants were analysed. Proportion of infants with protective level of antibody was 90% for new-borns, 45% for 4-month-olds, and 15% for 8-month-olds.	Earlier measles vaccination before 8 months of age may be warranted in the population.

Table 5.2: Continued

Author/Year/Location	Study Design	Time frame	Description	Conclusion
Shilpi, 2009, Bangladesh	Longitudinal (Serological)		Serological study for 157 mother-infant pairs. Method: repeat serum samples from mother-infant pairs were taken. Antibody tested with ELISA method. Protective antibody level determined at 200mIU/ml. Final sample of children follow-up until 7.5 months was 24. 97.6% infants were protected at birth. Among 2 t0 5 month-olds, only 25.5% were protected. None of the infants had protective antibody after 5 months.	If supported by larger-scaled studies, measles vaccination could be advanced to before 6 months.
Borras, 2012, Spain	Cross-sectional (Serological)	2012	Serological study. Paired sample, pre- and post- vaccination for children aging 9 to 14 months were taken. Method: Measles IgG ELISA, with detection level at 150mIU/ml Total 51 children sampled. Maternal antibody detected in 45.1% of 9-month olds, 39% of all infants younger than 15 months. For children vaccinated at 9 months, response to vaccination was 74%. Seroconversion was 100% at 13 months.	Advancing the first dose of measles vaccination from 15 months to 12 months is the correct strategy to reduce susceptibility of infants to measles.

5.3.1 Seroconversion studies

Six studies looked into seroconversion after measles vaccination in infants who were vaccinated at various ages. Out of the six studies, two produced evidence to support a later age of vaccination at 15 months, on the basis that seroconversion rate was higher, and vaccine efficacy was higher at 15 months as compared to 12 months (De Serres et al., 2012; Redd et al., 2004).

In 1992, Redd et al found that infants vaccinated at 9 months were less likely to seroconvert compared to infants vaccinated at 15 months (Redd et al., 2004). However, this difference was significant for babies of mothers born before 1963. For younger mothers born after 1963, the seroconversion rates for vaccination age of 9 months and 15 months were not significantly different.

In 2011, De Serres et al described the beneficial effect of later vaccination at 15 months compared to 12 months in terms of higher vaccine efficacy (De Serres et al., 2012). Similar to the study by Redd et al, De Serres' study population was a group of high school students, likely born to older mothers who acquired immunity to measles via natural infection.

Three studies suggested that vaccination for infants younger than 12 months was beneficial. Ichikawa et al studied the effect of vaccination at 6 months for healthy premature infants born before 34 weeks of gestational age in Japan, and found that all recipients seroconverted (Ichikawa et al., 2013). However, this study was limited by its small sample size (17 infants). In addition, the vaccine strain used was AIK-C, which was different from other more popular, commercially available strains such as Edmonston-Zagreb, and Schwarz.

In a relatively small trial in Guinea-Bissou, Martins et al found that 92% of 139 infants vaccinated at 4.5 months responded by developing detectable antibody, whereas 77% developed sufficient antibody deemed to be protective (Martins et al., 2008). When these children were followed up, it was noted that early measles vaccination at 4.5 months was protected against measles and hospitalisation for measles infection. In other words, if the children developed measles infection, the disease was less likely to be severe. This was further supported by the lower overall mortality rate within the treatment group, with the control group manifesting mortality rate of approximately four-times as high as the infants vaccinated at 4.5 months, although the finding was not statistically significant. Thus the authors recommended early vaccination in situations with high risk of measles transmission, such as during outbreaks.

In a similar vein, Helfand et al observed in a large-scale randomized trial that for immuno-competent children, being vaccinated at 6 months appeared to augment their immune response to measles vaccine administered at 9 months, compared to children who just received a single dose at 9 months (Helfand et al., 2008). Another reassuring finding in Helfand's study was that improved vaccine efficacy when given at 6 months was not associated with increase in adverse events, which strengthens the argument for early vaccination in regions where infants experience early-onset vulnerability to measles infection.

However, four years after Helfand's study, Kurubi et al conducted a longitudinal serological survey for infants after they received the first measles vaccine at 6 months, and was not able to reproduce the high seroconversion rate (Kurubi et al., 2009). The poorer outcome was likely attributable to two factors. Firstly, there was difference in methodology in that infants were not followed up after the 2nd dose at 9 months. As seen in Helfand's study, the 6-month dose actually primed the immune system for the subsequent dose at 9 months to increase the ultimate seroconversion rate. Secondly, there were a relatively high proportion of infants with residual maternal antibody (69%), which interfered with successful seroconversion.

5.3.2 Serological studies

16 articles described levels of measles antibody tested at various points of time during infancy.

Depending on the frequency of serological sampling and age range chosen, infants were reported to have lost maternal antibody to measles virus as young as within the first 3 months of their lives, especially in studies that followed up infants from birth(Leuridan et al., 2010; Manirakiza et al., 2011; Oyedele et al., 2005; Shilpi, Sattar, & Miah, 2009; Waaijenborg et al., 2013). This observation was reported across various countries, regardless of socio-economic standings. In Nigeria (Oyedele et al., 2005), less than half of 3-month-olds had sufficient antibody to be deemed as protective against measles. In Netherlands (Waaijenborg et al., 2013), by 3.3 months, infants born to previously vaccinated mothers were already susceptible to measles infection. Likewise in Nigeria's neighbouring country, only 14% of infants younger than 3 months in the Central African Republic were still protected against measles, and all became vulnerable as they grew older than 3 months (Manirakiza et al., 2011). In Bangladesh, 25% of infants younger than 5 months had protective level of measles antibody, and none were protected after 5 months (Shilpi et al., 2009).

Even when measles serology was measured at later ages, studies generally noted early loss of antibody among infants. The age group which susceptibility was first noted ranged from 3 to 6 months. In other words, infants in all the study populations had become susceptible to measles infection before they reached the recommended age for first measles vaccine at 12 months. Jani et al noted that eight percent (8%) of infants as young as 6 months old demonstrated evidence of recent measles infection in a non-outbreak situation, suggesting that infants had lost immunity against measles at least 3 months before reaching the scheduled age for measles vaccination (Jani, Holm-Hansen, et al., 2008). Gagneur et al also noted that the mean concentration of antibody in French infants fell below the protective threshold at 6 months (Gagneur et al., 2008). At the other end of the passive immunity spectrum, Gagneur et al found that French infants had measles antibody below the protective threshold after they were 10 months old (Gagneur et al., 2008), whereas Borras et al described persistence of antibody up to 14 months in a group of Spanish infants (Borras et al., 2012).

Generally, the age group by which all infants completely lost their anti-measles antibody ranged between 3 to 12 months, although majority of the studies reported maximal vulnerability between 4 to 9 months (Jani, Holm-Hansen, et al., 2008; Karimi et al., 2004; Kim et al., 2004; Leuridan et al., 2010; Martins et al., 2009; Techasena et al., 2007; Zhang et al., 2012). So far, the body of evidence was supportive of early measles vaccination, possibly before 12 months in view of early susceptibility to measles infection in young infants.

5.3.3 Miscellaneous studies

Consistent with findings of early susceptibility through serological studies, Dominguez et al described their observational study during a measles outbreak in 2006 in Catalonia Spain, that 50% of measles cases reported occurred in infants younger than 15 months, the age when first measles vaccine was scheduled (Dominguez et al., 2008).

5.3.4 Premature infants

Two studies specifically involved premature infants (Gunes et al., 2007; Leineweber et al., 2004). In both studies, susceptibility to measles in premature infants manifested earlier than term infants.

Leineweber et al found that 38% preterm neonates born at 27 gestational weeks and earlier in Switzerland had no measles antibody at birth. In contrast, all neonates born at 28 weeks and older had measles antibody (Leineweber et al., 2004). Despite having higher antibody level at birth, borderline-premature neonates were not protected for long. Six months after birth, less than 20% of infants born after 32 gestational weeks retained immunity to measles, whereas all infants born earlier than 32 weeks were vulnerable to measles infection.

Five years after Leineweber's study, Gunes et al also noted that preterm infants (<37 gestational weeks) in Turkey not only were less likely to be born with anti-measles antibody, they were also more likely to be susceptible to measles at 6 months of age (Gunes et al., 2007).

5.4 Discussion

5.4.1 Study limitations

The findings from this review should be interpreted in light of possible limitations arising from identification and selection of articles.

There was significant heterogeneity in study design, age of study participants, types and strains of vaccine, length of follow-up, laboratory analysis, definition of antibody titres, as well as study outcomes. Similarly, assessment of publication bias was limited by the heterogeneous nature of the literature included in this review.

The exclusion of non-English papers from full review could have an effect on the synthesis of data and generation of conclusion pertaining to age of vulnerability and vaccine effectiveness, because similar studies from non-English speaking populations were not appraised.

As most of the studies employed a non-probability sampling method, it was possible that infants who participated in the studies differed from infants whose parents declined participation in terms of sociodemographic details, nutritional and health status. The impact of variation in such factors on infant vulnerability to measles infection and immunogenicity of measles vaccine could be reviewed in future when more data become available.

Lastly, evidence on methods and recommendations to reduce infant susceptibility, other than revising the vaccination schedule, could not be extracted because such information was not systematically described in the reviewed articles.

5.4.2 Implications for future research

Larger scale, longitudinal population studies on the long-term effectiveness of early measles vaccination are desirable, as evidence has shown that immunity induced by vaccination declines over time and increases the likelihood of measles outbreak in adults due to secondary vaccine failure.

The needs of growing subgroups of children, such as preterm infants have to be taken into account when vaccine recommendations are made. Compared to term infants, their lack of passive immunity and delayed maturation of immune systems made them even more vulnerable to measles infection, thus they require increased protection through better herd immunity, or when that is not achievable, earlier vaccination. Despite evidence that suggested early vaccination could induce T-cell functions and confer immunity against measles, it remains to be established whether this is also true and safe for preterm infants.

More studies are required on the developmental aspects of infant immune system, as well as the factors responsible for generation and maintenance of immunity against measles that differentiate infection-induced from vaccine-induced immunity. The findings of such studies may potentially aid in the development of a more potent measles vaccine with long-term effectiveness compatible with that of naturally-acquired infection.

5.5 Summary of findings

Successful universal infant vaccination programme had changed the population immunity against measles and the epidemiological patterns of disease outbreaks. It has been reported that infants have lost their protective maternal antibody to measles as young as 3 months of age in highly vaccinated populations. This gap in immunity would remain until the time they develop active immunity to measles vaccination. Combined with a vaccination policy that recommends first dose of measles vaccine at 12 months, this created a wider window of vulnerability in infants, especially if they were born preterm.

Thus, judging from the available evidence, lowering the age of eligibility to first dose of measles vaccine to 6 months and following-up with a booster dose at 12 months or later is feasible and beneficial in highly vaccinated populations aiming to eliminate measles outbreak. However, the long-term effectiveness of such a regime needs to be periodically updated with more serological studies as the population immunity is constantly evolving.

It appeared that the Malaysian MOH's move to lower the age of first MMR to nine months in accordance to WHO recommendation was evidence-based, but the said evidence might not be timely, or up-to-date, as the said recommendation was made in year 2009 while the Malaysian MOH lowered the recommended vaccination age only in 2016 (World Health Organization, 2009). Evidence from the past decade already suggested that measles vaccination at nine months was likely to be too late, and a newer vaccination strategy such as further lowering the recommended vaccination age is indicated.

In conclusion, while a major change in first vaccination age to younger than 9 months may only be possible to implement at the national level after its safety and efficacy are well-established through large-scale studies, it is feasible to minimize the vulnerability in infants too young for measles vaccination through encouraging parents to vaccinate their children according to the recommended schedule, and maintain herd immunity by maximizing coverage of measles vaccine for all eligible persons.

Having established that the optimal vaccination time frame for infants should occur before nine months, and is feasible as early as six months, this thesis will continue with an evaluation of the degree of parental adherence to the existing immunization schedule.

CHAPTER 6: AGE-APPROPRIATENESS OF CHILDHOOD MEASLES VACCINATION IN MALAYSIAN PRE-SCHOOL CHILDREN

6.1 Introduction

In Section 2.5.2, a review of the literature has established that a small number of vulnerable individuals could propagate a measles outbreak even in a highly vaccinated community(Dominguez et al., 2008; Park et al., 2013). This vulnerability could be due to either non-vaccination, or delayed vaccination beyond the recommended age of 12 months when the child is expected to lose his maternal acquired immunity against measles.

Literature review in Section 4.3.1 also presented the growing body of evidence in developing and developed countries that delayed vaccination contributed to measles outbreaks even in countries with high overall vaccination coverage, with outbreaks being reported when the proportion of children who delayed vaccination was as low as 20% (Akmatov et al., 2008; Fadnes, Nankabirwa, et al., 2011; Hu et al., 2013; Jeong et al., 2011; Le Polain de Waroux et al., 2013; Lernout et al., 2014).

From 2009 onward, until the time of the most recent measles outbreak in 2011, Malaysia had been maintaing an annual coverage of above 95%, but the proportion of children who were vaccinated on time was not known. As delayed vaccination is often overlooked when evaluating the success of a vaccination programme, this chapter presents results of a study aimed at determining the level of age-appropriateness of measles vaccination and its correlates for Malaysian preschool-children as a probable gap in population immunity and contributory cause of the measles outbreak.

The following sections will start with methodology in Section 6.2, followed by results in Section 6.3, brief discussion in Section 6.4, then study limitations in Section 6.5, before concluding with summary of findings in Section 6.6.

6.2 Methodology

6.2.1 Data sources

Up until 2011, the year of measles outbreak in Malaysia, the standard reporting format for childhood vaccine coverage was the administrative coverage. The timeliness of vaccination in the children population was hitherto unreported. Traditionally, details on aspects of vaccination unreported by administrative method could be supplemented by community or household surveys which followed methods designed by international health agencies. The three methods widely followed by researchers are Expanded Programme on Immunisation (EPI) cluster survey by WHO, the UNICEF Multiple Indicators Cluster Survey (MICS) and the Demographic and Health Survey (DHS) by ICF International (Burton et al., 2009). However, these surveys were not conducted in Malaysia.

In Malaysia, large-scale household surveys that had been conducted were the Malaysian World Health Survey (WHS 2002), and the National Health and Morbidity Survey (NHMS) which is conducted every 10 years. While the WHS 2002 had a module on child health and vaccination (World Health Organization, 2003), for NHMS the child health module was only included in the NHMS 2016, which was concluded in May 2016 (Noor Ani, 2016).

The WHS 2002 dataset thus became the most recently available source for age-appropriate vaccination coverage data among Malaysian children because the questionnaire collected details on their dates of birth and dates of vaccination. In addition, Malaysia had experienced a measles outbreak in year 2004, which invites the question of whether the timeliness of vaccination among the children population had played a role in the 2004 outbreak. Hopefully the information obtained from the WHS 2002 can yield clues on the possible causes of the recent 2011 outbreak.

6.2.2 The World Health Survey

The World Health Survey (WHS) was an initiative by the World Health Organization to monitor national health systems and health outcomes by using a standardized, valid and reliable household survey instrument. The WHS was conducted in collaboration with selected countries across the globe between year 2002 and 2004 to represent all regions of the world. The study sampling was done probabilistically so that it was nationally representative of rural-urban residence, gender, education, age distribution and racial compositions. To adjust for population distribution, sampling weights were assigned, and non-response was corrected via post-stratification weights.

In Malaysia, the local collaborator for WHS 2002 was the Institute of Health Systems Research. Despite its name, Malaysian WHS 2002 was actually conducted between 2 March 2003 and 16 April 2003.

6.2.2.1 Sampling method employed in the WHS 2002

The survey employed multistage, stratified sampling with proportional allocation. Stratification was by state and urban-rural location. Within each stratum, a three-stage sampling process were performed.

Using maps containing information on Enumeration Blocks and Living Quarters (LQs) which were obtained from the Department of Statistics Malaysia, the whole of Malaysia was divided into contiguous geographical areas with artificially created boundaries called Enumeration Blocks (EB), which were made up of about 100 Living Quarters (LQs)[11]

[11] **Living Quarters**: A living quarters (LQ) is a place which is structurally separate and independent and is meant for living. The terms, 'separate' means a structure is surrounded by walls, fence, etc. and is covered by a roof, while 'independent' means it has a direct access via a public staircase, communal

per enumeration block. LQs were randomly sampled from EB on a probability of 0.76%. Within each sampled LQ, an adult aged 18 and above was randomly sampled as the respondent to answer the questionnaire.

Throughout Malaysia, a total of 7528 LQs were sampled. If there was a child aged five years or below in the living quarter, then the guardian was invited to answer questions pertaining to the child's health. If two or more age-eligible children were in the same living quarter, the youngest child was selected. If there were no eligible child in the living quarter, then the part of questionnaire on child health was not answered.

The sample obtained in the survey had been compared with the estimated population for year 2003 and the sample deviation indices had been calculated by the WHS 2002 team to show no significant deviation from the Malaysian population. Thus the sample was concluded to be representative of the population of Malaysia in 2003 (Institute for Health Systems Research, 2006).

passageway or landing (that is, occupants can come in or go out of their living quarters without passing through someone else's premises.

Table 6.1: Comparison of WHS 2002 survey sample and Malaysian population census 2003

Characteristic	WHS sample		2003 Census	
	Weighted count	%	Count	%
Age				
0-4	2192996	10.1	2966000	11.8
5-14	5042894	23.2	5347700	21.3
15-29	5434426	25.0	6732100	26.9
30-44	4471609	20.6	5244200	20.9
45-59	2983265	13.7	3158600	12.6
60-69	1008009	4.6	991000	4.0
70-79	402098	1.9	452100	1.8
80+	157074	0.7	156600	0.6
Missing	16386	0.1	-	
Gender				
Male	10841914	49.9	12752000	50.9
Female	10866843	50.1	12296200	49.1

6.2.2.2 Study tool employed in the WHS 2002

There were two sets of questionnaires, the household and individual health data. Household data focused on health expenditure, insurance coverage, and indicators of wealth. On the other hand, individual data dealt with detailed health information such as sociodemography, description of the health state, risk factors, diseases and deaths, health care utilization, health system's responsiveness and social capital (Institute for Health Systems Research, 2006).

The questions that yielded information on childhood vaccination were contained in the section of "coverage". Vaccination history for the youngest child in the household who was five years or younger at the time of survey was obtained. In WHS 2002, only details of two vaccines, the DPT and measles vaccines were covered.

From the publication of WHS report by the IHSR (Institute for Health Systems Research, 2006), the coverage for measles vaccine was calculated for children aged 12 to 23 months old and reported to be 79% (compared to the administrative coverage of 94% reported by MOH in 2003).

6.2.3 Vaccination coverage

For the purpose of this thesis, vaccination coverage was calculated for all children aged five years and below, instead of 12 to 23 months, as the under-five group has been found to be most susceptible to measles and its complications (Centers for Disease Control and Prevention, 2012).

6.2.4 Parameters used to report vaccination coverage

6.2.4.1 Administrative coverage

The standard parameter used globally to report and compare vaccination programme performance is the administrative vaccination coverage, also called immunisation coverage, which is reported annually.

Vaccine coverage is expressed as a percentage and calculated using formula 6-1 as shown below (World Health Organization, 2004b):

$$\begin{aligned}&\mathit{Annual\ coverage\ for\ vaccine}\\&= \frac{\mathit{Number\ of\ infants\ who\ receive\ the\ required\ dose\ in\ the\ last}\ 12\ \mathit{months}}{\mathit{Total\ number\ of\ eligible\ infants\ at\ the\ start\ of\ reporting\ period}}\end{aligned} \qquad \textbf{6-1}$$

Eligibility of infants is determined by the age recommendation as per the national protocol. In the case of Malaysia, eligible infants are those who are twelve months old. The data for both numerator and denominator are captured from the administrative databases such as birth and service provider registries. Local data are aggregated to form the national coverage, and reported annually to international child health coordinators such as WHO and UNICEF.

Coverage calculated from administrative data could be biased because of errors in numerator (children vaccinated) or denominator (target population). When the numerator is small because of vaccinations under-reporting at lower administrative levels or at the private sector, coverage can be underestimated. Overestimation in coverage can also occur when children who get vaccinated outside the eligible age range are erroneously included in the numerator. Likewise, inaccurate denominator can bias the vaccine coverage, especially when population census is not updated or inaccurate population growth projection is used.

6.2.4.2 Survey coverage

Often lauded for its greater precision compared to the administrative coverage, survey coverage as its name implies is obtained from community-based surveys. The proportion of infants who have been vaccinated is calculated from all age-eligible (as predefined by the survey team), and in the case of Malaysia, twelve months old infants sampled during the survey period. Vaccination information is determined by looking at parent-held vaccination records, by asking the child's caretaker to recall, or both.

The common issue that often arise with different sources of vaccination information is the validity of recall-based information compared to the health card. Some authors found vaccination histories provided by parents based on recall were not reliable (Bolton, Holt, et al., 1998; Goldstein, Kviz, & Daum, 1993), whereas other studies concluded that parental recall was comparable with health record when calculating vaccine coverage for research purposes (Fielding, Cumberland, & Pettitt, 1994; Hayford et al., 2013; Pless & Pless, 1995; Rossi et al., 2004).

Despite its advantages, vaccination coverage calculated from survey method can be more expensive, logistically more complex and more difficult to administer compared to administrative coverage, unless items targeted at studying children's vaccination history could be incorporated into existing surveys, such as the WHS, UNICEF Multiple Indicators Cluster Survey (MICS) and the Demographic and Health Survey (DHS) (Burton et al., 2009; World Health Organization, 2012b).

6.2.4.3 Age-appropriate vaccination indicators

In view of the limitations of annual vaccine coverage, public health researchers have proposed new indicators to monitor vaccination programme performance. One such indicator is the age-appropriate vaccination coverage, also called timely vaccination coverage, which effectively measures the proportion of eligible infants whose vaccination occurs within the timeline recommended by the health authority.

The definition and calculation for age-appropriate vaccination coverage is not consistent, but vary by researchers and countries. In some countries, vaccination is considered age-appropriate as long as it falls within a recommended age interval. For example, an early study defined age-appropriate MMR vaccination to be one that fell between 366 and 517 days according to then American Academy of Pediatrics guidelines (Bolton, Hussain, et al., 1998). Another study conducted in South Africa defined age-appropriateness of MMR vaccination by WHO, was between 9 to 12 months (Fadnes, Jackson, et al., 2011). Vaccinations that occurred outside the accepted range were considered untimely.

In countries which specify time points for vaccination (usually expressed as months of age), age-appropriate vaccination could be defined as one that occurs on the date a child attain the recommended age(Rossi et al., 2004), within days (Bielicki et al., 2012), or a month (Dombkowski, Lantz, & Freed, 2004; Le Polain de Waroux et al., 2013) of the recommended age, depending on the degree of precision required for data analysis.

Compared to administrative vaccine coverage, age-appropriate coverage is considered a better measure of the quality of vaccination service, as it not only reflects the proportion of infants vaccinated as soon as they lose the protection from maternal antibody, but also monitors the quality of care in terms of follow-up and patient tracing (Bolton, Hussain, et al., 1998; Jeong et al., 2011).

6.2.4.4 Population level indicators of age-appropriate vaccination

Age-appropriate vaccination coverage is a more accurate measure of the proportion of the population who are optimally protected by vaccination at a correct age. However, it could not inform the local policy makers of the magnitude of population vulnerability caused by untimely vaccination.

To measure the cohort effect exerted by individual vaccination delay, researchers have proposed the concept of vulnerable, or at-risk period, expressed as the total length of time spent before receiving the needed vaccine divided by number of children in the cohort (Bielicki et al., 2012). For non-vaccinated children, they were considered vulnerable for the whole length of time from birth until the time of data collection, either at time of survey or end of the reporting period (Rossi et al., 2004). Existing literature has advocated the use of such indicators to better monitor the quality of vaccination services (Bolton, Hussain, et al., 1998; Rossi et al., 2004). However, this indicator which reflects the cohort effect of vaccination delay has yet to be used in the routine reports of the vaccination programme.

6.2.5 Study variables

6.2.5.1 Dependent variables

The status of measles vaccination was analyzed separately according to whether the child was vaccinated at the time of study, and vaccinated at appropriate age as recommended by World Health Organization. The operational definition for each type of vaccination is given below.

- Age-appropriate vaccination: A child was given measles vaccine at 12 months of age. A child who got his measles vaccination one month or longer after the intended age was considered to be inappropriately vaccinated, or delayed.
- Vaccination at time of study: A child had history of measles vaccination at time of survey, regardless of age when the vaccine was given. The vaccination coverage thus calculated is the simple vaccination coverage, inclusive of age-appropriate and inappropriate coverage.

Both sources of vaccination history: guardian recall and health record, were collected in the WHS 2002. However, vaccination history based on recall was only used for general calculation of vaccination coverage at the time of study. For the purpose of age-appropriate vaccination coverage calculation, a valid date of vaccination is required. Therefore only children with valid health record of vaccination dates were included in the analysis of age-appropriate vaccination coverage.

6.2.5.2 Independent variables

Independent variables of interest were chosen based on literature reviews that showed various levels of associations between vaccine uptake and personal or family characteristics. The main variables used as means of comparison were given as follow:

- Age of child
- Sex of child
- Ethnicity of child
- Type of health facility where child was born

Other variables of interest were also included as follow:

- Age of head of household (the respondent)
- Education status of respondent
- Occupation of respondent

6.2.5.3 Data processing and analysis

Data analysis was done using the Complex Samples Analysis mode of the SPSS 19.0 statistical software. Complex Samples Analysis is the statistical tool of choice for complex sample designs such as multistaged, stratified, weighted or clustered sampling. In contrast, conventional statistical analysis mode assumes observations in the data file are obtained through probability sampling method, therefore unsuitable for the purpose of this thesis (IBM Corp, 2011).

*(a) **Descriptive analysis***

The vaccination data were described in terms of difference between independent variables such as age, sex, race, place of birth. Frequencies of independent variables among the immunized and non-immunized children were reported.

Vaccination coverage was calculated as the proportion of children who had received a dose of measles vaccine at the time of survey. Age-appropriate vaccination coverage referred to the proportion of children who received measles vaccine by the age of 12 months. Delayed vaccination was defined as vaccine received a month or more after the recommended age of 12 months.

*(b) **Inferential analysis***

For categorical data (sex, ethnicity, education of parent) chi-square test was used to examine the associations between the variables and vaccination status. Percentage estimates were analyzed using complex sample analysis module from SPSS Statistics version 20 (IBM Corp). Logistic regression was used to test correlates between child characteristics and delay in measles vaccination.

Vulnerable time per child was calculated after actual age of vaccination was known. Preventable vulnerable time referred to the time duration expressed in months per child, derived from the average of cumulative non-vaccinated time spent before ultimately receiving the measles vaccine in children up to the age of 60 months.

$$Vulnerable\ time\ per\ child\ (month) = \frac{1}{N}\sum_{i=1}^{N}(x_i - 12),$$

$$x\ being\ the\ age\ in\ months\ when\ vaccination\ finally\ occurred,$$

$$or\ age\ of\ an\ unvaccinated\ child\ at\ the\ time\ of\ WHS\ survey.$$

For the purpose of this thesis, children were taken to be vulnerable to measles infection as soon as they passed their first birthday. For example, children at five years old who had not received any measles vaccine (single component or MMR) were taken as being vulnerable for 48 months.

6.2.6 Permission and Ethical consent

Written approval for using the Malaysian World Health Survey 2002 dataset had been granted by the World Health Organization Press (ID: 119827, date 25 June 2013).

Ethical approval had been obtained from National Institutes of Health Malaysia (ID: NMRR 13-938-16913, date 6 Novermber 2013).

6.3 Result

A total of 1461 children under-five were sampled throughout Malaysia during the WHS 2002. Their sociodemographic characteristics are displayed in Table 6.2.

Table 6.2: Sociodemographic characteristics of children in Malaysian World Health Survey 2003

Variable	Weighted Percentage (%)	95% CI
Gender		
Male	53.8	(50.7, 56.8)
Female	46.2	(43.2, 49.3)
Birth Facilities		
Government-owned	28.9	(26.2, 31.6)
Private-owned	6.9	(5.5, 8.5)
Unknown	64.3	(61.3, 67.1)
Age group (months)		
12-23	37.1	(34.1, 40.2)
24-35	36.2	(23.7, 28.9)
36-47	23.2	(20.7, 26.0)
48-59	12.7	(10.9, 14.7)
60	0.9	(0.4, 2.0)
Ethnicity		
Malay	60.2	(57.1, 63.2)
Chinese	17.3	(15.2, 19.6)
Indian	8.6	(6.8, 10.7)
Sabahan & Sarawakian natives	6.0	(4.9, 7.4)
Others	8.4	(6.9, 10.3)
Guardian's Education		
None	5.3	(4.2, 6.8)
Incomplete primary	6.8	(5.4, 8.6)
Completed Standard 6	17.6	(15.3, 20.1)
Completed Form 3	20.0	(17.6, 22.6)
Completed Form 5	34.5	(31.7, 37.5)
Completed Pre-U/Basic Degree	13.8	(11.8, 16.0)
Master/PhD	2.0	(1.3, 2.9)
Guardian's Occupation		
Government	11.3	(9.5, 13.3)
Non-Government	30.5	(27.7, 33.5)
Self Employed	12.8	(11.0, 14.9)
Employer	6.0	(4.6, 8.0)
Unemployed	39.3	(36.4, 42.4)

6.3.1 Coverage of first dose of measles vaccine

Not all guardians of the sampled children in the WHS 2002 were able to produce the home-based health card upon request. The WHS 2002 questionnaire allowed vaccination information to be given based on both health card (or any supporting document) and memory recall. In the sample, 30.1% of children had no valid vaccination record.

As seen in Table 6.3, when recall was taken as valid source of vaccination information together with health card, the combined coverage for measles vaccine at the time of WHS 2002 survey was 70.0% for all children under-five. However, when vaccination by recall without supporting documentation was classified as “non-vaccinated” and excluded from analysis, the coverage for measles vaccine became 62.7%, which was 7.3% below the one calculated from both recall and card.

Table 6.3: Measles vaccine coverage, Malaysia (2003)

	Count	**Weighted proportion (95% CI)**
Total	1461	
Measles vaccine coverage among surveyed children (card and recall)	1038	70.0% (67.1,27.2)
Measles vaccine coverage among surveyed children (card only)	928	62.7% (59.6, 65.6)
Timeliness of measles vaccine coverage		
Age-appropriate	762	50.5% (47.5, 53.6)
Premature (before 6 months)	4	0.2% (0.1, 0.6)
Delayed	162	11.9% (10.0.14.1)
Vaccinated with no valid record	110	7.4% (5.9,9.2)
Not-vaccinated	423	30.0% (27.2,32.9)
Vulnerable time (per child)		
Due to non-vaccination	7.1 months (6.4,7.8)	
Due to delayed vaccination	0.7 month (0.5,0.8)	

6.3.2 Age-appropriate measles vaccination coverage

The analysis of age-appropriateness of vaccination coverage was restricted to 928 children with valid health records (See Figure 6.1).

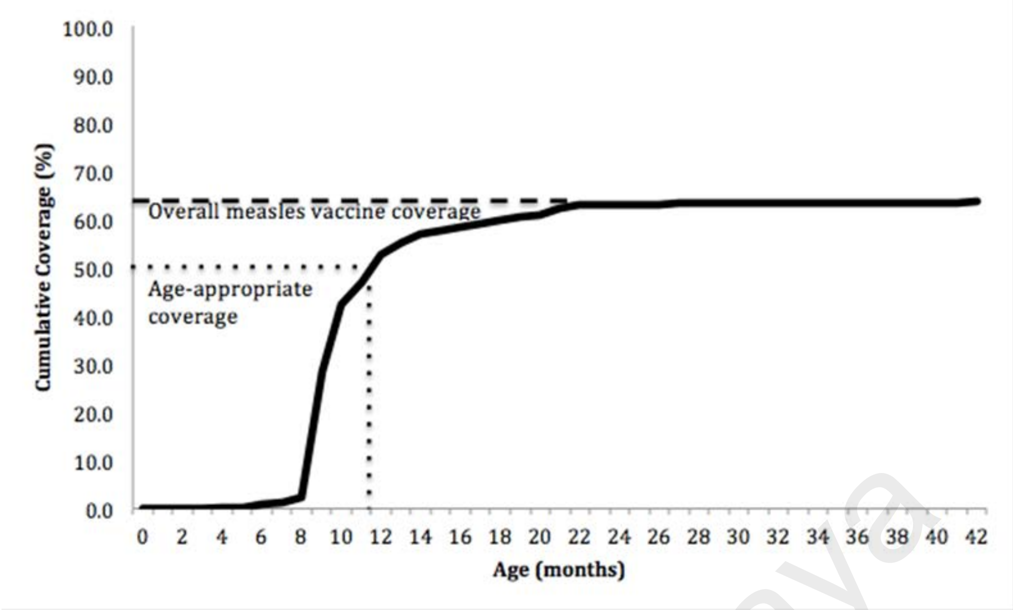

Figure 6.1: Cumulative measles vaccine coverage for children under five in WHS 2002

The age-appropriate measles vaccination coverage was 50% for all eligible children in the WHS cohort (regardless of presence of valid vaccination record) and 81.0% of all children with valid vaccination record.

The remaining 19.0% of the children received measles vaccination thereafter up to the age of 42 months, which put the most-delayed children vulnerable to measles infection for up to 30 months after their first birthday.

Only 0.2% of the vaccination occurred prematurely, before the age of six months. Although not technically a delay, premature vaccination not following scientific evidence on infantile immunity development and health recommendations was still considered untimely for the purpose of this analysis (World Health Organization, 2009).

6.3.3 Cohort effect caused by individual delayed vaccination

Non-vaccination and delayed vaccination created 7.1 preventable vulnerable months per child in the Malaysian WHS population against measles infection (95%CI [6.1, 7.8]) months per child.

Delayed vaccination alone accounted for 0.7 preventable vulnerable months per child in the Malaysian WHS children population against measles infection (95% confidence interval 0.5 to 0.8 months per child). However, when cohort effect was calculated for different regions within Malaysia, the magnitude of vaccination delay and resultant gap in population immunity for the under-five population in East Malaysia (comprises of Sabah and Sarawak) was less severe compared to Peninsular Malaysia, although the difference is not statistically significant.

Table 6.4: Cohort effect of delayed vaccination by region, 2003

Region	Vulnerable time per child (non-vaccination) (95% CI)	Vulnerable time per child (delay) (95% CI)
Malaysia	7.06 (6.35-7.77)	0.67 (0.51-0.84)
Peninsular Malaysia	7.25 (6.46-8.04)	0.71 (0.53-0.89)
East Malaysia	6.23 (4.63-7.84)	0.51 (0.08-0.94)
Sabah	7.26 (4.77-9.76)	0.15 (0.00-0.30)
Sarawak	5.43 (2.79-8.06)	0.79 (0.02-1.57)

6.3.4 Correlates of vaccination delay

In the univariate logistic regression model, testing association between delayed vaccination and attributes of children (refer to Table 6.5), children born in a private health facility, age of three years and above, having parents/guardians who were self-employed were more likely to be delayed in receipt of their measles vaccine. Being a native child in Sabah or Sarawak, or having a guardian who had completed primary school or secondary school education were more favourably associated with age-appropriate vaccination.

Multivariate logistic regression model was done. Among children and caregiver attributes, being born in a private centre (adjusted OR 2.08; 95% CI[1.19, 3.65]) and having a parent/guardian who was self-employed (adjusted OR 2.53; 95% CI[1.44, 4.46]) remained as the strongest correlates for vaccination delay. Having a caretaker who was not employed had a weaker association with delayed vaccination, while other correlates such as being a Sabahan or Sarawakian child of native descent, having a caretaker who had at least completed primary school and secondary school but did not pursue tertiary education were associated with improved age-appropriateness in measles vaccination.

Table 6.5: Logistic Regression model for delayed measles vaccination

	Crude OR (95% CI)	P	Adjusted OR[12] (95% CI)
Ownership of birth facility		<0.01	
Government	1		1
Private	2.33 (1.40-3.89)		2.08 (1.19-3.65)
Unsure	1.63 (1.22-2.17)		1.37 (0.90-2.06)
Sex of child		0.83	(Excluded from model)
Boy	1		
Girl	1.03 (0.79-1.33)		
Age of child		0.14	
12-23	1		1
24-35	1.03 (0.74-1.43)		1.03 (0.74-1.44)
36-47	1.45 (1.02-2.07)		1.46 (1.00-2.11)
48-59	1.41 (0.95-2.09)		1.48 (0.98-2.23)
60	0.78 (0.17-3.59)		1.02 (0.22-4.84)
Ethnicity		0.08	
Malay	1		1
Chinese	1.17 (0.83-1.65)		1.03 (0.72-1.49)
Indian	1.47 (0.87-2.48)		1.58 (0.92-2.73)
Sabah & Sarawak natives	0.54 (0.31-0.96)		0.55 (0.31-0.98)
Others	0.95 (0.60-1.50)		1.01 (0.63-1.62)
Gender of guardian		0.03	
Male	0.75 (0.58-0.97)		0.82 (0.53-1.27)
Female	1		1
Education of guardian		<0.01	
None	0.44 (0.17-1.15)		0.33 (0.11-1.00)
Incomplete Primary	0.49 (0.19-1.29)		0.33 (0.11-0.97)
Completed Standard 6	0.22 (0.09-0.53)		0.15 (0.06-0.41)
Form 3	0.31 (0.13-0.75)		0.22 (0.08-0.59)
Form 5	0.38 (0.16-0.88)		0.28 (0.11-0.73)
Pre-Uni/Primary degree	0.49 (0.20-1.18)		0.39 (0.15-1.02)
Post-graduate	1		1
Occupation		0.05	
Civil servant	1		1
Private employee	1.25 (0.80-1.94)		1.54 (0.95-2.52)
Self-employed	1.80 (1.09-2.97)		2.53 (1.44-4.46)
Employer	1.58 (0.79-3.18)		1.97 (0.92-4.18)
Unemployed	1.03 (0.67-1.58)		1.70 (1.01-2.87)

[12] AOR were adjusted in a final model if univariate analysis yielded a p of less than 0.25. Only variables with results in the column were included in the final model.

6.4 Discussion

The schedule for childhood vaccination is designed to offer greatest protection to an infant, whereby vaccination should be initiated as soon as the infant starts to lose maternally conferred antibody. Therefore, a true measure of the population protection level against disease should include the proportion of infants covered at the appropriate age, and any proxy indicators that could reflect the magnitude of population vulnerability caused by failure to vaccinate on time.

However, unless specifically monitored and calculated, the presence and severity of delayed vaccination among infants is not detectable by the annual vaccination coverage, as long as the children eventually obtained their vaccination before the end of the reporting year. Although not systematically studied, the existence of untimely vaccination in year 2003 could have added to the population's vulnerability that culminated in the measles outbreak in year 2004. This should serve as a valuable historical lesson to public health policy makers striving to attain optimal herd immunity and eventual eradication of measles from the country.

Findings from the Malaysian WHS 2002 dataset suggested that on top of non-vaccination, delayed vaccination created an additional layer of vulnerability to measles infection. In the WHS 2002 sample of children, only half received measles vaccine at the stipulated age. These findings are consistent with other studies on timeliness or age-appropriateness of vaccination, which generally demonstrated that apparently high vaccination coverage rates could mask high rates of delayed vaccination (Akmatov et al., 2008; Dannetun et al., 2004; Hu et al., 2013; Le Polain de Waroux et al., 2013; Lernout et al., 2014; Park et al., 2013). This could be a contributing factor for failure to eliminate measles in the country, and calls for additional vaccination indicators apart from annual vaccination coverage.

Apart from age-appropriate vaccination coverage, the preventable vulnerable time to measles could potentially be used as a proxy indicator of damage to actual population immunity. Within the WHS 2002 sample of children, up until their fifth birthday, every child in the study population spent an average of 0.7 months being vulnerable to measles infection due to delayed vaccination, which was easily preventable by being compliant to the vaccination schedule. For regional comparison, the cohort effect of delayed vaccination in East Malaysia was less severe in comparison to Peninsular Malaysia. This is consistent with the finding from logistic regression that native children in Sabah and Sarawak were more likely to be vaccinated in a timely manner. Compared to age-appropriate vaccination coverage rate, the vulnerable time-per-child indicator has a narrower confidence interval, therefore is a more precise indicator of quality of vaccination service at the local level. This finding will be of great use to local health administrators in view of the need to improve the effectiveness of the existing vaccination services and to benchmark performance of vaccination quality against the national standards.

The observation that native children of East Malaysia (Sabah and Sarawak) were more appropriately vaccinated according to schedule compared to those in Peninsular Malaysia is surprising, as it defied the logical assumption that rough geographical terrains in East Malaysia would prevent parents and infants from accessing vaccination service in a timely manner. Findings from in-depth interviews of parents in the subsequent chapter (Section 8.3.6.1) suggest that parents of indigenous ethnicity who were less well-off financially tended to be appreciative of the health services provided by the public sector, and valued advice from health providers more. This could perhaps explain the higher compliance of children of indigenous parents to the vaccination schedule in general. However, this finding needs to be interpreted with caution, taking the historical and methodological context of WHS 2002 into consideration, in that sampled LQs in East

Malaysia were most likely accessible by road transport rather than settlements in inaccessible locations which were uncharted by authorities. In all likelihood, parents residing in remote rural areas of East Malaysia would be inaccessible by both health personnel and survey enumerators, thus their vaccination behaviour would not be captured.

Multivariate logistic regression also suggested that being born in a government health facility encouraged age-appropriate vaccination. A possible explanation is that vaccination and well-child clinic services are provided by the public health clinics as a part of the maternal-child health continuum. A baby born in the government facility is routinely given the child health card and advised for subsequent vaccination follow-ups in a health facility nearest to his home. However, as there is no central or regional vaccination database, this continuity may be lost if a child loses his card, or moves to a new location or another health facility.

Only 0.2% of the children received their vaccination before the earliest recommended age of 6 months. These might also reduce vaccine effectiveness due to persistent maternal antibody and immaturity of the young infants' immune system. In addition, from the perspective of a public health policy maker, this reflected on the providers' non-compliance to the national schedule, and could add to the risk of measles outbreak by lowering the overall herd immunity.

6.5 Study limitations

As the primary respondent for individual health questionnaire (refer Table 1) was the adult of the living quarter, the WHS protocol did not make special provision to take nationally representative sample of children under-five. Participation of children hinged on selection of living quarters. Unlike other childhood immunisation-specific survey such as the EPI cluster survey (World health Organization, 2008) by the World Health Organization, if the sampled living quarter had no age-eligible child, that living quarter was not replaced because the child health portion of questionnaire was optional. However, in the Malaysian country report, overall the gender, age structure and population distribution for children and adult appeared balanced and comparable with the national figures, which implied that the cohort of children in the WHS 2002 would be nationally representative (Institute for Health Systems Research, 2006).

Another limitation in this study also arose from the cross-sectional nature of the Malaysian WHS. The up-to-survey-date measles vaccination coverage referred to the proportion of children who had received their measles vaccine anytime between their first birthdays and the date of survey. A child who had not been vaccinated on the date of survey would therefore be counted as non-vaccinated even if the child ultimately obtained measles vaccination after the survey. However, as the proposed average vulnerable months per child was not intended as an estimate of individual immunity, it was still a suitable proxy indicator of the population's susceptibility to infection due to gaps in vaccination not captured by simple vaccination coverage.

6.6 Summary of findings

High overall vaccination coverage for the population masked the reality that children did not receive measles vaccine on time. Age-appropriate vaccination coverage more accurately reflected the adequacy of protection in infants compared to administrative coverage or up-to-survey-date coverage, whereas vulnerable time due to vaccination delay could be a better indicator for the magnitude of population-level vulnerability due to individual delay. Delay in vaccination was associated with being born in a private health centre and having a parent/guardian who was self-employed or unemployed; while being a native child in Sabah and Sarawak was favourably associated with age-appropriate vaccination.

Having established the understanding that delayed vaccination as contributed by policy recommendation and individual delays is deletarious to herd immunity against measles infection, and that Malaysian parents were not compliant to national immunization schedule, it is now fitting to examine the reasons underlying delayed, or non-vaccination among Malaysian parents.

CHAPTER 7: VACCINATION SERVICE MANAGEMENT – CHALLENGES FACED BY PROVIDERS

7.1 Introduction

The 2011-2013 measles outbreak in three major cities in Sarawak occurred on a background of high annual measles vaccination coverage in excess of 90%. Among the reported cases, nearly a quarter were unvaccinated, indirectly showing a failure of the health system in reaching out to some pockets of the population. On the other end of the spectrum, approximately a quarter had been vaccinated; implying that the vaccines they previously received had failed to generate sufficient and long-lasting protection against measles.

The occurrence of these measles outbreaks are suggestive of gaps in the health system, namely, ineffective vaccines and insufficient uptake of vaccination services. Identifying and rectifying such gaps are important from a public health point-of-view. If we could vaccinate the hard-to-reach pockets of population, and ensure that vaccines delivered are effective, the resultant herd immunity would likely be able to prevent further outbreaks and achieve measles elimination.

A successful vaccination session is made up of two components: access to vaccine provider, and administration of vaccine in an optimal condition. Inadequate access could be due to social and material deprivation, gender inequity, poor awareness (Corsi et al., 2009; Dugas et al., 2009; Jeong et al., 2011; Mitchell et al., 2009; Schempf et al., 2007) or vaccine hesitancy on the parents' part (Dube et al., 2013; Kempe et al., 2011), which will be discussed in the subsequent chapter on the parents' perspectives.

Vaccination failure could also be related to a number of health providers' characteristics, such as, vaccination knowledge, beliefs and practices (de la Hoz et al., 2005; Herzog et al., 2013; Nikula et al., 2011), and commitment to form a trusting relationship with parents (Benin et al., 2006; Brown et al., 2012; Leask et al., 2012). Other institutional factors such as maldistribution of health facilities and providers, long waiting time, administrative and bureaucratic barriers have also been associated with poorer outcomes (Abdulraheem et al., 2011; Babirye et al., 2014; Dietz et al., 2000; Schempf et al., 2007; Sharma, Singh, & Sharma, 2015). While these findings have been extensively described in international studies, there is a dearth of research to investigate whether similar issues are seen in Malaysian health facilities.

This chapter aims to describe vaccination services and management in both public and private health facilities in Sarawak, describe vaccine provider's knowledge, and cold chain maintenance practices. The following sections will start with methodology in Section 7.2, followed by results in Section 7.3, a brief discussion in Section 7.4, study limitations and implications in Section 7.5 to 7.6, before concluding with summary of findings in Section 7.7.

7.2 Method

This is an operations research and aimed to study the vaccination service and management. A mixed-mode approach was utilised. It consisted of direct observations and semi-structured interviews of the vaccine providers. The scope of the study included vaccination practices and clinic policies regarding vaccination service.

7.2.1 Study population

This included all clinics (public or private) offering vaccination service to children in the three major cities (Kuching, Bintulu and Miri) involved in the 2011 measles outbreaks in Sarawak.

7.2.2 Sampling frame

All public and private clinics which offered child health services in the three major Sarawakian cities with measles outbreak were included in the sampling frame. At the time of study, a total of 122 clinics provided childhood vaccinations (see Table 7.1).

Table 7.1: Public and private clinics offering vaccination to children in districts facing measles outbreak

City/Town	**Number of clinics offering vaccinations**	
	Government health clinics (Public)	**Private medical clinics**
Kuching	27	37
Bintulu	12	13
Miri	13	20
Total	52	70

7.2.3 Sampling method

Letters were sent to the Medical Officer-in-charge and nursing sister of each of the selected public clinics. The letters contain a description of the research and a request for opportunity to survey their vaccination practices. Similar letters were posted electronically to the private practitioners or paediatricians.

Follow-up telephone calls were made to the clinics approximately one week later to request permission to conduct the research. At least two attempts at calling a clinic were made before listing the clinic as non-respondent.

7.2.4 Sample size

Sample size was calculated based on prevalence of good adherence among vaccination providers of 0.16 using single proportion formula (Yuan et al., 1995).

Taking precision of 0.025 at 95% confidence interval, the sample size required was 107 clinics.

After considering the non-response rate of 20% (Azira et al., 2013), the sample size was expanded, and universal sampling was performed.

7.2.5 Sampling unit

All clinics listed were contacted and invited to participate in the study. Eligible respondents were personnel involved in the vaccination programme or service. Involvement was defined as doing initial screening for children who presented to the clinic for vaccination, handling the cold chain and vaccine, and keeping track of vaccination records.

In the case of public sector, the respondent from each clinic was the nurse-in-charge of vaccination on the day of survey. For private sector, the clinic respondent was the doctor himself/herself as private practitioners do not usually delegate medical procedures to clinic assistants.

Clinics which did not offer vaccination services (certain private practitioners and some public clinics with no maternal and child health services) were excluded.

7.2.6 Study variables

(a) ***Independent variables***

Several independent variables of interest were chosen based on literature review as discussed in Chapters 2 and 3.

- Location of clinic
- Demographic background of respondents who provide vaccination services
- Position of respondents in the clinic
- Length of service

(b) ***Dependent variables***

Outcome variables of interest are listed as follows:

- Performance of cold chain (see operational definition below)
- Knowledge of vaccination staff regarding vaccine storage, handling and management
- Vaccination service delivery
    - Clinic policy
    - Management issue

(c) ***Operational definitions***

- Cold chain: referred to a set of equipments and procedures to store and maintain the vaccines so that they remained in a potent state. A functioning cold chain was one that adhered strictly to standards, for instance, those recommended by World Health Organization(World health Organization, 1998a).
- Knowledge of vaccination staff: this was categorized into the following domains.
    - Vaccination schedule in Malaysia
    - Vaccination techniques
    - Adverse events associated with vaccination and management plan.
    - Contraindications to vaccination
    - Cold chain
- Service delivery: this referred to the process of organizing and distributing vaccination service so that it reached its target population
    - Clinic policy: these were divided into following.
        - Access: Hours of service, waiting time, screening, referral
        - Vaccine handling: documentation, storage and regular maintenance
        - Reminder and tracking of defaulters
        - Continuous education for provider and parents
    - Management:

- Resources available: time, personnel, vaccination supply
- Other challenges

7.2.7 Study instruments

(a) Cold chain checklist

This checklist was adapted from the World Health Organization's refrigerator and cold-chain checklist, recommended for supervisors and personnel directly responsible for vaccine storage and handling at all levels of health system (Sarawak State Health Department, 2013; World health Organization, 1998a).

(b) Questionnaires

Two sets of questionnaires were used. Both questionnaires were in English. No translation was made, since all health providers in Sarawak use English for clinic documentation and formal communication.

1. Questionnaire on knowledge regarding vaccination practices and the cold chain system for the respondents.
   a. There were 14 items. Estimated time to complete was 30 minutes.
   b. This was adapted from the Canadian Capital District Health Authority immunisation learning module (Whelan et al., 2011) and from the Performance Assessment Report on health worker training in India by the National Institute of Health and Family Welfare and World Health Organization (Nandan & Jafari, 2009).
   c. Questions were divided into five domains: vaccination schedule, route of administration, contraindications, adverse events and cold chain maintenance.
   d. Good knowledge in each domain was defined as ability to answer all questions correctly.
2. Questionnaire on clinic policy related to vaccination service delivery, and vaccine management.

a. This questionnaire consisted a number of semi-structured, open-ended questions.

b. Domains assessed:

    i. Delivery of vaccination services (clinic hours, waiting time, reminder and recall)

    ii. Vaccination procedures

    iii. Information and education

    iv. Resources

    v. Challenges

    vi. Possible improvement

c. The questionnaire was based on Dr Donald Haley's research tool on childhood immunisation programmes (Haley, 1999). This was in turn adapted from Dietz's questionnaire to evaluate vaccination clinic policies and practices, which had been pretested and validated (Dietz et al., 2000; Haley, 1999). (*Written permission granted by original author*).

7.2.8 Data collection

Written informed consent to conduct interviews was obtained from the respondents prior to administration of questionnaire.

In each clinic, data were collected through direct observation on the cold chain equipments and documentation. Observation findings were entered into a standardized checklist. Simultaneously, one set of self-administered questionnaires was given to the vaccine provider on duty in the clinic on the day of data collection. By completing the questionnaire, the health provider answered all three topics on vaccination service delivery; vaccine management; as well as knowledge on vaccines in the national vaccination schedule. At the end of 30 minutes the questionnaires were collected.

7.2.9 Data processing and analysis

Data were coded, entered and analysed with the SPSS 19.0 statistical software.

Before data analysis, key variables were cleaned by checking for inconsistencies and outliers.

(a) ***Descriptive:***

For all study variables, the major analysis was descriptive in nature, consisting of counts and simple frequencies. For assessment of providers' knowledge on vaccines and cold chain management, each question which was answered correctly was given a score of 1, while each incorrect answer scored 0. The score was expressed as a proportion of the question answered correctly in each domain of vaccine management.

(b) ***Inferential analysis:***

Independent t-test and one-way ANOVA were performed to compare scores on vaccination- and cold chain-related knowledge between the types of health providers, length of service and demographic background.

7.2.10 Ethical considerations

Ethical approval had been obtained from National Institutes of Health Malaysia (ID: NMRR 13-938-16913). Approval from Sarawak State Health Department was obtained before commencement of study.

7.3 Results

7.3.1 Background of Respondents

A total of 102 respondents consented to participate in the study. The response rate was 85%. All respondents from the public clinics consented, while non-response came only from the private practitioners. Reasons given by practitioners for non-response included: retirement, no longer seeing paediatric patients, or lack of interest.

The socio-demographic background of respondents are listed in Table 7.2. A vaccination provider in the public clinic was more likely to be female, of Sarawak of native ethnicity and working as a nurse.

Table 7.2: Background of providers

Characteristics	Public (N=38) n (%)	Private (N=64) n (%)	*p* value
Gender[a]			<0.001
Male	0 (0.0)	45 (70)	
Female	38 (100)	19 (30)	
Ethnicity[a]			<0.001
Malay	11 (29)	17 (27)	
Sarawakian natives	21 (56)	5 (8)	
Chinese	6 (16)	36 (56)	
Indian	0 (0.0)	6 (6)	
Position[a]			<0.001
Doctor	0 (0.0)	64 (100)	
Nursing Matron/Sister	3 (7.9)	0 (0.0)	
Staff Nurse	14 (36.8)	0 (0.0)	
Community nurse	21 (55.3)	0 (0.0)	
	Mean (95% CI)	**Mean (95% CI)**	
Age of providers(years)[b]	31.8 (28.8, 34.7)	49.3 (46.8, 51.8)	<0.001
	Median =29.0	Median= 50.0	
Length of service in current post (years) [b]	7.7 (4.9, 10.6)	23.3 (20.9, 25.7)	<0.001
	Median=4.0	Median=24.0	

a. Statistical test: Chi-square test
b. Statistical test: Independent t test

7.3.2 Vaccination service and management

Compared to public clinics, one-third of private clinics required appointments for vaccination (see Table 7.3). The purpose of the appointment was not to arrange a specific time slot for doctor consultation, but to ensure availability of vaccines, especially those not included in the MOH's Expanded Programme on Immunisation. Majority of these clinics gave appointments on the following day to avoid a long waiting time. Although the private clinics differed from public clinics in terms of the parents having to wait for an appointment date, none of the parents interviewed perceived this to be an issue.

Table 7.3: Accessibility of service

Vaccination service	Public (N=38) n (%)		Private (N=64) n (%)		*p* value
Appointment needed for vaccination[a]	0 (0)		20 (31)		<0.001[c]
Service available in evenings[a]	7 (18)		49 (77)		<0.001
Service available during weekends[a]	5 (13)		60 (94)		<0.001
Vaccination at home[a]	24 (63)		0 (0)		<0.001 [c]
	Median	Mean (95% CI)	Median	Mean (95% CI)	
Waiting time[b] (minutes)	30	24.8 (19.0, 30.6)	26.0	24.9 (19.9, 29.9)	0.983

a. Statistical test: Chi-square test
b. Statistical test: Independent t test
c. Fisher's exact test <0.001

Although appointment system is not fully enforced in public sector clinics, in practice all the maternal and child health visits were scheduled and appointments would have been set during the prior visit. This policy was introduced under the Personalized Care programme under MOH and aimed to facilitate continuity and rapport building between parents and the same health provider. The appointments were frequently not kept, however, especially among parents with difficulty accessing the clinics. Thus in reality, public sector health providers more often had to vaccinate walk-in patients in addition to patients with prior appointments. Even though walk-in patients tended to increase workloads for vaccine providers and complicate the task of estimating daily vaccines needs, the walk-in system actually served as a safety net to prevent a child's attrition from the vaccination schedule. By preventing attrition and defaults, the clinic's performance in terms of vaccination coverage will eventually improve.

While all public clinics offered walk-in vaccination for all children during operating hours, less than 20% of them were open after 5pm and during weekends. In contrast, more than three quarters of private clinics were accessible to parents after working hours. Only the public clinics reach out to children with special needs in their homes to administer the needed vaccines.

Contrary to public opinion and news reports on long waiting time at public facilities(Chan, 2014; Lakshiny, 2015; Roslan Johari, 2007), the waiting time in public and private clinics did not differ significantly. This was probably because waiting time was self-reported by the respondents and was not validated by objective measures like time-motion study.

Table 7.4: Opportunistic Vaccination

Vaccination Service	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
Children screened for vaccination during unscheduled illness visits	24	63	31	48	0.15
All needed vaccinations were given in one visit	9	24	9	14	0.28
Statistical test: Chi-square					

Not all public clinic staff routinely screen the children for vaccination status when the latter visit the clinics during acute illnesses (see Table 7.4). This could be because children with acute illnesses were routinely seen first by the Assistant Medical Officers[13] who were not required to be proficient in maternal and child health-related promotive

[13] The Assistant Medical Officers are also known as Medical Assistants. They provide preventive, curative and rehabilitative health services under the supervision of medical officers.

health programmes, and thus might have limited experience in vaccination. Hence, opportunities to catch-up on the children's vaccination schedule and to educate parents might be lost due to this standard operation procedure in public health clinics, namely, management by purpose of visit.

The proportion of private providers who screened the vaccination status for children presenting with illness was lower than the public sector clinic practitioners. Two-thirds of public vaccination providers performed opportunistic screening but less than half of private medical practitioners did so. This finding, while disappointing, is not unexpected, given that private doctors in solo practice had explained during interviews that they were under pressure to expedite clinical consultation for their patients and minimize waiting time for others.

There was no difference between public and private providers in terms of willingness to administer all required vaccinations within one visit. According to vaccination guidelines, a child who lags behind in his vaccination schedule is recommended to receive all the required vaccines within the same visit, in order to immunise the child optimally (Centers for Disease Control and Prevention, 1993; "Recommended Immunization Schedules for Individuals NOT Previously Immunized.," 2016). Regardless of types of practice, 82.4% of all providers were reluctant to give more than two vaccines simultaneously. The reasons given by vaccine providers included fear of increased risk of adverse events following vaccination such as fever and seizures, as well as difficulty convincing parents who were put off by the anticipation of pain suffered by their children due to multiple inoculations.

This phenomenon of vaccine hesitancy among public and private vaccine provider is a cause of concern. By limiting the number of vaccines received per child, it could lower the final vaccination coverage for him/her. In addition, by putting off some vaccines until the next visit, a provider is putting the child at further risk of contracting the diseases. For example, a previously unvaccinated child might need up to five vaccines if he first presented to the clinic at 12 months of age: Bacillus-Calmette-Guerin (BCG), Hepatitis B, combined DTaP-IPV-Hib, Japanese Encephalitis, and MMR. With the widely practised two-doses-per-visit approach, it would take minimum three visits for a child to receive the first dose of each vaccine. This would unnecessarily increase the total number and costs of clinic visits to complete the whole vaccination schedule. This cost might overwhelm a poor family, and the parents might decide not to return to the clinic for subsequent doses.

From a public health point of view, in addition to increasing risk of disease outbreaks, provider hesitancy also widens the inequity in health. This is so because the effect of undervaccination, namely, ill health, would be more acutely felt by children who could not access health facilities easily due to geographical or financial reasons. It therefore stands to reason that the issue of provider hesitancy needs to be addressed by policy makers in order to improve the overall vaccine coverage within a community.

While more than three quarters of private practitioners kept basic vaccination records (type of vaccine, name of patient and date), only a couple had proof of documenting adverse reaction arising from vaccination or to report such incidences to the health department (see Table 7.5). This might limit the comprehensiveness of local surveillance data for Adverse Events Following Immunisation (AEFI), and subsequently affect the patient's ability to obtain redress.

Table 7.5: Management of Patient and Vaccination Information

Information	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
Maintaining record on vaccination information	38	100	49	77	0.001
Documenting adverse reaction to vaccination	20	53	2	3	<0.001
Reporting adverse reaction to health department	9	24	2	3	0.001
Statistical test: Chi-square					

Public providers received more updates and continuous education regarding vaccination (see Table 7.6). From the respondents' explanations, the local health department offered updates routinely to all public clinic nurses, whereas private doctors depended on pharmaceutical companies for updates when new vaccines were marketed. Public providers were also more likely to be incentivised to vaccinate population under their care compared to their private counterparts, as vaccination coverage was an essential component in annual performance appraisal for health providers working in maternal and child health clinics.

Table 7.6: Education and Support for Providers

Type of Support	Public (N=38)		Private (N=64)		*p* value
	Median score	Mean score	Median score	Mean score	
Continuous Medical Education on vaccine and cold chain (session/year)[a]	2.0	1.8	0	0.6	<0.001
	n	**%**	**n**	**%**	***p* value**
Formal training on vaccine and cold chain for new staff[b]	38	100	4	6	<0.001[c]
Staff given incentive to increase vaccination rate[b]	18	47	0	0	<0.001

a. Statistical test: Independent t-test
b. Statistical test: Chi-square test
c. Fisher's exact test <0.001

With reference to the Malaysian immunisation schedule, most childhood vaccines had to be given multiple times at recommended intervals. Therefore, it is reasonable to say that ensuring children attend vaccination sessions at the stipulated time has implication on improving the likelihood of full immunisation and overall herd immunity. However, comparison of performance between public and private vaccine providers suggested that public providers were superior in detecting and tracing defaulters (see Table 7.7).

Table 7.7: Detection and Tracing of Defaulters

Vaccination Service	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
System to identify children who are behind their schedules	38	100	17	27	<0.001
Minimum 3 phone calls to defaulters	36	95	16	25	<0.001
Home visit for defaulters	37	97	0	0	<0.001[a]
Outreach services	11	29	0	0	<0.001 [a]
Reminding parents about upcoming appointment	16	42	5	8	<0.001
Statistical test: Chi-square test a. Fisher's Exact test <0.001					

For public clinics, when parents defaulted appointments and did not respond to telephone calls, providers made up by organizing outreach teams and home visits to attempt to vaccinate the defaulters, even in the remote areas. This was not feasible for individual medical practitioners who needed to remain full-time in their clinics, probably explaining the low performance of private practitioners in detecting and tracing defaulters of vaccination.

In terms of education to the parents, both public and private practitioners offered some reading materials to educate the parents on vaccination (see table 7.8). However, public clinics demonstrated significantly better continuity of care, from offering health information on vaccination during antenatal follow-ups, to counselling for defaulting parents in attempts to resolve any deterring factors in accessing the public vaccination service.

Table 7.8: Education and Support for Parents

Type of education/support	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
Antenatal education on childhood vaccination	21	55	3	5	<0.001
Distributing reading material on vaccines	17	45	33	52	0.50
Types of reading materials					
Posters on vaccines	3	8	4	6	0.75[a]
Newspaper cuttings on vaccines	1	3	0	0	0.19
Discussing and solving parents'issues on vaccinations	38	100	25	39	<0.001
Statistical test: Chi-square test a. Fisher's Exact test 1.00 b. Fisher's Exact test 0.37					

7.3.3 Cold Chain Maintenance Practices

Many clinics had standard procedures on monitoring and maintaining the refrigerator for vaccines storage, as protocols could be obtained from the local health department for free (see Table 7.9).

Table 7.9: Cold chain Guidelines and Plans

Steps to maintain cold chain	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
Standard procedure on temperature monitoring	38	100	56	88	0.02
Back-up for power failure (alarm, generator)	23	61	15	23	<0.001
Statistical test: Chi-square test					

Despite having written plans, majority of the clinics did not have the necessary equipment to maintain the cold chain should a power failure occur, with private clinics significantly worse-off compared to public ones.

Public clinics were more likely to have functioning and appropriate equipment such as refrigerators, thermometers and cold-boxes. Therefore, public providers were better in maintaining an intact cold chain. Apart from better hardware, attitude wise, the staffs in public clinics were more likely to be completely compliant to cold chain protocols in comparison to private practitioners, who were more likely to comply with some of the recommendations (see Table 7.10). For the purpose of this study, full compliance was defined as complete adherence to the WHO recommendations, whereas partial compliance was defined as adherence to some but not all of WHO recommendations.

However, both public and private practitioners were unfamiliar with procedures to handle minor technical issues in the cold chain, such as, abnormal temperature, refrigerator malfunction or power outage.

Table 7.10: Aspects of Cold Chain Care

Aspects of Cold Chain Care	Public (N=38)		Private (N=64)		*p* value
	n	(%)	n	(%)	
Equipment					
Appropriate type of refrigerator (pharmaceutical, top loading, double door)	38	100	49	78	0.001
Compliance with refrigerator maintenance Full compliance Partial compliance	 22 16	 58 42	 8 56	 13 88	 <0.001
Dedicated refrigerator for vaccine	33	8	34	54	0.001
Temperature maintenance					
Compliance to temperature maintenance Full compliance Partial compliance Non compliance	 27 11 0	 71 21 0	 7 47 10	 11 73 16	<0.001
Vaccine storage and handling					
Compliance to vaccine storage guidelines Full compliance Partial compliance	 26 12	 68 32	 4 60	 6 94	<0.001
Availability of cold box	38	100	3	5	<0.001
Proper use of cold box to maintain cold chain Full compliance Partial compliance			(Cold box not routinely used)		
Contingency plan					
Display contingency plan	38	100	4	6	<0.001
Handling disruption in cold chain Fully prepared Partially prepared Not prepared	 3 35 0	 8 92 0	 0 18 46	 0 28 45	<0.001
Preparedness to troubleshoot abnormal temperature Fully prepared Partially prepared Not prepared	 3 28 7	 8 74 18	 0 17 47	 0 27 73	<0.001
Statistical test: Chi-square test					

7.3.4 Providers' knowledge on vaccination and cold chain

The public health providers, who were all nursing professionals, did significantly better than the doctors (private providers) in terms of vaccination schedule, recommended injection routes and cold chain maintenance (see Table 7.11).

The private providers were superior to nurses on matters pertaining the more advanced aspects of vaccination like contraindications and managing adverse events following vaccination.

Table 7.11: Knowledge on Vaccination and Cold Chain

Aspects of Vaccination	Public (N=38)		Private (N=64)		*p* value
	Median score (%)	Mean score (%) (95% CI)	Median score (%)	Mean score (%) (95% CI)	
Schedule	100	87 (79.5, 94.1)	100	75 (67.2, 82.7)	0.02
Route of vaccine administration	100	96 (93.6, 99.3)	50	50 (43.9, 56.0)	<0.001
Contraindications	50	34 (22.0, 46.3)	100	78 (70.1, 86.1)	<0.001
Adverse events post immunisation	20	24 (18.6, 29.7)	60	55 (50.1, 59.8)	<0.001
Cold chain	92	91(88.1, 94.2)	50	56 (50.6, 60.7)	<0.001
Statistical test: Independent t test					

In summary, public health providers gave better service in terms of community outreach and continuity of care, were more knowledgeable on the basic, day-to-day operations of vaccination, and were more compliant to vaccine storage guidelines. Private practitioners were comparatively better in service accessibility and knowledgeable on advanced management of vaccine-related medical events.

7.4 Discussion

7.4.1 Variations in vaccination service and management

In public health clinics, nurses were the main managers and providers of vaccination service. Nurses who were directly involved in vaccination service were also likely to be younger and junior in service, as nurses who gained seniority in service would eventually be promoted to managerial and administrative positions. In contrast, all private vaccinators, being general practitioners, were doctors. In order to begin and maintain a thriving private practice, a provider must have had considerable years of working experience. This could probably explain the marked difference in the personal background between public and private providers of vaccination. However, this in no way suggests that private vaccinators are more superior in vaccinating children. The competency of a vaccinator depends on theoretical knowledge, on-the-job training, compliance to standard operating procedure and adequacy of experience, which may be lacking in a private facility that tends to offer vaccination only on parental demand.

As private and public vaccination providers differed in terms of training, continuing medical education and organizational settings, their vaccination practices and knowledge also differed.

Providers from public and private facilities had similar performance in educating parents about vaccination, with public providers offering better support and continuity. For other aspects of vaccination service, there were considerable variations within and between private and public health facilities.

In ‘Standards of pediatric vaccination practices’ issued by Centers for Disease Control, vaccination should be organized so that it was readily accessible to patients (Centers for Disease Control and Prevention, 1993). For urban working parents, accessibility to vaccination service in most public clinics was hampered by their standard, 8am-to-5pm opening hours. In this respect, private clinics removed the time barrier by being open in the evenings and weekends.

In an effort to improve accessibility, the MOH had set up 1Malaysia Clinics since 2013 which opens for extended hours to service the poorer segments of the urban population. Child health services, including vaccination, are made available to working parents between 9am to 9pm every day, including on weekends. Theoretically, this will encourage busy and working parents to utilize the public vaccination service at their convenience. However, the performance of these new public health facilities has yet to be professionally assessed.

Accessibility is shown in previous studies to be increased by utilizing every clinical encounter to screen for vaccination status, and giving shots of all vaccines a child was eligible to within one visit (Centers for Disease Control and Prevention, 1993). However, over half of private practitioners and about two-fifths of public providers managing acute illnesses did not routinely screen for children's vaccination status. This might be due to constraints in time and treatment priorities in private practice, with the inevitable consequence of missed opportunities for timely vaccination for some children.

In addition, providers from both the public and private clinics were reluctant to administer more multiple vaccine shots, quoting reasons like concerns about pain, perceived risk of increased adverse events and parental anxieties. Hence, provider education about safety and efficacy of multiple simultaneous vaccination is needed to reduce the need for parents to make multiple trips back to the clinic in order to prevent eventual default of vaccination schedule and improve final vaccination coverage.

Despite their better performance in vaccination record keeping, public clinics still relied heavily on manual records for vaccines and patient movements. Periodic hand-searching was done to identify defaulters. In comparison, majority of private practitioners had already digitalized their patient and vaccine databases, which would have facilitated follow-up and tracking of defaulters but unfortunately defaulter tracking was not routinely practised by private vaccine providers.

Another issue with quality of vaccination service is the competence of vaccine providers. All providers had knowledge gaps regarding vaccination contraindications and managing serious adverse events following vaccination. Nurse providers in public clinics scored substantially worse, as less than 20% of the public clinic staff could answer questions regarding these two aspects of vaccination.

A high proportion of public providers had inadequate knowledge on the contraindications and serious adverse events related to vaccination. This finding was consistent with previous studies on providers' knowledge (Cohen et al., 2003; Nikula et al., 2011). Majority of public health providers who failed to answer anaphylaxis-related questions explained that such events had never occurred in their clinics, which probably explain their lack of knowledge. Furthermore, in public clinics, medical emergencies were routinely managed by assistant medical officers rather than the nursing staff. However, this is still sufficient cause for concern, as serious adverse events such as anaphylaxis and convulsions are medical emergencies and could be rapidly fatal. Thus, all first-line providers of vaccination are strongly recommended to be periodically updated in resuscitation and management of adverse events related to vaccination.

Private practitioners had significantly lower knowledge scores regarding cold chain maintenance compared to public providers. The cause for this knowledge gap could be attributable to the lack of involvement of medical officers in vaccination and cold chain management in government facilities. As a result, many medical practitioners may not be familiar with vaccine storage and handling until after they set up their private practices. Measures to improve awareness amongst medical practitioners are therefore indicated.

7.4.2 Cold Chain Maintenance Practices

In addition to knowledge and limitations in vaccination service policy, it appeared that cold chain was another vulnerable link in the vaccination service, especially for private providers. This finding is consistent with previous studies which demonstrated shortfalls in the quality of vaccine storage and handling (Azira et al., 2013; Rao et al., 2012; Yuan et al., 1995).

Although all clinics were equipped with at least one refrigerator, not all refrigerators fulfil the recommended standards. For example, nearly one-quarter of private facilities stored vaccines in single-door, dormitory-style combined freezer/refrigerator units which were not recommended on the basis of poor temperature control performance (Centers for Disease Control, 2014; World Health Organization, 2015). Even in clinics with appropriate equipment, having a dedicated vaccine refrigerator was not always possible, with medical or biological products being stored in the vaccine refrigerator. This was also not recommended because it resulted in frequent opening of the refrigerator door and temperature instability.

Another cause for concern was the inability to maintain the temperature of the environment surrounding vaccines within the strict limit of 2°C to 8°C, as per recommendation by the ministry (Hanjeet et al., 1996). This problem was prevalent in both public and private health facilities, affecting 23.8% of all facilities. Incidentally, similar findings were reported in cold chain studies done in Malaysia during the past decade (Azira et al., 2013; Hanjeet et al., 1996).

Additionally, there were various degrees of noncompliance to temperature monitoring guidelines, which probably compounded the poor quality of the vaccine storage equipments. Both public and private providers lack knowledge about troubleshooting inappropriate storage conditions, despite emergency plan being displayed in all public facilities. This indicated inadequate training and awareness.

Such shortfalls could be costly to public health funders, because these might result in impotent vaccines being administered to the local children population, and subsequently increased the risk of outbreaks.

Regular updates to improve medical and technical knowledge on vaccines could thus be helpful in improving providers' awareness and performance. It appeared that mere display of written guidelines was no guarantee that providers would be well versed with the content. Therefore, enforcing strict storage and handling regulations in facilities providing vaccination service, via periodic feedback, audit and reminders, will improve adherence to prescribed standards.

7.5 Study limitations

The information on vaccination service provision was based on self-reporting. Findings might not reflect actual practices in the health facilities. Results and conclusion thus drawn might be discrepant from the end-users' experience. To address this discrepancy, in-depth interviews were conducted with parents regarding their clinic experience. Further gaps in vaccination services were found and reported in chapter 8.

Secondly, temperature observation was done using the pre-existing thermometers in the refrigerators. Therefore, there could be inaccuracies in temperature readings due to individual equipment failure. Future evaluation studies into cold chain maintenance should address this limitation by using a calibrated thermometer to compare against the thermometers in individual clinics.

7.6 Research Implications

The results were likely to be reflective of service rendered in all public health facilities, as they operate on the same guidelines from the Ministry of Health. Findings pertaining to private practice were probably true for private clinics serving urban population with similar socio-economic characteristics. This is because demands for vaccination service in the private health facilities are driven by the clients and are very much affected by financial capacity of the parents.

Probable focus for further research includes validating aspects of vaccination service delivery by performing time-motion study, and quantifying patient attendance in time series trials. These findings can potentially inform policy makers to improve the delivery of vaccination service, especially in public clinic where overcrowding and understaffing are known problems (Ling, 2015; Puthankattil, 2013).

In addition, there is a need to explicitly associate knowledge of vaccine providers with outcomes of vaccination service, for example, parents' satisfaction, and individual clinic's vaccination coverage. However, this will not be feasible without a centralized vaccination database.

7.7 Summary of findings

Variable shortfalls were identified in the vaccination service provision, the scope of which differed according to type of ownership of the health facility, be it public or private.

Public health facilities were strong in outreach and continuity of vaccination care, whilst private health facilities were more accessible to modern-day working parents.

For all types of facilities, opportunistic vaccination, medical and technical knowledge pertaining to vaccination were factors that could adversely affect the quality vaccine and immunity thus conferred.

The findings so far presented the view that limitations in health service organization and quality assurance could have played a role in the 2011 measles outbreak. Another aspect of the health system is its capacity to respond to the needs of the population. Meeting the expectation of parents is equally important in ensuring the acceptability of the vaccination programme. This is presented in the subsequent chapter through an exploration of users' perspectives on childhood vaccination service.

CHAPTER 8: NON-VACCINATION FROM PARENTS' PERSPECTIVES

8.1 Introduction

In Chapter 7, we have explored the provider's management of the cold chain and vaccination, and uncovered a few gaps in the vaccination service provision which could potentially act as catalyst in measles vaccine failure. However, no service is complete in absence of a service recipient. Thus, it is needful to examine the parent's perspectives on various causes of non-vaccination.

Numerous studies had been conducted to study the phenomenon of non-vaccination among children in both developed and developing countries. Many of the studies done were based on the Rosenstock's health belief model (Rosenstock, 2005; Rosenstock et al., 1988). Applying the health belief model, vaccination can be seen as a health behaviour after parents weigh several important factors such as vaccine necessity, effectiveness and safety profile.

The decision to vaccinate, or the not, is rooted in a complex social, cultural and belief system, which we can attempt to understand and modify to effect a behavioural change (Alfredsson et al., 2004; Bardenheier et al., 2004; Bond et al., 1999; Casiday et al., 2006; Evans et al., 2001; Flynn & Ogden, 2004; Smith et al., 2011). The core of parental decision making on whether to accept or reject a vaccine is founded on the perceptions of costs and benefits of the said vaccine.

After a decision is made, it would finally transform into action after being catalyzed by social cues, such as the advice of someone from a person's social network, or a media exposure on a measles outbreak for example. Among the documented social cues, social network (peer, media, health professional) is the most widely stated reason which influences parents to accept measles vaccination (Flynn & Ogden, 2004; Poltorak et al., 2005).

One other important determinant of parents' vaccination behaviour is access to the service. In developing countries, available evidence showed that vaccination uptake is frequently limited by poor access to vaccination service (Dugas et al., 2009; Mhatre & Schryer-Roy, 2009). Access to vaccination care is not determined by geographically distance alone. It also encompasses other aspects like: personal time schedule, affordability, willingness of the people to negotiate the health system, and cultural compatibility(Norris & Aiken, 2006).

Ethnographic studies conducted in other countries with multiracial populations showed that ethnic and linguistic minorities could feel disempowered in the mainstream health organizations. The respondents also expressed the need for more respect of their cultural identity and power of autonomy (Priest et al., 2012; Van Herk et al., 2012). These findings illustrate that patient's expectations health service go beyond the need for safety and health protection, but also encompass cultural responsiveness.

A conceptual understanding of the factors affecting parental decision making in vaccinating their children and barriers impeding access to vaccination are thus important considerations to be taken into account in planning a meaningful immunization programme that ensures near-total coverage of the children population. In Malaysia, available literature on non-vaccinating behaviour and its determinants amongst parents were mainly quantitative studies (Awadh et al., 2014; Shamsul Azhar et al., 2012). At the time of writing, studies using detailed qualitative method to explore parents' experience with MMR vaccination service or barriers to accessing vaccination service in Malaysia were not yet available.

This study was conducted in Kuching, Sarawak where a measles outbreak had occurred in 2011, indicating gaps in acceptance of MMR vaccine in the population. As the capital of Sarawak, Kuching is home to a multi-ethnic population, including Malay, Chinese, Iban, Bidayuh, Indian and other indigenous races which have different belief systems and practices pertaining to uptake of health services, including vaccination.

In region undergoing economic transformation such as Sarawak, uneven infrastructural and wealth distribution is likely to produce pockets of population living in material deprivation, and reduced means to access vaccination services. The multi-ethnic composition of the population in Sarawak adds another layer of complexity to the acceptability and utilization of vaccines.

This study aimed to explore Sarawakian parents' knowledge experience and attitudes on measles immunization programme, their decision making process regarding vaccination, barriers faced when attempting to obtain vaccination for their children and their needs for a better health service.

The following sections will start with methodology in Section 8.2, followed by results in Section 8.3, a brief discussion in Section 8.4, and study limitations in Section 8.5, before concluding with summary of findings in Section 8.5.

8.2 Method

The method is reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) (Tong, Sainsbury, & Craig, 2007).

8.2.1 Research team and reflexivity

8.2.1.1 Personal characteristics

All interviews were conducted by the researcher, who had attended several training programmes and workshops on qualitative methods.

8.2.1.2 Relationship with participants

There was no prior relationship established with the participants. At the time of interview, care was taken to explain the objectives of the study to potential participants to gain their trust and consent. The reasons for researching parental decision making and circumstances leading to non-vaccination were explained in detail. Potential participants were made to understand that the interviews were not designed to find fault with them or their action, but to explore their experiences, feelings and opinions about vaccination in order to identify components in the vaccination service that required improvements.

In this study, my biases were born out of being a health provider and wishing to understand the circumstances and factors that made the parents decide not to vaccinate their children with the MMR vaccine. As a health provider, I advocated for infant vaccination against measles and all other vaccine-preventable diseases (VPDs). I would like to improve on infant vaccination service within the current institutional capacity and resource allocation. As a researcher, I expected the participants to talk about how they accessed or tried to navigate the health care system, their experiences with the vaccination service specifically, and child health service in general. I realised that my background could potentially impact on my participants' confidence in freely expressing themselves. In order to nurture rapport with the participants and avoid stepping over boundaries, I refrained from using questions that could be interpreted as accusatory, such as "Why had you not vaccinated your child." Instead, every effort was made to communicate with the participants as they are experts in their children's health status, and their opinions on MMR vaccine would be much valued. This had helped to make participants feel comfortable in disclosing their doubts about MMR vaccination, and perhaps better understood in terms of their experiences with the health system.

Potential participants were fully aware of the researcher's designation as a medical doctor prior to the interview. However, they were reassured that the researcher was not a member of their clinical management team, and therefore there was no conflict of interest. In addition, participants were repeatedly reassured of the confidential nature of the interviews and their identities would not be disclosed to any party.

I also refrained from making judgment about parents' demeanour or interaction with their family members during the interview sessions. I was aware of my role as an 'instrument' during the data collection. Therefore, I set aside my own opinion as I listened to the parents' opinion. Subsequently I transcribed and reviewed what they had described as their opinion of the child health, health providers, vaccination service.

8.2.2 Study design

8.2.2.1 Theoretical framework

The methodological orientation underpinning this thesis was phenomenological study. The researcher's intention at the outset of this study was to explore parents' perspectives, thoughts and feelings about the phenomenon of not taking up MMR vaccine for their children despite recommendation by health authorities and the wide availability of MMR vaccine.

8.2.2.2 Participant selection

This study aimed to collect a diversity of views regarding non-vaccination; so all parents who defaulted MMR vaccination for their children were potential participants. A participant would be a mother, father or guardian who had at least a child aged between one year and seven years (between commencement of eligible age for MMR vaccination and school entry, when each would be given the second measles vaccine by the school health team).

The names and particulars of unvaccinated children were obtained from two sources: the official measles case notification database, and health clinic registries from the clinics situated around Kuching.

As all medical practitioners were mandated to notify measles cases to the State Health Department, the official measles case notification database captured all parents of children who had contracted measles and who had presented to any health facilities within the state. Together with patients' demographic and disease details were the children's vaccination status. All children who were reported as unvaccinated were traced according to the contact details as reported by their physicians. Health clinic registries for children attending major government health clinics were also manually searched to identify children who failed to return for their MMR vaccination.

Parents were traced and approached through the telephone. All parents were contacted twice before attempts at recruiting were stopped. For parents with no or invalid telephone contacts, at least one home visit was made before the potential parent was deemed 'untraceable'. Parents of children who were successfully traced were invited to participate in the study.

The sample size depended on saturation of emerging themes, where gathering new data no longer sparked new ideas (Dworkin, 2012). However, to ensure complete and accurate data collection, a minimum of twelve participants was recommended (Guest, Bunce, & Johnson, 2006). At the conclusion of data collection period, a total of twelve parents were recruited. Ten of whom were mothers while two were fathers. The gender of participants was not controlled for, as the defaulter tracing was based on contact numbers given by parents to the health authorities when they registered. In most cases, the numbers belonged to the mother, most probably because the mothers were the main caregivers. In one instance, the contact number belonged to the father but upon learning the purpose of the call, the father requested that all future correspondence be continued with the mother as he was of the opinion that the mother was better informed about the health status of the child.

8.2.2.3 Setting

The location for interview was decided by the participant, for example in a private room of a health clinic, or in the participant's place of residence. Six participants preferred the clinic, while another six requested to do the interviews in their own homes. From my observation, participants were generally more at ease in their own homes. This could be because the clinical environment was deemed threatening, associated with unpleasant medical procedures and laced with an element of coercion from health practitioners. However, the participants' homes had the disadvantage of having the interviews interrupted by intermittent distraction from children or other family members.

The interviews with participants were often conducted in the presence of the latter's spouse and children. It was noted that the presence or absence of a spouse during the interview could exert some influence on the content of a participant's narratives. The presence of the spouses had enriched the interviews on several occasions by offering their own experiences and opinions. They also verified and validated the participants' recall of past events. However, when the decision not to vaccinate was not mutual between the couple, the spouse's presence during the interview could result in important stories being withheld by the participant. For instance, one mother commented on her spouse's fear of health authorities and his reluctance to let their child be seen by health providers from the public sector, which went against her personal views. Had her husband been present during the interview, it was likely the mother would not have expressed this particular aspect of her opinion.

8.2.2.4 Data collection

*(a) **Interview guide***

The interview guide was semi-structured and guided by the Health Belief Model (Rosenstock et al., 1988). The initial guide contained topics which included perception towards measles and its vaccine, barriers to accessing vaccination service, and parental needs for a better vaccination service (see Appendix D).

Under each topic, prompts were designed to initiate the conversation. The prompts on possible factors influencing non-vaccination were drawn from the literature. They were included to stimulate the flow of conversations, and to facilitate the participant's thought process when there was prolonged awkward silence or the participant's facial expression indicated that such issues were never contemplated upon.

In the interview process, it was revealed that participants could not respond well to the first topic on knowledge regarding measles and MMR vaccine. I realised that beginning the interview on knowledge about measles tended to increase the participants' stress. As this could be viewed as potentially threatening, it was subsequently avoided. Instead, the topics and prompts were modified to explore the participants' experiences, thoughts and feelings when their loved ones were medically diagnosed with measles (see Appendix E).

*(b) **Interview sessions***

Face-to-face, in-depth interview was chosen as the method of data collection. Compared to focus-group discussion method, the one-to-one interaction in in-depth interview method provided parents the confidence to admit to personal weaknesses, especially when the issue of interest was a potentially sensitive one, because defaulting vaccination was viewed unfavourably by health authorities. Participants could also express their negative opinions about aspects of the vaccination service provision by the health centres, which they might not disclose to health providers.

Depending on parental preference, two languages were used during the interviews, namely, English and Malay. It took approximately 60 to 90 minutes to complete each interview. Each participant was interviewed at least once. Some participants were interviewed twice to reach saturation of data. Each interview was recorded with two digital audio recording devices and transcribed verbatim. Transcripts were not returned to the participants.

8.2.3 Analysis and reporting of findings

All personal identification was removed from the transcripts and a subject code was assigned to each transcript. Each participant was assigned an anonymous identifier based on four personal characteristics, namely age in years, ethnicity, highest level of education attained and employment.

The transcribed interviews were checked against the audio recordings by the researcher. Each transcript was checked and imported into Text Analysis Markup System Analyzer, which is shortened to TAMS Analyzer, version 4.47b2ahMav. TAMS Analyzer is a qualitative data management and analysis tool. It allows digital assignment of codes to texts, as well as subsequent extraction, analysis and saving of coded information. TAMS Analyzer is an open-source software released under the General Public License, which guarantess end users the freedom to run, study, share and modify the software (Weinsten, 2011).

The analysis process followed qualitative content analysis method (Taylor-Power & Renner, 2003). The empirical data analysis began with a set of researcher-assigned themes and codes. These themes (for example perceived risk of MMR vaccine) and codes (such as vaccine-related deaths, autism) were derived from literature review.

The transcripts were read multiple times and scrutinised in detail to uncover meanings and themes. The transcripts were searched through, line by line to scan for themes of interest (for example, perceived risk of vaccine). Codes were then assigned to pieces of information revealed in the interview.

In addition to theory-driven codes as mentioned in the previous paragraphs, new codes were created from narratives which carried new meanings and concepts. Finally, codes were categorised by grouping them around unifying patterns to form new themes. The transcripts were also rechecked and reread to make sure common themes were really common across transcripts and not concentrated in one interview. Irrelevant and redundant materials were excluded from the analysis.

8.2.4 Ethical considerations

Ethical approval had been obtained from National Institutes of Health Malaysia (ID: NMRR 13-938-16913).

Informed consent was obtained from the participants. The participants signed an informed consent form prior to the interview. Selected contact information was obtained for the purpose of tracing when further interview was needed.

All participants were given a token of RM30.00 each for their time and travel expenses.

8.3 Results and Discussion

8.3.1 Sociodemographic background of parents

12 parents agreed to participate the study. Four participants were traced through measles case notification database as their children had been diagnosed with measles. For the remaining eight participants, their children had not suffered from measles. Instead, the participants were traced through health clinic registries, which indicated that their children had not received measles vaccination.

The sociodemographic background of parents is shown in Figure 8.1. The parents' age range was between 21 to 40 years old, with mean age of 33.5 years. Majority of the parents were Malays. There were one Chinese, one Iban, two Bajau-Suluk from the neighbouring state of Sabah, and one Filipina. Half the parents had tertiary education; a third received secondary education, while the remaining two parents had incomplete primary education. Majority of the parents work outside of home either in full-time or part-time employment.

Characteristics	
Ethnicity	
Malay	7
Iban	1
Chinese	1
Bajau-Suluk (Malaysian not in possession of identity card)	2
Filipina	1
Education Level	
Primary	2
Lower secondary	2
Upper secondary	2
Diploma/Degree	6
Employment	
Homemaker	6
Teacher	3
Civil servant	1
Manager	1
Business	1

Figure 8.1: Parent's sociodemographic background

8.3.2 Parents' perception about measles and its vaccine

Non-vaccinating parents generally had inadequate knowledge on measles. For five parents, question to explore understanding about measles was met with awkward silence. This was the case even for the three parents whose children had clinically confirmed measles. This inability of the local population to recognize measles probably signified that parents had not been given sufficient education about measles by mainstream media, school or health educators.

Educated parents generally acknowledged that they have heard or read about "campak", which was the official and academic terminology for measles in Malay language. However, half the parents were under the wrong impression that "campak" was a Malay translation for "chicken pox". This confusion could be because chicken pox is relatively more common than measles among Sarawakian children.

*"Campak is chicken pox, right?" (*30, female*)*

*"I have always thought measles is the same as chicken pox. We all in my village thought so." (*34, female*)*

Formal terminology which differed from local references to measles seemed to increase parents' confusion. The local terminology for measles is "jerumut". This term is not specific to measles, but encompasses all types of childhood infections characterised by fever and skin rash, for instance, viral rashes and roseola infantum.

Two parents who had had first-hand experience with a clinically diagnosed measles were able to describe measles accurately, from the fever, rashes, respiratory symptoms, to complications arising from the infection.

"*High-fever on and off, can be until 39 degrees, the fever. I was quite worried. Rashes yes, small ones, very small but covered the whole body... Hospital admission for lung infection, for one week…*" (40, female)

Measles was generally perceived as not dangerous due perhaps to parents' lack of knowledge on measles. However, for the few parents who had knowledge and experience on measles, the most threatening feature of measles was the accompanying fever. To them, the fever could trigger off convulsion, a phenomenon that was generally fearful for all parents.

"*We were most worried about the high fever. I read through internet that fever will be, like, not good for the brain. Fever can cause handicap in a child. Brain damage starts with fever.*" (40, female)

"*My child was so hot that day. Her cheeks and eyes were red. My mother said it was dangerous, if the fever went to the brain, there could be convulsion.*" (30, female)

Only one parent who witnessed deaths from measles infection explicitly said that measles itself was dangerous.

"*I was scared when he got measles. It could threaten his life. I had heard of so many cases of measles dying, children who could not be saved. Back in Sabah, two of my nieces got measles, they died.*" (21, female)

Other parents thought the threats of measles was exaggerated by the health authorities to promote parental compliance.

"*These are just scary names, the big scary diseases…*" (33, male)

For majority of the parents, vulnerability to measles and other illnesses was attributed to poor hygiene.

"*I did not expect my kids to have measles. I cleaned the house, and still he got it, I was surprised... Babies get measles easily, so you give baths everyday, change the clothes, clean the house to prevent it.*" (36, female)

"(Measles)*'s only dangerous to people living in dirty house. If a child lives in dirty house and gets a fever, it's likely he gets another infection.*" (30, female)

To some parents, vulnerability to measles infection was not a major child health issue. The first group of parents thought that measles was rare and therefore unlikely to affect their children.

"*But the chances of getting the disease is like winning Toto, it's quite slim.*" (33, male)

"*I've seen measles, but rarely.*" (30, female)

The second group of parents thought measles infection was part of growing up, so was not a serious issue. In fact, the lay logic demonstrated by these parents was not much different from the scientific logic of vaccination. The one distinction between allowing a natural infection and receiving a vaccine was probably the severity of disease, in which the vaccine will cause the mildest symptoms whereas natural infection could range from a mild disease to the most severe one.

"*Everyone must get measles, no?*" (33, female)

"*People said you need to get measles once to not get it anymore. Better if you get it early.*" (21, female)

Parents with low education attainment did not understand the word "immunization" or "vaccination" in both English or Malay language. The terminology understood by these parents was the spoken English word of "injection", which was a term used by nurses during daily clinic consultation.

Even for well-educated parents, vaccines were not identified by their names or natures as printed in the child health card, instead they were referred to by the time scheduled by

Ministry of Health. For example, MMR vaccine was frequently referred to as the "12-month injection". Ironically, parents were not very cognizant about the importance of complying to the stipulated timing of vaccination. Rather, they were more anxious about admonishment from nurses when they did not attend the clinic on time.

"*I never knew the one year injection was for measles, until you told me today.*" (33, female)

All parents were aware that vaccination could bring health benefits to their children. Benefits mentioned ranged from a general "makes the child stronger" statement, to a more specific one such as "prevents illnesses". However, none of the parents who favourably regarded childhood vaccination were able to name all diseases prevented by childhood vaccination programme in Malaysia. Question on diseases preventable by MMR vaccine was also met with long silence.

"*Children are at high risk* (of getting measles)*, because they are still young, there is not enough antibody. That's why the government asked to do injections, and we need to follow… We also need to take care of their food, and house environment…*" (34, female)

A couple of parents appeared to have basic knowledge about the functions of vaccines by accurately naming them and their supposed benefits. However, these same parents had refused all vaccinations. They did not seem to be convinced of the benefits of vaccines. Instead, healthy and religious lifestyles were perceived to be equivalent or more effective than vaccination.

"*Even vaccinated children get it* (measles) *too. We try to strengthen our immune system in any way we can. Lots of fruits, vegetable, cold showers…*" (33, male)

"*We can prevent* (disease) *with Sunnah food* (religiously prescribed)*, control our diet and healthy lifestyle… Vaccine is not 100 percent prevention... Previously people claimed that if* (you) *did not take Rubella vaccine your child will be handicapped. Thank God all* *four of my children are not handicapped even though I did not take Rubella* (vaccine). *So… it's not that not taking it will cause handicap in the children.*" (35, female)

8.3.3 Parents' decision making

8.3.3.1 Past experience

Parenthood presents new parents with unfamiliar challenges, obligations and expectations. Potentially frightening challenges they have to confront is child-related medical procedure such as childhood vaccination, and whether to allow their child to go through such procedure. In order to cope with such situations, parents tend to fall back on their personal experience and knowledge.

In their narratives regarding accepting or declining measles vaccination for their children, four parents described growing up in families in which childhood vaccination was a part of child care. Therefore when they started parenthood, they were already open towards vaccination.

"*We were taught from young that immunization was a must…*" (35, female)

"*All I know* (about vaccination) *comes from my mother, she had eight children and was very experienced. I took days off school to accompany her and my baby brother to the clinic…*" (30, female)

Having suffered measles and its complications in their childhood, or witnessing such events in close relatives also weighed substantially in the parents' compliance with childhood vaccination programme.

"*That measles, I ever got it when I was seven. My whole body was covered with growth (rash), when they sent me to the polyclinic, I had high fever, I had difficulty breathing, I could hardly sit up… I didn't want him* (child) *to have incomplete vaccination…*" (40, female)

For two-thirds of the parents, the role of vaccination in their childhood was minor and they described relatives from older generation, who enjoyed good health despite being unvaccinated since measles vaccine was not available then.

"*My parents didn't really care about vaccinations. My parents really took good care of us when we were children. My grandparents are over ninety years old, they live at countryside, they are so healthy, still very active.*" (33, female)

"*I don't know about importance of vaccination, is it that important? In the olden days, people did not get any injections but they remained healthy, do you get what I mean.*" (34, female)

Some even recalled seeing relatives who suffered ill effects due to vaccination, as well as those who did not suffer any consequences of non-vaccination.

"*My friend's children got symptoms after they were given injections. They were unhappy. So I was surprised that my children had no fever after the injection.*" (21, female)

"*About vaccinations, I shouldn't feel guilty if I follow healthy lifestyle. Because some of my friends, they didn't vaccinate their kids, and they're teenagers, very healthy. And that was the inspiration for us also.*" (33, male)

8.3.3.2 Social network

Aside from personal experience and knowledge on measles and its vaccine, the decision to vaccinate one's child may be affected by wider social influence.

Both poor and less educated parents relied heavily on friends and family members for health knowledge. Sometimes, friends and neighbours were the sole agents of knowledge through whom a parent gained knowledge on child health, albeit such information could often be quite erroneous.

"*My father-in-law is the one to ask me to send his grandchildren to the clinic…*" (36, female)

"*The village elders said, in case of measles do not take medicine, do not bathe the child. If you bathe the child, the rash will sink into the skin… Don't bring to the clinics, if you take medicine from the clinics the rash will not come out, and it is bad*." (33, female)

It also appeared that parents seldom sought or gave advice actively. Rather, they learned by listening to and sharing experience with other parents. For socio-economically disadvantaged mothers especially, this network acted as a cue for action to vaccinate their children and seek other necessary preventive healthcare. Such information would not have otherwise reached these mothers because there was no direct provider-parent contact previously.

"*I heard from my friends that nurses came to their houses to look for their children* (who defaulted well-child follow-up). *After that I saw them going (to the clinic), so I also follow and brought my child along*." (21, female)

"*I saw others bringing children to the doctors, so I also followed… My cousins, they said to me, we are taking our children* (to the clinic)*, you can take yours too… I'm relieved to see my children getting the same (treatment) as other children…*" (26, female)

Highly educated couples often preferred obtaining health knowledge online over discussing vaccination formally with acquaintances and relatives. This was observed among white-collar employees and professionals.

"*I subscribed to a health website, about diseases, diet, it would post to my Facebook and I only need to read it*." (30, female)

"*My knowledge? From reading magazine and Facebook page…*" (34, female)

8.3.3.3 Encounter with health system

*(a) **Antenatal and birth experiences***

Parents' narratives suggested that initiation and compliance to childhood vaccination programme were dependent on the mothers' engagement with antenatal health providers. Encounter with health providers during antenatal period and birth could either reverse or reinforce a parent's previous opinion on vaccination.

Antenatal health visits and births are pivotal points when mothers start to build trust in health providers and health advices they give, or otherwise. For socially disadvantaged parents especially, these encounters may serve as the only opportunity to gain accurate information about vaccination and other child health services. A mother living in poverty who previously shunned government facilities was finally convinced to get vaccination for her home-delivered son after a chance encounter with the government health providers.

"*People told me in hospital, mothers were tied up* (during labour). *I was scared. The private doctor said, if you go to hospital they might operate on you, I got even more scared. I had thought about giving birth in hospital, but I was scared when people said like that…* (Knowing about vaccination) *from the time my second baby got sick, he had bleeding from his umbilical cord… The nurse in hospital told me not to delay his injections. From that day onwards, I never delayed his injection even for one day.*" (21, Bajau-suluk, primary, homemaker)

It also emerged rejection of vitamin K and Bacillus-Calmette-Guerin vaccine at birth may predict future refusal of all other childhood vaccines, including MMR.

"*They take my wife away. The hospital is like a prison, you must follow everything that they do. After she* (the daughter) *was born, we told them no vaccination, but they still approached us trying to convince us, then one Medical Officer came and she's like,* *did you get vaccinations? Are you ok? You alright? Then the vaccination is good for her too. The way she said that was, ooooooh, it's just so arrogant, so prideful. It's like you know, if you want to convince us, that's not the way to convince us.*" (33, male)

(b) ***Trust in health providers***

Few parents formally discussed with health providers about childhood vaccination. For most, vaccination was passively accepted. This is especially apparent for parents who had gone through a period of inability to access primary care clinic services due to financial or geographical barriers. They tended to favour government-provided health services once the latter became accessible to them.

"*I believe in the clinic. If the nurse says it is good, I don't ask anymore.*" (21, female)

"*I have never heard of bad effects* (of vaccination). *The government surely will not do anything bad. I believe the clinic because many people go there. If I were the only one I worry, but I'm not the only one, there are many others…*" (26, female)

"*I will bring* (my children) *to the doctor, because they know what to do. Not like last time, we went through the hard time always sick, always fever.*" (40, female)

Even for the vaccine-compliant parents, their trust in health authorities was not without reservation. Beneath their expressed trust in public sector vaccination service, these parents had unvoiced doubts about the value of vaccination. However, they did not have the confidence to to question or criticize their providers as what the more opinionated, anti-vaccination parents did.

"*The nurses, they said the injection was for such and such purpose, I only said okay… I knew the doctors would answer if I ask, but sometimes what they said, I could not understand… I nod my head only.*" (26, female)

"*I will observe the person, if he/she looks unwilling to be asked, I would not ask question. If he/she looks busy, impatient, not happy to entertain you, only answer when you ask…*" (34, female)

To further complicate the trusting relationship between health providers and parents, the younger parents were now accustomed to receiving large volume of information online on a constant basis. For these parents, once they were exposed to online media coverage on possibilities of adverse events following vaccination and medical errors, it was natural for them to seek information online regarding risks associated with vaccines and reappraise the value of infant vaccination. Unfortunately, the information they acquired did not assuage their anxieties and suspicion of health provider's recommendation to vaccinate their children, especially when health providers failed to disclose vaccine-related risks to them during medical consultation.

"*It's not fool proof. Like flu vaccine, they just pick a bunch of popular flu viruses, put it together, make it a bit weak, hopefully your body can create a bit of immunity. It's just guesswork, it's pseudoscience… What do you do with your own kid when you know that vaccines can have side effects? Would you still take a risk? … We think it's insurance, but what if it's not insurance, it's a trojan horse?*" (33, male)

"*It contains heavy metals, right, like aluminium… I read in the drug insert. It's so unlikely we would inject mercury into our bodies right? I think doctors also know that mercury is dangerous, they know it but no, they cover it up. I don't know their agenda.*" (35, female)

The distrust expressed by parents could arise as a by-product of general scepticism towards governmental institutions or medical industries. Asymmetry of information when the ministries and related authorities disseminated vaccine-related information to the general public also seemed to have placed parents in a disadvantaged position, thus they regarded vaccination services with suspicion

"*Whenever you point the finger, like when I point the finger against the pharmaceutical company, they have their lawyers, their systems you know. But they put the blame on the layperson, on these antivacciners… Because if we go against what they do, they lose money… You can see the tactics those pharmaceutical companies use, it's dirty tactics. Because of that, we know something is not right.*" (33, male)

"*The Fatwa council did not talk about the detailed content of the vaccine, because they must work closely with the Ministry of Health. This information was not disseminated to the community because the council must get approval from the Ministry of Health first.*" (35, female)

Decreased trust in government authorities was accompanied by a heightened expression of self-reliance and assumption of personal responsibility over the children's health. It appeared that these parents had taken up the role of child protectors, having decided that they could not rely on the government to provide a well-researched, risk-proof service to their children. In contrast, parents who unintentionally defaulted vaccination had not expressed such level of anxiety.

"*Everybody is responsible for their own choices. Parents for their children.*" (33, male)

"*I asked, if I take all vaccines and anything happen to my child, is the doctor going to bear responsibility? Because this is my responsibility, my husband's responsibility. We did not make the decision not to immunize overnight. We had done our research and thought it out carefully*." (35, female)

These self-reliant parents tended to have gone through the phase of collecting stories on the side effects of vaccination from their family and friends, including online acquaintances. This active information seeking behaviour was not observed in parents who held neutral or favourable view towards vaccination. As illustrated by the narrative below, a mother who failed to find like-minded parents in her immediate social circle went online to seek friendship and validation for her opinions about vaccination in chat groups comprising parents with anti-vaccination tendencies.

"*I chatted with mothers* (whose children) *suffered and also with doctors who rejected immunization in the Facebook group. I didn't know whom else in Sarawak I could talk to.*" (35, female)

Moreover, even when advised by friends who supported infant vaccination, the parents who were hesitant about vaccination were not easily convinced because pro-vaccine parents were deemed as being ignorant of the undesirable characteristics of vaccines.

"*The ingredients of vaccines are not halal. They* (the friends) *vaccinated their children because they did not know*." (35, female)

Narratives suggested that parents had attempted to seek medical advice when they were contemplating to reject vaccination. These parents had hoped for more than a provider who forced the health authorities' recommendation for vaccination on them. They expected the health providers to listen to their concerns, alleviate their anxieties and support their perspectives on childhood vaccination. Unfortunately in all the narratives, none of the sessions with providers were deemed satisfying in addressing their concerns, let alone persuade the parents to regard vaccination in a more positive light. Ultimately, parents left the consultation sessions feeling more alienated than reassured regarding childhood vaccination. They were also offended by the patronizing attitudes of the health providers, which striped them of the freedom of making health-related choices.

"*Some doctors are very pushy. They bring fear somehow. They just said, if you don't do it, then you will suffer. Some of them tried to promise, but not all… Here in Malaysia, when you see just how the doctors and nurses treat us, there's no love. When you look at that, there's something wrong. We choose not to get vaccination and this is how you treat* *us? They were somehow very rude. Because we didn't want inject, then they didn't want to register baby in the check-up place…*" (33, male)

"*For me, doctors as medical people are not supposed to scare the parents that if you don't want injection your child will become like this* (sick). *This type of attitude should not have happened. The clinic staff? They did not accept my decision, they did not respect me. If a person do not want vaccine, you should still treat her as a patient…*" (35, female)

A recurring theme that emerged during the discussion with parents was the lack of rapport between providers and patients, where even the most educated and well-spoken parents found it difficult to establish good communication with health providers in the public facilities. Issues frequently encountered by parents were perceived verbal abuse, perceived unwillingness to engage in conversation, lack of knowledge on the providers' part, and seemingly evasive responses which prompted the patients to suspect that important information was withheld.

"*They told me to come on this day, if I came late, they raised their voices at me, they scolded… Sometimes I forgot about the appointment, sometimes I needed to work… If people told me off, I would not go back anymore*" (38, female)

"*The thing is the thought like that... Even doctors... It's like a military programme, you just follow what the head officer says. You can't question them. You disobey, they treat you bad, they ostracise you. So it's too bad the government is educated this way… so pushy and yet they're so reluctant to give information.*" (33, male)

"*I think the staff need to be educated. They did not know what was vaccine. They just know their job is to jab other's children… They cannot explain, or convince us. The least they could do is give me an answer, it's not that I would be satisfied with their answer, it's ok even if the answer is not something I like… As it is I want to know what exactly is the vaccine content, there's no answer when I ask the doctor*." (35, female)

Various external factors such as overcrowding and rigid consultation procedures acted in combination to make the child health clinic an unfavourable environment to impart knowledge or seek advice about child health.

"(you only get) *5 minutes with the staff. Outside* (the consultation room) *is full of people, if you open the door there are people waiting there… That's why I want to be fast. I think all the staff like to talk, but I feel sory for the many patients still waiting outside the consultation room…"* (30, female)

"*Maybe they* (the staff) *are busy, because there're many patients. If they take time to explain to me in detail, all patients will have to wait longer… I keep my questions to myself… Sometimes I see them so busy at work, and to ask questions in that situation… They said, okay mom thank you. When people say that you get the clue, so you get up and leave*." (34, female)

8.3.4 Barriers to Vaccination Uptake

8.3.4.1 Perceived health risk

From the narratives of parents who opted not to vaccinate their children, it was noted that their major concerns were additives in vaccines, such as Thiomersal, and that vaccines might be too much for the infants' immune system to cope with.

To vaccine-refusing parents, all vaccines were potentially risky and ought to be avoided. Thus, their children did not only default MMR, but also other vaccines on the national vaccination schedule.

"*There are heavy metals in the vaccines, for example Aluminium…*" (35, female)

"*There's a doctor, she made a video called 'Weapons of mass destruction' dealing with population control, and dumbing down people. She said that vaccinations were actually for that purpose. She said that when she was taught to be a doctor, a pregnant* *mother gets no vaccination, even a baby who was before six months, nothing… But now, all the vaccinations* (given) *before six months… before the child could communicate, they don't know anything. They cramped in everything into the child in six months, for us, we think, so many innoculations and she's so young…*" (33, male)

Furthermore, parents who already distrusted vaccination tended to attribute poor health in younger friends and relatives to to childhood vaccination. Storied circulated among vaccine-hesitant parents served both to strengthen their conviction and rationalise their decision not to vaccinated their children.

"*And we have some friends who said that their first child get vaccinated and the second one didn't. And the second one is much brighter, picking up things quicker, hardly gets sick… There's actresses who have children, they say that autism is caused because of their first inoculations. They say instead of progressing, they're regressing. Then you meet children who had full inoculations, sometimes some children can't even talk at age three. And then we found out that they had all the inoculations…*" …" (33, male)

"*My older children who got immunized, until they were three years old, they would need hospital admission twice a year, due to lung infection, vomiting and diarrhoea… Compared to them, my youngest two had no hospital admissions yet. They were also better* (in health) *at the same age*." …" (35, female)

When enquired directly whether scientific evidence would persuade them to immunize their child, the parents, having done extensive reading in the topic of vaccination, were confident that mere figures were not compelling enough. Instead, they might be more convinced by personal stories as told by other parents, as illustrated previously.

"*But statistics with just numbers, anyone can make up numbers. Numbers are not always right. Studies, there's a lot of flaws. A lot is fake science, a lot of it is not even properly done*." (33, male)

"*I am not so concerned about the effectiveness. It's all about the content. If the content of vaccine is halal, I have no qualms about immunizing my children*." (35, female)

8.3.4.2 Religious prohibition

One parent refused vaccination because of religious concerns over the cell lines in which viruses were cultured. Although the mother was unable to provide off-hand specific scriptural quotes that prohibited use of such ingredients in vaccines, the lack of positive support for vaccination in pre-existing religious literature appeared as a powerful deterrent for the parent.

"*Main reason* (refusing vaccination) *is the vaccine content, it is not* halal (religiously permissible)*… I've read the drug insert, most of the vaccines contained things like monkey serum, cow embryo… The animal may be okay, but the way they slaughtered the animal is not appropriate…* (Question: is there any specific provision in the scriptures?) *I am not sure*." (35, female)

Another parent was strongly opposed to vaccination and modern medicine, citing religious quotes that modern medicines were not religiously appropriate, and that medical practitioners had defied God by taking over God's role.

"*The word sorceries was "*pharmakeia*"* (in original scripture)*, where we get the word pharmaceutical from… Nowadays people are playing God. When you think about a human, when God created Adam and Eve, did he said take this syringe, take this injection, so to protect you against disease? …When you look at physicians in the bible, they are very low people, they are not high in the society. Now, we listen to everything they say. Back then they dealt with blood, …, they were ceremonially unclean… For me, I think innoculations will defile my baby girl and we choose not to put anything into her*." (33, male)

Coincidentally, both sets of parents thought that illness was an act of God, thus vaccination was unimportant as a means of prevention.

"*In Exodus 15, verse 28* (referring to Christian Bible) *it says if we diligently hearken to the lord, to his commandments, He will take away the diseases from us... for he is the God who heals us…*" (33, male)

"*In Islam we believe in concept of* Qada *and* Qadar*, meaning fate. If we don't take vaccine, and God says we remain healthy, we will be healthy. If we take vaccine and God says we will be sick, sickness will still occur*." (35, male)

8.3.4.3 Geographical barrier

Despite rapid urbanization and infrastructural development in Sarawak, one main reason for defaulting vaccination was inability to travel to the nearest clinic offering vaccination. An urban-dwelling parent could have as much difficulty as her rural counterpart in accessing the vaccinating clinic.

"*Hired vans will not go to the clinic, they only go to town centre. Even if they are willing to send me here, I still cannot go back. I need to walk from clinic to the main road, take a bus to the town centre. The journey home takes one hour… There is no more bus service*." (33, female).

"*I can't remember why* (I had not immunized my child)*… I was with my husband who worked in an oil palm plantation (at time of vaccination). The plantation was far from the hospital. If you wanted to go hospital, you could only hitch a ride in a pickup lorry if there was one. Going from the plantation to the town took one day. You started in the morning, you reached there the next morning...*" (26, female)

8.3.4.4 Financial barrier

Financial barrier was closely linked to geographical accessibility issues. Since attendees of public clinics are only charged the nominal fee of RM 1, which is often waived for poorer patients, the only substantial expenditure associated with the clinic visit was the transportation cost.

From mothers' narratives, it appeared that many governmental health clinics were poorly served by the public transport system. Thus mothers who did not own cars had to resort to hiring commercial vehicles, which could be expensive, although most mothers stayed within 20 kilometres from the nearest clinic. For the poorest families, the cost of transport could take up 10 percent or more of their monthly income, making regular monthly clinic visits unaffordable.

"*Now my husband gets roughly RM500 in one month, what can you do with that? It pays for the house rent, water and electricity. House rent is RM400 per month, sometimes there is no money left. The transport to clinic costs RM25, and another RM25 back. Yes it's true my house is just beside the main road,* (Question: why can't you take a bus?)*, but she needs to be carried, and I have to take the baby along. My child is delayed for many injections, for many months, because there is no money*." (26, female)

One parent had avoided public health facilities because she erroneously believed that she had to pay for health service, that the clinic and hospital would detain the child/ patient if parents failed to settle the medical charges, indicating the existence of communication gap between public health providers and the poorest segment of the society.

"*People told me that in hospitals if you cannot settle the payment, you go home and they keep your child there*." (21, female)

A father who was the sole breadwinner acknowledged that he had delayed or missed multiple vaccinations for his children. Because he was so overwhelmed with pressure of earning a living, he was forced to forego vaccination trips for their children. To make ends meet, he took up various part time jobs outside his formal employment. Although he struggled to make time for vaccination sessions in the clinic, he was not always successful due to physical exhaustion, memory slips and tight work schedule.

"*I seldom follow the timetable given by the nurses. I sometimes work outstation, sometimes I was too tired. Yes my wife tried to remind me but I needed to work. It's not the clinic's problem, it's my fault. My pay is RM640 after deduction for Employee Providence Fund and bank installment. I have to work outside office hours, like renovate houses, odd jobs as mechanic, wielder and guard. Sometime I work until the next morning. Vaccination is important, but how about food for the family? Who gets food for the family if I don't work? Most important is staying alive. If my financial situation improves later I surely will give more time to the family*." (36, male)

8.3.4.5 Mobile Population

Often, in attempt to improve financial prospects, poorer families found themselves moving from city to city, seeking for jobs which were often temporary in nature.

Keeping up with the child vaccination schedule thus became a daunting task for these families, with the bread earners travelling from one locality to the next, taking informal employment like construction work, plantation work and other similar manual jobs.

Mothers recounted their experience of settling down in a new town or district, not knowing the whereabouts or the means of going to a clinic that offered childhood vaccination. The matter was further compounded by the loss of formerly formed social network, which had acted as knowledge channel, and source of moral support for the less resourceful mothers.

"*Not that I did not know* (about the vaccination)*, I didn't know how to go the government clinic. I had no friends there. A neighbour said it did not matter, I could go to private clinic, it was the same thing*." (26, female)

"*My husband was a contract worker, we were always moving house.* (On the date of vaccination) *I was squatting at someone's place, I was stranger to that place, difficult to find* (clinic)." (38, female)

8.3.4.6 Inconvenient hours

Financial pressure did not only afflict previously discussed parents who came from socio-economically deprived background. Some financially stable parents were equally unable to vaccinate their children as recommended. These are the parents with difficulties taking time off from a job that they cannot afford to lose.

Most government clinics are open only during normal office hours of eight to five, Monday to Friday. Thus, the majority of parents who worked similar hours had difficulty taking time off from their work. Furthermore, the high patient load and long waiting hours in public clinics might compel a working parent to take a day off duty, which might be undesirable for the parent. Ultimately, they might resort to getting vaccination service from private practitioners, or not getting the vaccination at all.

"*Normally we can't take half-day off, at the bank there's no such thing. Let's say we have appointment* (at the clinic)*, I just ask my boss to go out for a while, maybe one, or* *two hours. Then I come back and replace the hours.* (Question: Meaning?) *I stay back to do overtime.*" (40, female)

"*Once I start working, the office will not let me out* (until the day ends). (Question: Why is that so?) *You will not believe me, but if I go at 8 AM, I can only return by 12 PM, just for one injection. There is not enough clinic staff, what can you say?*" (30, female)

8.3.4.7 Citizenship status

Issue pertaining to proof of nationality affects both immigrants with no travel documents, and citizens with no valid national registration. As everyone in the country is subject to Immigration Law, such parents avoided government institutions because they fear the consequences of being found out.

A few parents had such fear of violating immigration rules as the reason for not attending public health clinics. This issue was not only raised by non-Malaysian parents, but also by poor parents who were born in Malaysia but did not manage to obtain vital documents such as birth certificates and identity cards.

"*It's not my fault* (for not immunizing the child) *because I am not local. If you don't have identity card, police catch you. I am scared of going to jail. Here you need to bring identity card everywhere. Now my child finally gotten his birth certificate, it's not difficult now*." (36, female)

"*My husband is from Sabah, he also has no identity card because he was not registered for birth. My son has no birth certificate because he was born at home. I brought him to hospital one week after giving birth, the hospital asked for my antenatal card, I had none. The hospital said since he was born at home they would not support his birth registration.*

I kept on asking, I was worried, … because people catch you if you don't have documents. The staff will not help you if you are not someone important." (21, female)

A Malaysian child who has a valid birth certificate or national registration identity card (NRIC) is entitled to various privileges, among others, free health care in public clinics, and supplementary welfare allowances if he has special needs. All that a parent needs to do is to produce a valid identity card during registration at the clinics. However, parents with no documentation interpreted such administrative procedure as act of rejection. Consequently they preferred to use private medical service, and only for acute illnesses.

"*Once when he was two years old, he got measles. We brought him to a private doctor. The doctor asked us to go hospital, I already wanted to, but my husband and mother-in-law refused because they were too scared. Hospital was like police station to them…*" (21, female)

8.3.4.8 Vaccine supply

Another hurdle in being compliant to a child's vaccination schedule was vaccine shortage. At least one pair of parents mentioned that they gave up after making trips to the clinic only to be told that the needed vaccine was out of stock. If there were no defaulter tracing mechanism in the clinic after the vaccine stock was replenished, parents could be lost to follow-up. Such was the case for a mother, who belatedly realized that MMR vaccination had been missed when her child contracted measles at six years old.

"*When they said there was no stock, twice, so my husband and I decided not to take the injection. Then we missed it because we were busy at that time. Because of my work, I was traveling a lot, and to arrange a new appointment was really... My husband could not* (take him to the clinic)." (40, female)

Another mother was more fortunate. After the mother finally lost interest in attending more failed vaccination sessions, the clinic staff managed to track her down three months after the vaccine arrived.

"*Three times I went to the clinic, but there was no vaccine. I waited for my turn to see the staff, and then I was told sorry no stock you can go home. At least you could inform me earlier but no, must wait until I was in the consultation room. So many visits for nothing, at the end I was lazy to go*." (34, female)

8.3.4.9 Fear of admonishment by providers

Other reasons that cropped up during discussion were less explicitly stated by parents. Rather, they reflected parents' own phobia or guilt over mistakes associated with other practical aspects of vaccination, such as remembering the appointment date.

One mother who missed her child's MMR vaccine appointment because she was unable to visit the clinic in an unfamiliar town did not attempt to attend her former clinic after returning to her hometown, until the time her child was diagnosed with measles. She explained that she feared admonishment from the clinic staff for missing the appointment.

"*I knew she had not had her injection, but I did not dare to go clinic, I was scared that people will scold me. I am very forgetful. I had been late* (for other appointments), *they scolded. So if people scold, I am too scared to go again*." (38, female)

Another mother misplaced the baby's home-based card and was only able to locate it after three months. She had hesitated about going to the vaccination clinic without the health card, because she believed the clinic would not allow it. However, in reality it was a non-issue because the clinic in public sector is required to keep a copy of vaccination record for any infant registered with it. It had not occurred to the parent that she could ask the clinic staff for help, like issuing a new card.

"*I remembered her appointment, but without a card I could not bring her to clinic.* (Question: why can't you just tell the nurse?) *If there was no card the nurse would not be able to do anything*." (30, female)

8.3.5 Parents' needs

8.3.5.1 Outreach and tracing

Among the strategies adopted by governmental clinics to ensure better compliance, the one most favourably received by parents was the home visit conducted by clinic nurses.

Most parents were happy if a nurse visited them at their home to check on the baby and advise the parents to resume follow-up in the clinic. Some parents even voiced their hope for the clinic staff to administer the vaccination at their home in view of transport difficulties.

"*I got a surprise when the doctor and nurses came to my house* (to locate child who defaulted vaccination session)*, I was happy but I was shy. The nurse, she knew me…*" (36, female)

"*Sometime I could not go to clinic, if the doctor could come to my house to give injection, it would be much easier*." (36, male)

Some parents were more reserved about having home visitors but acknowledged the benefit of such outreach efforts.

"*Of course we don't like to be disturbed at home… But this is for health…*" (30, female)

Other parents suggested reminder service, such as telephone call or text messages to alert them about their child;s upcoming appointment.

"*Best if they can call me, don't call too early, I will forget. Do it like the day before…*" (38, female)

8.3.5.2 Empowering the parents

Although all parents thought that health information pertaining to childhood illnesses and vaccines as given by the health authorities were insufficient, they were divided as to the amount of such information.

Whereas majority of parents merely requested for more information dissemination by health authorities especially matters related to childhood diseases and vaccination, parents accustomed to doing their own research on childhood vaccines were more concerned about being allowed to make informed choices.

"*I can't remember about measles, we lack knowledge on measles and its danger. A bit more knowledge would help, yes. The parents need to be aware of the importance of taking vaccination, you know? We are not doing enough in terms of giving details to parents…*" (40, female)

"*I prefer if they* (clinic nurses) *can explain more. The reading material is just for reading and not for answering questions. Sometimes you can't understand even after reading. If we want to know more, we still have to ask.*" (33, female)

"*We would like the community to be educated in matters of vaccination. Parents must know all about vaccine, its content, side effects. Then whether they want to immunize or not, should be their own choice. But they must know the truth. No parents should make vaccination decision without knowledge.*" (35, female)

8.4 Discussion

In this study, parents who defaulted MMR vaccination comprised a wide socioeconomic spectrum within an urban setting. This ranged from parents who were hardly educated and living in poverty, to parents who had at least tertiary education and working as professionals.

In terms of vaccination behaviour, parents who did not vaccinate their children could generally be categorized into two distinct groups, passive users who were generally compliant but had inadvertently defaulted a vaccine or two, and active refusers who deliberately declined all forms of vaccines (Benin et al., 2006; Dube et al., 2013; Peretti-Watel et al., 2015).

Not surprisingly, parents who had first-hand experience with the dangers of measles were more likely to originate from poorer socioeconomic background, a setting where measles infection propagates easily. Incidentally, parents who had witnessed cases of measles were also appreciative of free vaccination to protect their children against measles. This is evident from parents' narratives and supported by previous study (Martirosyan et al., 2012).

For these parents, default did not occur because they had taken their children's health lightly, nor was it because they were opposed to vaccination. Rather, they appeared to have accepted vaccination and well-child clinics as part of routine childcare. In this respect, any non-adherence to the vaccination schedule appears to have stemmed from external barriers.

The forms and magnitude of these vaccination barriers may vary widely, from financial and geographical barriers to forgetfulness and frustration with health services. It is interesting to note that a parent's journey to the vaccination clinic could be deterred by relatively frivolous reasons, reflecting the local community's indifferent attitudes towards infant vaccination. This seems to be contrary to the impression of community-wide compliance as suggested by the high annual vaccine coverage statistics.

To appreciate the parents' thought process and actual vaccination behaviours (which could be at odds with their thoughts) remain a challenging task, albeit an indispensable one if we are hoping for a maximal level of population immunization and disease eradication. Policy makers from other countries were also faced with similar situations, and researchers in other parts of the world have already proposed several frameworks to better predict the probability of parents' vaccination choices.

Studies have shown that parental attitude towards vaccination could not be conveniently categorized into the mutually-exclusive groups of acceptance and refusal (Dube et al., 2013). Acceptance of vaccination is more appropriately seen as a continuum, ranging from vaccine advocates who fully endorse the benefits of vaccination to the rejecters who distrust all vaccines (Benin et al., 2006; Downs, de Bruin, & Fischhoff, 2008; Gust et al., 2005; Keane et al., 2005; Leask et al., 2012; Peretti-Watel et al., 2015). Thus, depending on the degree of faith a parent has in vaccinating his/her child, his/her decision making can be variably sensitive to a range of factors from the external environment, socio-economic circumstances to structural issues like vaccine access, supply and quality of service. The less faith he/she has in a health intervention, the more likely his/her health action will be interrupted by an external influence.

The Health Belief Model hypothesized that utilization of a health service or adoption of a health practice requires a person to go through a rationalization process of weighing his desire to avoid an illness, and his belief that a specific health action will prevent or ameliorate the said illness. It was assumed that demographic, socio-psychological, and cultural variables exert influence on a person's perception and these factors indirectly affect a health decision (Janz & Becker, 1984).

When such health decision is not an intervention for a person's existing disease, which is often associated with definitive symptoms and suffering, but rather a preventive measure which introduces a foreign antigen into a person's previously healthy child, the decision making becomes delicate. This is so especially when vaccination itself carries a risk of adverse event, irrespective of how small the risk could be.

From the narratives of most parents in this study, who were passive acceptors and inadvertent defaulters of vaccination, it was quite apparent that their vaccination belief and practices were overwhelmingly decided by external influences such as socio-economic and structural factors. In the process that commences from a parent making the decision to take a child for vaccination, then making the trip to clinic, finally getting the vaccination and the days which follow during which parents deal with any side effects, parental decision to vaccinate almost always hinged upon financial capacity and service accessibility. For most of the parents who were interviewed, the desire to prevent illness or improve the child's health was less apparent.

The findings regarding attitudes and experiences of Sarawakian parents were in reality closer to the outcomes of studies from underdeveloped countries such as Africa and parts of Asia (Dugas et al., 2009; P. H. Streefland, A. M. Chowdhury, & P. Ramos-Jimenez, 1999), or those marginalised populations in developed countries. In those studies, parents generally held views that ranged from indifference to favourable towards childhood vaccination. However, exogenous factors had hampered attempts to vaccinate their children. Such hindrances could come from their socioeconomic environment, cultural background, gender differences, and the availability or accessibility of health services.

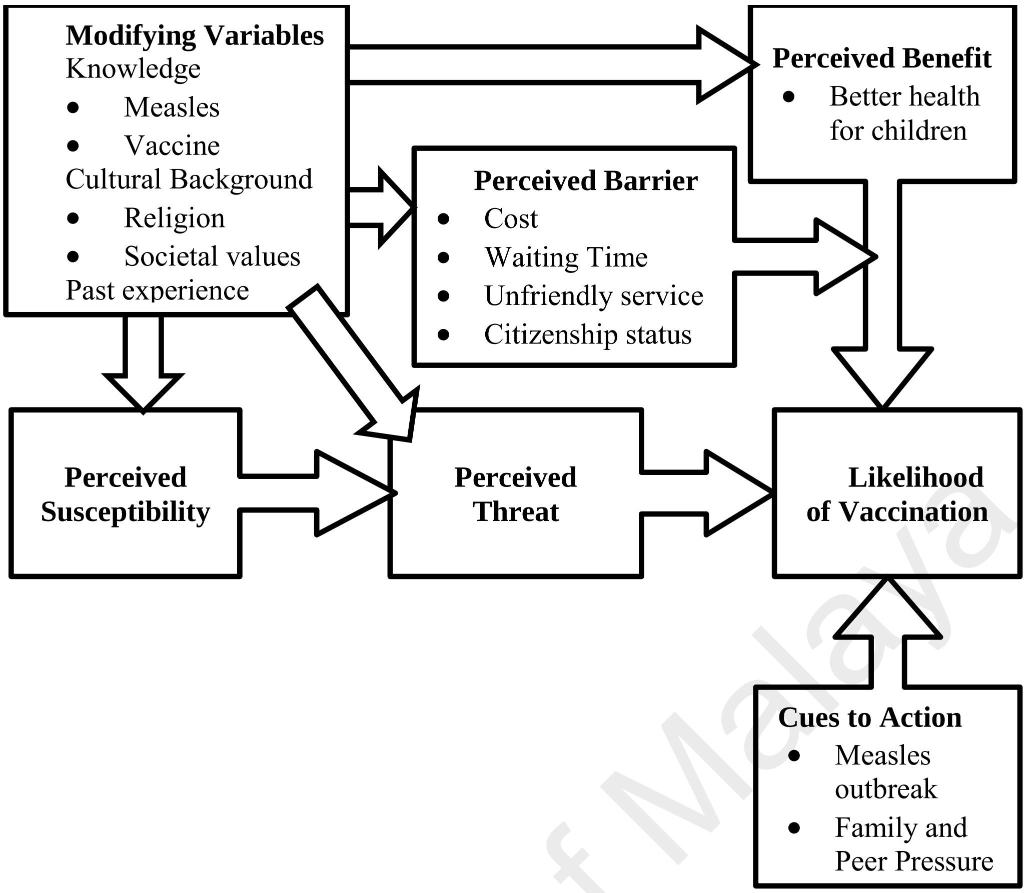

Figure 8.2: Parents' decision making based on Health Belief Model

In this respect, the Health Belief Model (figure 8.2) is less effective in conceptualizing and explaining the parents' ultimate vaccination behaviour, especially in a setting where modifying factors such as socio-demography and financial pressure exert a heavy influence on the actual access to the vaccination service. This is because the Health Belief Model premises itself on parents arriving at a rational decision after weighing the potential risks and benefits of a vaccine, besides taking into consideration the degree of threat from the disease. The decision-making process in the Health Belief Model requires abstract thinking, and the formation of a logical conclusion after processing a myriad of health-related information. As observed during the interviews, most parents did not think in the same fashion as depicted by the Health Belief Model. This could be attributed to multiple modifying factors, for example, lack of access to health information, lack of critical thinking skills and disempowerment.

One major hurdle faced by parents when attempting to comply with vaccination schedules appears to be financial difficulties, despite the fact that health services at government clinics are virtually free. Financial problems were found to co-exist with other obstacles to accessing facilities such as transportation, nomadic lifestyle, and citizenship. These problems are not easily overcome by short-term financial aids given through welfare or other single-agency initiatives. This is so as they are the products of interaction between various agencies such as immigration, health, social and financial institutions. Families with limited financial means in accessing health care in the study sample were prone to suffer social isolation in parallel, further rendering them vulnerable to misinformation, unhealthy lifestyle, disease occurrence and worsening deprivation.

For parents at the lower rungs of social hierarchy, a more appropriate model to describe their ultimate vaccination behaviour is the Maslow's Hierarchy of Needs (Figure 8.3), in which a person will fulfil his needs in a specific order, starting from survival, then safety, love and belonging, esteem, and lastly self-actualization(Maslow, 1943). Maslow's Hierarchy of Needs succinctly explains why a parent would default vaccination, even though he may have viewed childhood vaccination favourably by the logic of the Health Belief Model.

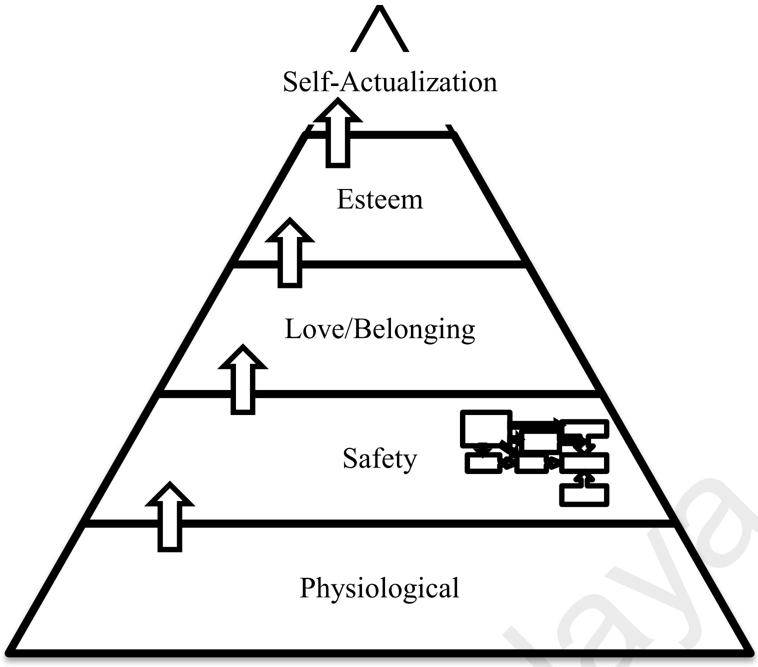

Figure 8.3: Maslow's hierarchy of needs

A person will first and foremost take care of his basic needs directly impacting on survival such as food, shelter, water and electricity. In the case of poor parents, ensuring the family's survival might entail hopping from one place to another to seek job opportunities. For these mobile families which were already displaced due to poverty, the mother and children might become more vulnerable from disruption of their family and social ties. The parents might therefore have limited means to use preventive health service, and will only use the medical service in the case of serious illnesses.

Should attempts to understand vaccination behaviour be made using the Maslow's framework, the conceptualization of risk and benefit of vaccination forming the cornerstone of the Health Belief Model will fit into the 'safety' rung, which is of secondary importance as compared to the most important physiological needs rung. Therefore, to consciously decide for or against vaccination may be less relevant for socially disadvantaged parents as childhood vaccination presents no immediate and tangible benefit in terms of survival. That act of vaccination is only likely to bring about a heightened sense of safety and security, which becomes important only after the fulfilment of basic needs. For a struggling parent living in an urban, cash-dependent setting, he might not be able to appreciate such an abstract health benefit in decreasing the likelihood of illness for an apparently disease-free offspring, whose survival is already threatened by the more immediate material risks. Understandably, vaccination would not be a priority, at least, not until after the basic physiological needs have been fulfilled.

We can now see that for Sarawakian parents, satisfaction of the basic physiological needs alters vaccination behaviour more than parental attitudes and beliefs. We thus propose a framework on parents' ultimate vaccination behaviour as shown in Figure 8.4. Basic needs can be seen as the most important and influential modifying variable, and it can independently exert influence on parents' perception and their likelihood of vaccination. After the basic needs are met and parents are not encumbered by material hardship, then only they are better able to carry out cost-benefit analysis regarding vaccination. Material circumstances which dictate survival and parent's thought process are in turn governed by a complex interplay between personal, institutional, community and structural factors.

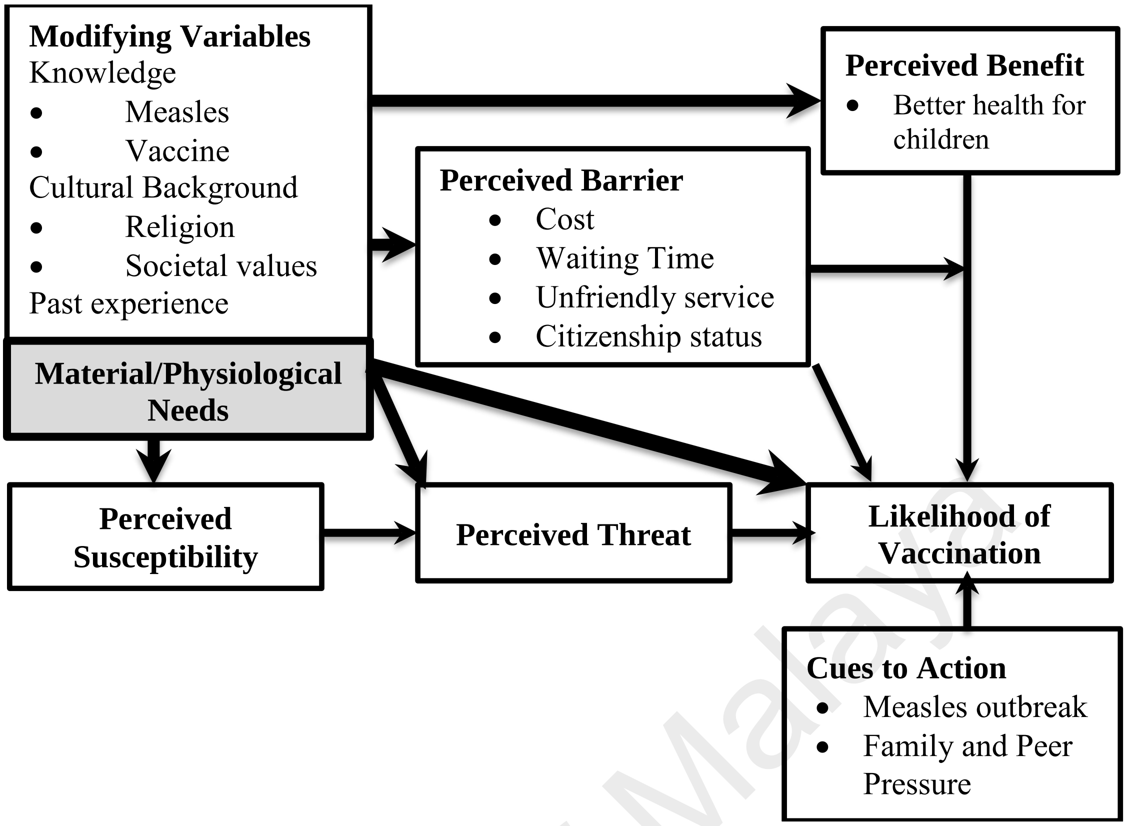

Figure 8.4: Proposed theoretical framework on vaccination behaviour

Therefore, in order to encourage the poor parents to voluntarily seek vaccination for their children, the pressing need is to improve material circumstances rather than to communicate more information on vaccination and its benefits. After satisfying the basic needs, people could start to contemplate on more abstract issues such as safety, better health prospects and other higher needs according to Maslow's hierarchy. Therefore, only with satisfaction of basic needs could the Health Belief Model best explain the parents' vaccination behaviour.

When the poor people in the community are constantly relocating to earn a living, it becomes impossible for the Ministry of Health to provide proper tracings and follow-ups, which are of central importance in maternal and child care. Whilst building more health centres helps to better serve the needs of the community, such measures are most effective when accompanied by improvement in the availability, affordability and effectiveness of the public transport system.

Again, in order to improve uptake of vaccine among socioeconomically disadvantaged parents, the local Department of Health needs to work extremely closely with other agencies, such as, Immigration Department, National Registration Department, Public Works Department, City Council, Education Department and Welfare Department. This is so because health and health seeking behaviour often follow poverty reduction and improved health equity (Evans, 2008).

Another observation from the parents' narratives is the importance of antenatal healthcare and events surrounding childbirth in establishing their first contact with a nurse or a doctor, thus opening the opportunity to create awareness about childhood vaccination. Here, the role of maternal and perinatal health providers in promoting vaccination could not be over-emphasized. Even a narrow window of opportunity during a short hospital admission has been shown to initiate mothers into childhood vaccination (as seen in Section 8.3.3.3a).

A child of a mother so initiated not only ceases to be the potential reservoir of infection, but he/she also becomes a source of inspiration for other mothers. The role of initiated mothers as agents of change is evident from the recurrent statement of 'knowing about vaccination service because 'I saw other children going'. This is especially important for poor mothers with no other means of knowing about public health policies and services. In addition, this will greatly lessen the work burden of community nurses by reducing the need of performing targeted home visits and other outreach efforts in order to track vaccination defaulters.

8.4.1 Vaccine hesitancy – an emerging issue

Having attempted to understand the vaccination behaviour of parents who favourably viewed vaccination but were impeded by material barriers, it is also necessary to look into the group of parents who refused or questioned the necessity of vaccination.

Among the expanding segment of well-educated and high-income Malaysian parents, vaccine refusal and hesitancy is becoming an emerging issue. Having weighed the pros and cons of vaccination as described by the Health Belief Model, these parents may have concluded that vaccination is not beneficial to their children. Major concerns brought up in the vaccine-refusing parents' narratives are perceived health hazards of vaccine, and religious prohibition.

Similar findings were reported in developed countries like the United Kingdom and United States, where stalled progress in measles vaccination programme, and reduction in measles vaccine uptake had resulted in an increase in measles cases (Gostin, 2015; Poland & Jacobson, 2012; Saint-Victor & Omer, 2013). Researchers believed that this phenomenon was related to the now-debunked claim of the association between MMR vaccine and autism in Dr Wakefield's research paper, which was published in 1998 (Godlee et al., 2011; Wakefield et al., 1998). Although this paper was subsequently retracted, parental trust in health authorities has been slow in recovering (Dube et al., 2013; Poland & Jacobson, 2012; Poland & Spier, 2010).

Despite the 2011 outbreak, parents' knowledge on measles remains poor. This could be partly due to lack of media exposure on the last outbreak, as compared to outbreaks of new emerging diseases like rotavirus gastroenteritis or viral respiratory syndrome. In fact, when parents were asked for examples of dangerous diseases during childhood, they mentioned such diseases as reported by mass media, and explained that for a disease to warrant news coverage, it must be serious. Here, the power of mass media in shaping the people's health belief is clearly demonstrated. Thus, besides neighbourhood social networks, we could also consider utilizing mass or social media as an adjunct channel, to maximise dissemination of measles-related information.

Even among vaccine-compliant parents, in-depth interviews suggest that they had many unexpressed doubts and concerns about childhood vaccination. These parents' compliance to the national vaccination recommendation had hinged upon their high regard for medical professionals and cultural norms that value submission to authority. However, with almost universal access to mobile devices and social media among urban, financially well-off parents, they will be actively or passively exposed to a myriad of health and vaccine-related information that could undermine their faith in vaccination, irrespective of the validity and veracity of the said information.

Here, the role of the internet in disseminating unverified information about vaccine cannot be ignored (Dube et al., 2013). Information on virtually any conceivable topic is increasingly spread through what are known as the Web 2.0 applications (social media, online discussion forums, real-time chats) rather than conventional means. Although conventional media such as the newspaper, television and radio still comprise formal communication channels utilized by governmental institutions in Malaysia, Web 2.0 applications are significantly more powerful in recent years because of their comparatively wider user base, interactive nature, and speedier dissemination of news. As a result, health messages could be spread virally across geographical boundaries on the web or through smart devices, and ultimately influence parental decision making at an unprecedented magnitude compared to pre-Web 2.0 era.

A further complication arises for public health authorities when they wish to utilize this new technology, because there are now more parties involved in the measles vaccine debate, as compared to the simple, provider-patient discourse in the past. Apart from the vaccine communicators and their intended clients (the parents), there exist a growing number of active and vocal anti-vaccine activists who exert far-reaching influence over parents through Web 2.0 applications (Betsch & Sachse, 2012; Larson et al., 2011). Furthermore, evidence shows that parents are easily convinced by anecdotal and personal accounts on supposed vaccine-related injuries and sufferings from fellow parents. In contrast, parents do not trust statistics given by scientists and health authorities on the miniscule risk of vaccine-related adverse events, and the warnings on morbidities and deaths associated with measles (Betsch & Sachse, 2012; Hilton, Petticrew, et al., 2007). Thus, with the advent of the internet and smart devices, the task of competing against anti-vaccine campaigners and building parental trust specifically towards measles vaccine, and generally towards all other childhood vaccines becomes more daunting than before.

The success of the national expanded vaccination programme in reducing the incidence of measles had created a generation of young and inexperienced parents who had not witnessed the debilitation and death caused by measles infection. As a result, measles gradually ceased to be a threatening disease in the parents' minds. Now, the parents' attention is drawn to the adverse health events following vaccination, leading them to conclude that vaccinating a healthy child with the aim to reduce the already small risk of infection carries with it diminishing returns, and is therefore not desirable.

The study findings revealed that official statistics about effectiveness of vaccines and the minimal risk of adverse events would not reassure vaccine-hesitant parents adequately. As long as there are no firm statements from trusted sources to convince the parents on the absolute safety of measles vaccine, or to refute the claim that vaccines are religiously prohibited, parents' doubts would continue to linger, and they would remain as vaccine refusers.

The differential importance attributed to scientific evidence between health professional and parents arose because the parents did not conceptualize risk the way health providers did. From parents' narratives, it appeared that numbers and statistics were less important when they weigh the benefits and potential harms of vaccination. To the parents, it did not matter if the studies showed that the risk of adverse events following vaccination was miniscule, once an adverse event occurred, the statistics became meaningless and the child would experience the event in its entirety.

A mere reproduction of statistics to refute claims of anti-vaccine advocates, whether such claims are in fact correct or erroneous, may not gain much ground with the parents. Compared to facts and figures, parents who are already undecided about vaccination may resonate with public figures whom they perceived to be likeable, and free from any hidden agenda (Opel et al., 2009). This sentiment was clearly illustrated in section 8.3.4.1 in which a parent quoted the case of an actress who advocated against vaccination as his source of inspiration.

Upon realising that vaccines were not risk-free, parents tend to weigh on whether to vaccinate or not for the benefit of the child, drawing upon their own knowledge and values, as well as from their peers. This may be the reason why parents were prone to trust accounts and anecdotes from other parents, especially famous personalities whose children were purportedly disabled due to vaccination. Firstly, as fellow parents the parents were able to empathize. Secondly, accounts from other parents may be regarded as impartial and free from vested interests. Thirdly, the relatively small number of anti-vaccine advocates causes them to appear as the disadvantaged party when pitched against the health authorities and pharmaceutical industry. These anti-vaccine advocates may thus be perceived as whistle-blowers and the champions of parents from non-medical background.

As MMR vaccine has been the subject of contentious debate, study on vaccination uptake has to take into account both parents' and providers' perceptions and attitudes. Health providers play an important role in encouraging parents to accept vaccination. This is evident from parents' narratives of avoiding clinics because they were in fear of admonishment from vaccine providers. In parallel, for educated and empowered parents, although they were not fearful of the vaccine providers, the value they assigned to medical advice depended on perceived trustworthiness of health providers.

Parents in this study expressed varying degrees of trust in vaccine providers working in the public sector. The more educated and internet-savvy parents appeared to be, the less trust was given to vaccine-related information given by health providers. This reduced level of trust stemmed not from previous medical mishaps, perceived poor knowledge nor incompetence in the providers, but from the high-handed way doctors or nurses communicated with parents when they were discussing vaccination or the feasibility of "opting-out" from routine vaccination.

From the parents' viewpoints, there is a misalignment between the intention of health providers and their own. The modern-day benefit of vaccination, as discussed earlier, is now far less tangible and obvious as compared to the pre-vaccination era. This is further compounded by the inherent risks of adverse events associated with vaccination, therefore causing the overall costs of vaccination to escalate. As vaccination is a classic example of public good, being non-excludable and non-rival, more parents might have come to the logical conclusion to remain as free riders[14] and enjoy the herd immunity afforded by other vaccinating infants.

Clearly such parental decision-making based on individual benefit is at odds with the utilitarian approach of the public health providers. In fact, as younger members of our society were brought up in an era where self-expression and independent thinking were highly valued, an authoritative approach when giving health education as used by the health providers with varying success would no longer be sufficient to encourage this group of new parents to immunize their children. Furthermore, as the average educational attainment of the population improves, it could be expected that this proportion of parents with similar worldviews would increase in future.

For the moment, uptake amongst children has been maintainable through the Personalized Care, a patient-centred defaulter tracking and outreach programme run by all clinics under the Ministry of Health. However, with the expansion of community-based health services and competition from other new programmes for adolescents, special-needs children, disabled adults and elderly, resources for the Personalized Care are expected to be squeezed in the future. Thus, a more sustainable and cost-efficient approach needs to be crafted in order to improve on the existing vaccination coverage if measles elimination is to be achieved in the near future.

[14] A free rider, also known as free loader, is a person who consumes public good without contributing to the cost of providing it (Culyer, 2014).

8.5 Study limitations

By the sampling strategy, parents who participated had not vaccinated their children against measles for one reason or another. The proportion of parents who were hesitant and unconvinced about the necessity of childhood vaccination would thus be higher than the general population.

Due to the fact that non-vaccinating parents are a minority in the society, tracking of these parents based on official records were challenging. It was not possible to study the parents' perspectives systematically under socio-economic categories like ethnicity, income, education and family size. This study also did not attempt to address issues like gender and ethnic difference in perceiving vaccination needs or barriers. However, as this study only aims to gain insight into parental concerns about vaccination, in particular MMR vaccine, and possibly explore ways to regain parental trust in the vaccination service, this 'in-depth understanding' is deemed more appropriate than an 'overall picture' approach.

There was limited representation from parents of Chinese descent. Thus, certain experience and perception specific to the Chinese community may not have been explored. Further culture-specific studies on health beliefs and value system may be needed for effective, targeted communication efforts.

8.6 Summary of findings

Failure of parents to vaccinate their children for MMR vaccine is a complex issue with contributing factors such as geographical access, availability of health services and other public amenities, parent's socioeconomic status, individual experience and value system.

When parents consciously make the decision about vaccinating their children, their thought processes were consistent with some dimensions of the Health Belief Model:

perceived threat from disease, perceived susceptibility, perceived benefits, perceived barriers and cue to action. However, the outcome or ultimate vaccination behaviour was so frequently and heavily influenced by modifying external variables that the thought process was not immediately apparent. On the other hand, classical examples of decision making according to Health Belief Model were more clearly seen in well-to-do parents who were not encumbered by physical and material hardships.

Despite differences in health beliefs, the felt needs of parents were quite similar across cultural backgrounds, with all expressing the desire for more open communication and increased empowerment in making informed decisions pertaining to the uptake of vaccination services towards better health outcomes for their children.

CHAPTER 9: GENERAL DISCUSSION AND CONCLUSION

9.1 Introduction

This thesis seeks to uncover the reasons behind the 2011 measles outbreak. This outbreak has suggested that a national aggregate coverage for measles vaccine exceeding 95% may not be sufficient to deter an outbreak. For a programme that requires uptake by almost every infant in the country, the implementation of measles vaccination on a population level may still entail many problems. Therefore, it is crucial to assess the quality of vaccination programme implementation and analyse important factors that might have contributed to failure of building population immunity against measles.

The challenges and gaps identified in the provision and uptake of measles vaccination will be discussed in depth in the following sections, starting with issues in running a successful national immunisation programme in Section 9.2, followed by policy implications in Section 9.3, research implications of study findings at Sections 9.4, and the conclusion in Section 9.5.

9.2 Gaps in the national measles immunisation programme

9.2.1 Non-vaccination

One of the main threats to a long-running immunization programme is to maintain its success by keeping a high vaccine coverage. This is achievable by maintaining parents' trust in the need and safety of vaccines, so that they will continue to take up measles vaccine for their children.

For the 2011 measles outbreak, non-vaccination was an important factor. This was evidenced by the observation that one-quarter of the patients had no history of vaccination. This study revealed that parents who did not vaccinate their children could generally be divided into two groups. The first group comprised parents who were poor and relatively less educated (and these parents form the majority of vaccination refusers) and the second group were affluent and well educated parents.

The most common reason given by parents who did not vaccinate their children against measles was the inability to access vaccination service in a timely manner. Obstacles to accessing vaccination service were financial difficulties, geographical barriers, transport problems, unclear citizenship status, families with mobile lifestyle, and conflict between vaccination appointments with parents' work schedules.

Parents who had access problems were generally less affluent. In absence of access barriers, they would readily vaccinate their children when instructed by health providers, although they might remain ignorant of the benefits of measles vaccination. However, seemingly minor hindrances, for example fear of admonishment from health providers, and vaccination appointments that clashed with working hours, had stopped them from bringing their children to the clinics. This could perhaps be explained from the perspective of hierarchy of needs, where vaccination becomes of secondary importance when families struggle to fulfil basic needs such as food and housing. Therefore, for the majority of non-vaccinating parents who could not access vaccination service, the pressing need is to alleviate their material hardship. If outreach vaccination service is offered to them, an enabling environment can be created where children can be vaccinated on time.

Other than inability to access service, the other main reason for non-vaccination was vaccine hesitancy among the affluent, well-educated and religious parents. They chose not to vaccinate because they perceived vaccination to be religiously inappropriate, or harmful to their children. These parents also did not perceive vaccination as beneficial.

Vaccine-hesitant parents can be defined as a heterogeneous group who "share varying degrees and motives of indecision and who hold an intermediate position along a continuum ranging from full support for vaccination to strong opposition to any vaccine" (Peretti-Watel et al., 2015). They may decline a vaccine but not all vaccines, or delay a vaccine, or eventually accept it despite their reluctance and doubts (Dube et al., 2013).

These study findings revealed that several important factors contribute to vaccine hesitancy. These include distrust of health providers, influence from family and peers, and lastly perceived low value of vaccination. This is consistent with studies on vaccine-hesitant behaviour of parents from developed and developing countries in America and Africa (Briss, Shefer, & Rodewald, 2002; Mitchell et al., 2009; Sanou et al., 2009; Smith et al., 2011; P. Streefland, A. M. Chowdhury, & P. Ramos-Jimenez, 1999).

As new vaccines were made available and combination vaccines were being developed from existing single-component vaccines, vaccination decisions were likely to be more complex and challenging for parents. Moreover, the advent of social media and smart devices had enabled rapid, borderless communication of vaccine-related information. Sharing of vaccine-related concerns and uncertainties among parents around the world had led to the increase in the number of vaccine-hesitant parents (Larson et al., 2014).

It is important to note that regardless of the cause of non-vaccination, be it access issue or vaccine hesitancy, the parents with predisposing risk factors might be clustered within the community. For example, poor parents tend to reside in the same neighbourhood, and vaccine hesitant parents tend to share the same philosophy and hold regular gatherings or send their children to the same schools. When the critical vaccination coverage for measles elimination was calculated, the mathematical model assumed random mixing of non-immune and immune persons throughout the population (Fine, Eames, & Heymann, 2011; World Health Organization, 2009). However, as seen in this study, the high-risk children were not randomly or homogenously dispersed in the community. Instead, they tend to move in the same social circle as other non-vaccinated children. This implies that the required level of measles vaccine coverage might be much higher than the calculated 95%. In fact, studies had shown that higher degree of social clustering was associated with higher risk of epidemics, and thus required higher critical vaccine coverage compared to a homogenous population (Fine, 1993; Fox et al., 1971). This might have explained the occurrence of measles outbreak in Malaysia despite the overall measles vaccine coverage of 95%.

9.2.2 Untimely, delayed vaccination

The other threat to measles vaccination programme is failure to vaccinate infants as soon as they become vulnerable to measles infection (age-appropriate vaccination). Delayed vaccination was likely to be the other main factor that contributed to the 2011 outbreak in Malaysia. Delay in vaccination had been shown to increase the risk of measles in young infants whose passive immunity had waned. Moreover, the implication of delayed vaccination goes beyond the risk on individual infants. When delayed vaccination occurs frequently enough and children receive their vaccines much later than intended, the population is rendered susceptible to measles outbreak because herd immunity will be compromised, despite a deceptively high administrative coverage.

Vaccination that is inappropriate for age occurs for two reasons. The first reason is delay on the parent's part in obtaining the vaccination for the infant. The second reason lies in inappropriate age-recommendation in vaccination schedule imposed by the health authorities.

Seroprevalence studies conducted around the world in the past decade (2003-2013) had suggested that for infants born to previously vaccinated mothers, at least a third would have become completely susceptible to measles infection by the age of six months. If

Malaysian infants have similar immunological profiles as their overseas counterparts, at least a third of each birth cohort will remain vulnerable for six months until they are scheduled to receive measles vaccine at twelve months old if they followed the old MMR schedule before year 2016. In 2016, MOH rescheduled the first MMR to nine months, thus reducing the expected period of vulnerability to three months. This would be the minimal period of infant vulnerability even if all the parents were perfectly compliant with the measles vaccination schedule. Unfortunately, data analysis from the WHS 2002 had shown that only half of Malaysian children were vaccinated according to schedule. This could likely be a contributory factor to the 2004 measles outbreak in Malaysia. It is also not unreasonable to postulate that the previous recommended timing of MMR vaccine at 12 months had resulted in six months of susceptibility in infants, and had negatively impacted on effective vaccine coverage, which subsequently contributed to the 2011 measles outbreak in Malaysia.

9.2.3 Challenges associated with vaccination service provision

Various minor departures from the standard operating procedures in vaccination service management and technical aspects of the cold chain maintenance have been observed in both public and private providers of measles vaccine in this study. In addition, vaccine provision is also complicated by a number of physicians and providers who themselves are vaccine-hesitant. This vaccine-hesitancy was observed among private and public vaccine providers who were not willing to administer more than two vaccines in an opportunistic encounter with a defaulting child, for fear of parental anxiety, even when giving all indicated vaccines within one visit is a practice highly recommended by the World Health Organization (Centers for Disease Control and Prevention, 1993;

World Health Organization, 2016)and there could be a high possibility that the said child would not return to the clinic.

Aside from gaps in knowledge and technical know-how, limitations in human resources were found to be a major challenge in running vaccination services, particularly in public health facilities. Although the supply of vaccines and cold chain equipment are generally adequate in all public sector clinics, the same cannot be said of human resources. This observation is consistent with findings by other authors in Malaysia which had been published in the mainstream media (Alhadjri, 2016; Choong; Panirchellvum, 2015). This was substantiated by narratives of parents interviewed in this study. Parents mentioned overcrowding, long waiting time and short consultation time in public facilities. These experiences, apart from being the reasons as to why children default measles vaccination, also serve as a testimony to the magnitude of human resource constraints in most public health facilities in Sarawak.

In addition, there is no full adherence to existing vaccine storage and handling guidelines. This could generally be attributed to staff shortages in the public sector clinics. Vaccine management is but only a fraction of work duties assigned to health providers in public facilities. A community clinic nurse's daily duties include but are not limited to running daily maternal and child health consultation sessions, defaulter tracing, performing outreach services and home visits, conducting patient education, and reporting a multitude of statistical returns for each health programme run by the clinic (Public Service Department Malaysia, 2008).

Such technical incompetency and attitudinal hesitancy are not only detrimental to the quality of vaccines served by said health professionals, but these gaps in service also indirectly affect vaccine uptake amongst the community served by the clinics. This becomes especially relevant when parents' acceptance towards vaccination could be influenced by their experience of interacting with health providers, and fear of admonishment by vaccine providers was repeatedly given by parents in this study as a reason of not attending the clinic for their children's vaccination appointments.

It may be argued that attitudes of health providers are less relevant for educated parents compared to the uneducated ones, as the parents who refused vaccination in this study had already made their decision prior to meeting their children's physicians. They also seemed to have low level of confidence in health providers who came across as active proponents of vaccination. However, studies do show that knowledge, attitude and belief of health providers did influence the uptake of vaccine amongst the patients they serve (Dube et al., 2013; Nikula et al., 2011). Thus it may not be unreasonable to postulate that, had the physicians possessed stronger convictions about the benefits of vaccination which outweighed the theoretical risks of vaccine-associated adverse events, or had they have more technical knowledge on each vaccine, perhaps they would not be deemed as "ignorant", "pushy" or in similar unfavourable light by vaccine-refusing parents.

So far, the gaps identified in the provision of vaccination service were minor. However, it could not be denied that these imperfections had collectively cause parents to regard health providers or vaccination service in a less positive light. This could eventually exert an impact on parental acceptance and uptake of measles, which ultimately render the population susceptible to a measles outbreak.

9.3 Implications for policy

In view the challenges in providing timely, age-appropriate vaccination to infants, and difficulty in monitoring uptake of measles vaccination especially by private providers, there is a need for a policy on better vaccination service surveillance tool nationwide.

This could be achieved through the creation of a centralised database, which receives feedback from every district in the country. The use of electronic vaccine information system as a surveillance tool is vital for real-time feedback on vaccination performance, and should be instituted in public health clinics to minimize human error, expedite identification of children who were falling behind schedule, and facilitate audit of records. Moreover, a state-wide or nation-wide vaccination database will have an the additional advantage of ensuring continuity of care for mobile patients who are at high risk of defaulting vaccination.

The importance of a centralized vaccination database could not be overstated. It is pivotal in ensuring adequate surveillance and monitoring of age-appropriate vaccination coverage, as well as identifying high-risk subpopulations such as vaccine-rejecting parents or vulnerable populations. When such a database is in place, health authorities will be well placed to start monitoring new parameters that will more accurately reflect the performance of a mass vaccination programme.

Routine collection of data on delayed vaccination entails only information on date of birth, demographic information of interest, and date of vaccination, which could be done when an infant was registered. A central database will enable computation of age-appropriate vaccine coverage and its derivatives, for example, magnitude of delay, with or without proxy indicator of vulnerable period per child can better reflect the true population immunity against measles. As an added advantage, indicators on delayed vaccination can also be used as a tool for comparing and monitoring the effectiveness on the delivery of preventive health services.

The failure to vaccinate sufficient number of children may have to be tackled with a two-pronged approach based on the identified gaps. The first being minimization of delayed vaccination and the second, promoting acceptance towards measles vaccine. These two approaches will be dealt with in turn in the following paragraphs.

The first approach is minimization of delayed vaccination, which involves changes at many layers of the health service. At the provider-patient interface, both physicians and parents will need to be provided with accurate information to guide their decision on the timing of vaccination, in order to minimize unnecessary delays in the absence of medical contraindications.

At the ministry level, policy makers may consider a review on the age-recommendation for first measles vaccination, pending further evidence on vaccine safety and local serological profile. Following the new 2016 measles vaccination policy, MMR will be administered at nine months followed by a second dose at twelve months. At nine months, the effectiveness and safety of single-component measles vaccine has been well proven (World Health Organization, 2009). However, cumulated evidence from the last decade has pointed towards early loss of passive immunity in infants as young as three months. It, therefore, stands to reason that the age for measles vaccination could be further lowered to six months as studies have shown that most infants have lost a considerable proportion of their anti-measles antibody by then. Recent studies have also yielded encouraging results on measles vaccine effectiveness when given at six-months old, so long as a second dose is administered at the end of one year (Gans et al., 2013). Whether or not a policy change with regard to age recommendation for measles vaccine in Malaysia could be achieved will most likely be informed by newer and larger population-based trials, which should become the direction of future research in Malaysia.

The second approach is promotion of acceptance towards measles vaccination which must be viewed in light of the heterogeneity in the factors that led to non-vaccination.

This is important for vaccination programme implementation on the ground, where discrepant economic development and uneven improvement of education level among the people prevail between and within districts in Sarawak. Difference in material circumstances and overall access to health information resulted in a heterogeneous group of parents who have different vaccination needs and issues. Therefore, health authorities could no longer rely on age-old, one-way technique of health education as a blanket strategy to persuade parents to comply with vaccination recommendations. Instead, MOH needs to start tapping into local communities for knowledge and aid.

For public health policy planners, there are additional resource-friendly methods that have been proposed to combat vaccine hesitancy, which have been put into practice in developing countries with restrictions in capacities. These methods include social mobilization, the use of public icons and the empowerment of health professionals at all levels to communicate with vaccine hesitant parents and the strengthening of pre-existing surveillance systems (Saint-Victor & Omer, 2013). In this thesis, poor parents' narratives showed that social connection with neighbours and elders was the only channel through which they learnt about free, essential health services offered at public sector clinics.

The urban poor families also had their share of challenges in accessing important services such as free preventive health care, public transport and education despite their relative geographical proximity to the said facilities. These last pockets of unimmunized children are the most important in elimination efforts, as they are likely to be the last stronghold of perpetuated measles outbreaks. Therefore, the presence of knowledgeable local volunteers can do much in enlightening and empowering the parents to start utilizing vaccination service.

By focusing and varying vaccine promotion efforts on high-risk locations or pockets of population, we can potentially avoid high costs and wastages associated with mass delivery of vaccine as is usually done during supplementary immunisation activities during outbreak control. It will be helpful for local health workers to study the causes of non- or delayed-vaccination in their localities before deciding on whether they need to deal with issues of material deprivation that competes with vaccine-seeking behaviour, or parents who have low confidence in measles vaccine. By taking targeted remedial steps, it would hopefully avoid the wastage of resources and improve local uptake of the vaccine.

For the growing segment of highly educated parents who are vaccine-hesitant, information given by the authority is deemed incomplete. They prefer to do their own research on vaccines before forming their own judgments regarding benefits and risks to their own children. After weighing personal gains against perceived risks from vaccination, a rational parent may logically decide to free-load upon the existing herd immunity at the expense of society's well being. This gives rise to the possibility that the community will eventually pay the price in the form of measles outbreaks.

Opening a two-way communication channel to allow discourse between vaccine-hesitant parents and health authorities can potentially ameliorate parents' cognitive biases and flawed risk perceptions. However, the effectiveness of such discourse rests on health providers who are responsive and empathetic to parents' concerns. From the narratives in Section 8.3.6.4, an opinionated health provider who strongly believed in the benefits of vaccination may find his motives and attitudes questioned by vaccine-hesitant parents. Conversely, should a health provider be less resolute in his views as regard the need for vaccination, the parents became concerned of possible "cover ups". For the better-informed parents, their trust in the health providers appeared to depend on how well the practitioners could offer a well-balanced opinion on the pros and cons of vaccination, as well as a perceived openness to intellectual debate. Seeing that parents place strong emphasis on unbiased information, future strategies in community education and parent counselling sessions should encourage health practitioners in public health sectors to expressly acknowledge the benefits and side effects of vaccination, address individual parent's concerns rather than dispensing impersonal statistics. This is more likely to help parents in reaching conscious, informed decisions based on sound health advice.

Health providers must also play their role by building good rapport with the parents. This is supported by studies that showed positive association between parents' satisfaction with child health providers and age-appropriate vaccination coverage (Bielicki et al., 2012; Schempf et al., 2007; Stockwell et al., 2011). It is also important that providers deliver vaccination service and advice in a sensitive manner, as parents are known to default vaccination because of poor provider-parent relationship.

Therefore, having a team of committed and competent local child healthcare providers is likely to improve preventive health utilization and regional age-appropriate vaccine coverage. This, in turn, is critical in building local herd immunity against future measles outbreak. Other than good policy makers, good vaccine providers working directly with the parents are important people in tackling the issue of failure to vaccinate. This effect will most likely work in tandem with well-maintained vaccine cold-chain managed by competent providers to ensure that vaccines delivered to infants are in optimal conditions, which will in turn address vaccine failure as a cause of continued outbreaks.

Having stressed the importance of commitment and competence of health care provider, it is worth mentioning that both are conditional upon good continual medical education for the health care providers. In fact, existing evidence has shown that practitioners with good knowledge are more intent on vaccinating the population under their care (Herzog et al., 2013). Improving and maintaining practitioners' knowledge should not rely on individual initiatives but requires considerable commitment from the governing bodies such as the Ministry of Health and Academy of Medicine Malaysia.

Finally, measles elimination and vaccination programmes need to undergo periodical evaluations and updates. Strategies need to be dynamic and be continuously informed by timely researches and field data on local ecology, disease epidemiology and population demographic changes.

9.4 Implications for future research

Population immunological profile would be informative in identifying regions with high-risk population, as well as yielding data on duration of immunity conferred by measles vaccine, which in turn will fill the research gap on prevalence of secondary vaccine failure in the Malaysian population. This is so because the huge success of measles vaccination campaign during the past three decades had given rise to a generation of adults who might possess shorter and lower level of measles immunity, compared to their predecessors who obtained their immunity via natural infection.

Another research direction which could better inform measles immunization programme is the objective measurement of vaccine quality to monitor the effectiveness of vaccines given to infants in each district. This is best done by a vaccine potency testing as the 'gold standard' of determining the strength of a vaccine and its immunological properties (McVey, Galvin, & Olson, 2003). A pooled, nationwide MMR vaccine potency analysis for all health facilities will adequately alert policy makers on districts facing problems with vaccine cold chain maintenance, so that remedial actions can be taken before the occurrence of an outbreak. This can be further supplemented by a well-organized case-control study to calculate MMR vaccine effectiveness in the Malaysian population, which may be different from other countries.

Having discussed primary vaccine failure, it is important to remember that young infants who are the subjects of this heated debate regarding age of first measles vaccination, precisely for the concerns that passive immunity would potentially cause primary vaccine failure if vaccination is given prematurely. In the results chapter, it is shown that premature disappearance of maternal antibody, rather than its persistence, is becoming the main threats facing young infants nowadays. Therefore, the next step in research will be to assess anew the feasibility, long-term safety and effectiveness of early measles vaccination in protecting young infants, especially babies who were born premature, in populations where vaccination coverage is high and maternal immunological profiles have been altered by vaccination compared to pre-vaccination era.

As disease elimination/eradication involves more political commitment and funding than merely running a vaccination programme, it would be prudent to conduct at least one econometric evaluation on measles elimination, and possibly followed by periodic re-evaluation as the country is currently going through trying economic times. As suggested by Field et al, a more robust analytical methodology ought to include important outcomes like vaccine costs, QALYs saved, vaccine risks, vaccine efficacy, potential for herd immunity, patient's autonomy restriction and disease burden (Field & Caplan, 2012). Policy-makers may use these results to compare across alternative interventions such as those aiming to improve general population health, rather than side-by-side comparison with measles hospitalization and treatment costs. Such studies will improve transparency, fund accountability and provide updated information on health policy changes regarding disease elimination, such as whether to step-up efforts or just postpone the time line for regional elimination.

9.5 Conclusion

As the saying goes, 'the last mile is the longest', to bring down measles case to zero from the already low incidence level is complex, and requires more socio-political commitment than the mere running of a vaccination programme. This is especially challenging when the population in Sarawak still faces complex structural and institutional barriers in accessing vaccination service.

The 2011 outbreak was likely attributable to non-vaccination and failure of providing age-appropriate vaccination to susceptible infants. Non-vaccination is associated with parental vaccine hesitancy and access barriers, while failure of achieving age-appropriate vaccine coverage is contributed by delays caused by policy recommendation and individual vaccination delays.

In this thesis, evidence has been shown to support early susceptibility to measles in young infants born to vaccinated mothers and the need for earlier vaccination age recommendation. Another contribution of this study is offering evidence to support incorporating age-appropriate vaccination indicators in evaluation and monitoring of vaccination programme. For this purpose, the setting up of a central vaccination database is highly recommended.

To promote vaccination, several measures are necessary. For parents facing access issues, efforts to reduce structural and systemic barriers by the MOH and local government is needed to ensure that children are vaccinated on time. In addition, health professionals who are competent in vaccine management and responsive to parents' needs are vital in improving vaccine uptake.

As highly educated parents are logically, although not rightfully, cool towards measles vaccination in the face of low disease incidence and high media coverage on vaccine-related adverse events, any success in regaining parental trust and community mobilization would probably spare the Ministry of Health from further financial burden of outbreak control and cost of running a protracted vaccination programme. Early programmatic planning for social mobilization, enlisting support of local leaders and full utilization of local knowledge are critical issues to be considered in addressing misinformation and misplaced risk perception regarding measles and its vaccine.

As with all other health programmes, successful population immunisation and disease elimination rely heavily on the presence of an effective health system. Strengthening the current health system, particularly addressing limited resources and lack of technical knowledge updates for vaccine providers, will address weaknesses in the vaccine service provision.

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LIST OF PUBLICATIONS AND PAPERS PRESENTED

1. Poster Presentation at 46th APACPH Conference Kuala Lumpur (17th to 19th Oct 2014): **Timeliness of Childhood Measles Immunization in Malaysian preschool children**
2. Oral Presentation at WHO Consultation on the Broader Economic Impact of Vaccines and Immunization Programmes, Bangkok; 24th to 25th November 2014: **Barriers to Measles Vaccination Service in Sarawak**.
3. Oral Presentation at 4th Asia Pacific Conference on Public Health, Pahang (7th to 9th September 2015):
   a. **Parents' decision-making & access to measles vaccination in Sarawak: A qualitative study**
   b. **Barriers in accessing measles vaccination in Sarawak: a qualitative study**
4. Oral Presentation at 6th International Public Health Conference, Malacca (31st May to 1st June 2016): Delayed vaccination and its association with measles outbreaks.

APPENDIX A

QUESTIONNAIRE ON VACCINATION SERVICE AND COLD CHAIN MAINTENANCE PRACTICES BY HEALTH PROVIDERS

Immunization Questionnaire for Health Clinic

The aim and objectives of the study have been sufficiently explained to me. I have not been pressurized to participate in any way. I understand that participation in this study is completely voluntary and that I may withdraw from it at any time and without any adverse consequences.

I know that this study has been approved by the Ethic Committee of the Universiti Malaya and Ministry of Health Malaysia. I am fully aware that the results of this study will be used for scientific purposes and may be published. I understand that information provided by me is confidential.

By completing this questionnaire, I consent to participate in this Study.

Name of Respondent	(Signed)	**Date**

A.	General Information		
1	District:	2	Clinic:
3	Interviewer:	4	Date of visit:
5	Name of Staff		
6	Race	☐ Malay ☐ Iban ☐ Bidayuh ☐ Melanau ☐ Other aborigines ☐ Chinese ☐ Others	
7	Age		
8	Gender	☐ Male ☐ Female	
9	Designation	☐ Doctor ☐ Assistant MO ☐ Staff Nurse ☐ Community Nurse ☐ Other (Specify) ____________________	
10	Total Years in Service		

Clinic Questionnaire

Vaccine Delivery

1.	Walk-in immunization offered during all operating hours of clinic	☐Yes ☐No
2.	Staff providing immunization is available during all operating hours of this clinic	☐Yes ☐ No
3.	Average waiting time for immunization appointment	☐ Seen same day ☐ ______ (number of days)
4.	Average waiting time for immunization service	☐______ minutes (walk-in) ☐ ______ minutes (immunization days)
5.	Immunization service provided during the following occasions: • Evenings • Weekends • School • Home visits	 ☐ Yes (______hours/month) ☐ No ☐ Yes (______days/month) ☐ No ☐ Yes (______days/year) ☐ No ☐ Yes ☐ No
6.	Immunization screening & referral integrated with other services.	

	Do the following staff screen and refer? • MCH staff • OPD staff • Home visitor Screening = assess immunization status and record the status in index card Referral = escort/direct to immunization provider	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
7.	Child receives all immunization (including catch-up immunizations) simultaneously within 1 visit.	☐ Yes ☐ No

Vaccine Handling

1.	Standard Operating Procedure & Guideline for vaccines administration, adverse reactions & contraindications	
2.	Documentation in home-based card of: • vaccine name • manufacturer • date • dose number • lot number • name of staff • adverse reaction	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
3.	Documentation in index card of: • vaccine name • manufacturer • date • dose number • lot number • name of staff • adverse reaction	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
4.	Adverse events are recorded and reported to JKN Sarawak	☐ Yes ☐ No
5.	Vaccine storage standards: • Temperature monitoring protocol/SOP • Back-up plan (e.g. alarm system, back-up power source)	 ☐ Yes ☐ No ☐ Yes ☐ No
6.	Vaccine inventory/accountability: • Maintain maximum 3-month inventory • Inventory report every 3 months • Report overstocked vaccines to matron/JKNS • Assure EEFO (earliest expiry, first out) • Assure vaccine wastage ≤ 25%	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No

Provider Education & Awareness

1.	Regular CME on immunization/vaccine/vaccine-preventable diseases for all clinic staff who administer, screen, refer & follow-up for immunization	☐ Yes (______days/year) ☐ No
2.	Documented training for new immunization staff (e.g. test, assessment)	☐ Yes ☐ No
3.	Incentive for clinic staff to increase immunization	☐ Yes ☐ No

	level (e.g. SKT, service award)	
Follow-Up & Assessment		
1.	Tracking/recall system in place: • Tracking system which identifies children aged 0-24 months who are overdue for immunization • ≥ 3 telephone calls for defaulters • Home visits • Outreach programmes • Recording immunization histories into clinic database	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
Parental Education & Awareness		
1.	Vaccine Information Statement (VIS) or reading material given to children's guardians.	☐ Yes ☐ No
2.	Types of material used to educate parents • Posters • Newspaper cuttings • Pamphlets • Videos • Others ____________________(specify)	 ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
3.	Do you adapt the education materials mentioned above to meet the needs of your patients?	☐ Yes (How? ________________) ☐ No
4.	Staff discusses reasons parents do not bring their children for immunization + solves the issues directly with parents	☐ Yes ☐ No
5.	Immunization information incorporated into antenatal and other health education programmes.	☐ Yes ☐ No
6.	Immunization incentive for parents	☐ Yes ☐ No
7.	Partnership with community organizations	☐ Yes ☐ No
8.	Use of media to publicize information about childhood immunizations • Local newspaper • Local radio • Local television • Others _______________________(specify)	 ☐ Yes (______times/year) ☐ No ☐ Yes (______times/year) ☐ No ☐ Yes (______times/year) ☐ No ☐ Yes (______times/year) ☐ No

5.	How many hours of operation are offered for immunization service? • Monday • Tuesday • Wednesday • Thursday • Friday • Saturday	 __________ hours/day __________ hours/day __________ hours/day __________ hours/day __________ hours/day __________ hours/day
6.	How do clients get their initial immunization service? (Check all that apply) • No real system • Link with birth records • Referral from OPD • Walk-in • Call and get appointment • Referral from other health facilities	 ☐ ☐ ☐ ☐ ☐ ☐
7.	Does the child need to be seen by doctor before vaccine is administered?	☐ Yes ☐ No
8.	What happens when a child is overdue for a vaccination? (Check all that apply) • Give another appointment • Tell parents to come back the next available day • Parent is given recall telephone calls about the next appointment • Parent is given recall mailing about next appointment • Home visit • Other (Specify) ____________________	 ☐ ☐ ☐ ☐ ☐ ☐
9.	If a child misses an appointment, how is the future appointment handled? (Check only one) • Identify as high-risk and put in special category • Managed like other children • Other (Specify) _____________________	 ☐ ☐ ☐
10.	Is there reminder service for upcoming immunization visits?	☐ Yes (How? __________________) ☐ No
B.	Resources	
1.	Are there sufficient immunization staffs to handle the workload?	☐ Yes ☐ No (How many more? ________)

APPENDIX B

QUESTIONNAIRE ON VACCINE KNOWLEDGE

The aim and objectives of the study have been sufficiently explained to me. I have not been pressurized to participate in any way. I understand that participation in this study is completely voluntary and that I may withdraw from it at any time and without any adverse consequences.

I know that this study has been approved by the Ethic Committee of the Universiti Malaya and Ministry of Health Malaysia. I am fully aware that the results of this study will be used for scientific purposes and may be published. I understand that information provided by me is confidential.

By completing this questionnaire, I consent to participate in this Study.

Name of Respondent	(Signed)	**Date**

A.	General Information		
1	District:	2	Clinic:
3	Interviewer:	4	Date of visit:
5	Name of Staff		
6	Race	☐ Malay ☐ Iban ☐ Bidayuh ☐ Melanau ☐ Other aborigines ☐ Chinese ☐ Others	
7	Age		
8	Gender	☐ Male ☐ Female	
9	Designation	☐ Doctor ☐ Assistant MO ☐ Staff Nurse ☐ Community Nurse ☐ Other (Specify) ____________________	
10	Provides immunization service	☐ Yes ☐ No	
11	Total Years in Service		

B.	Knowledge	
1	A child was last seen at 2 months old. He had received BCG, Hep B_1, Hep B_2, $(DTaP/IPV/Hib)_1$. He is 8 months old now. What vaccines will you give?	
2	What will you do if a child comes to you with temperature 38°C, pain and swelling at the site of injection?	
3	What is the route of administration and injection sites for the following vaccines? a) BCG ____________(route) ______________________ (site) b) DTaP/IPV/Hib ____________(route) ______________________ (site) c) Measles ____________(route) ______________________ (site)	
4	Which of the following is a **true** contraindication to immunization? (Circle only one) a) vaso-vagal response following a previous dose of the vaccine	

	b) known allergy to penicillin antibiotics c) anaphylaxis to previous dose of the vaccine d) fever 38°C	
5	OPV & MMR should not be given to children with primary immune deficiency disease. ☐ True ☐ False	
6	All of the following are Signs of Anaphylaxis, except: (Circle one) a) angioedema b) tachycardia c) wheeze d) hypertension	
7	In a suspected anaphylactic reaction in a clinic setting, epinephrine 1:1000 should be given: a) Intradermally b) Subcutaneously c) Intramuscularly d) Intravenously	
8	Maintaining the cold chain ensures that vaccines are stored according to the manufacturer's instructions at: a) 0°C to +4°C b) -1°C to +5°C c) +2°C to +10°C d) +4°C to +8°C e) +2°C to +8°C	
9	Vaccines can be stored in the vegetable bins of the refrigerator. ☐ True ☐ False	
10	All clinics that store vaccines must check the refrigerator/freezer temperatures every day. How many times per day? ____________________ When? ____________________________________	
11	Based on the vaccine vial monitor (VVM) below, this vaccine can be used.  ☐ True ☐ False  ☐ True ☐ False  ☐ True ☐ False  ☐ True ☐ False	
12	VVMs can measure exposure to freezing. ☐ True ☐ False	
13	The diluents of vaccines are not interchangeable. ☐ True ☐ False	
14	To compare between vials in the "shake" test, you need one TEST vial, and another vial that you are sure is not frozen. ☐ True ☐ False	

APPENDIX C

COLD CHAIN CHECKLIST

Name of Clinic ________________________________ Date: ____________________

Parameters	
Ice lined refrigerator	
Available Not available	
Deep freezers	
Available Not available Not functional	
Cold boxes	
Available Not available	
Frozen ice packs	
Available Not available	
Generator	
Available Not available	
Automatic voltage stabilizers	
Available Not available	
Dial thermometers	
Available	
Temperature chart	
Maintained Incomplete	
Vaccine storage in the refrigerator	
Proper Not proper	
Presence of other items with vaccines	
No Yes	

Penjagaan semua jenis peti sejuk, vaksin,*cold box,* penggunaan ais pakdanperalatan. Tandakan (√) diruang yang berkenaan.

Bil	Perkara	Ya	Tidak	Ulasan
1.	**Menggunakan peti sejuk yang sesuai**			
1.1	Jenis peti sejuk			
	i. *Pharmaceutical refrigerator*			
	ii. *Top loading refrigerator*			
	iii. *Double door refrigerator*			
	iv. *Single door refrigerator*			
1.2	Kedudukan peti sejuk			
	i. Jarak dari dinding belakang peti sejuk>20cm			
	ii. Jarak dari dinding tepi/sisi peti sejuk >30cm			
	iii. Jarak dari dinding atas peti sejuk> 40cm			
	iv. Jauh dari cahaya matahari			
1.3	Terdapat Label'Buka Bila Perlu' di pintu peti sejuk			
1.4	Plug/soket (bekalan elektrik) peti sejuk tidak berkongsi dengan lain-lain peralatan letrik			
1.5	Getah penebat dikeliling pintu dalam keadaan baik, tidak pecah dan pintu boleh ditutup rapat			
1.6	Ketebalan ais dinding peti sejuk beku (*freezer*)$\leq$1 mm			
1.7	Tidak terdapat minuman/makanan dalam peti sejuk (Peti sejuk hanya mengandungi vaksin, beg air batu			

Bil	Perkara		Ya	Tidak	Ulasan
	dan bekas berisi air)				
2	**Penjagaan suhu peti sejuk**				
2.1	Suhu dalam peti sejuk berada +2^{0}Chingga + 8^{0}C				
2.2	i.Jenis *thermometer*	- Minimax			
		- Dial			
		-Fridge watch			
		-Digital			
	ii.*Thermometer* berfungsi				
	iii.*Thermometer* digantung menegak di rak tengah peti sejuk				
2.3	Buku rekod suhu peti sejuk				
	i. Suhu direkod 2 kali sehari /setiap hari				
	ii.Tindakan yang diambil apabila suhu < 2^{0}C atau >8^{0}C (melalui pemerhatian/temubual dengan anggota bertugas)				
3	**Pengendalian Vaksin**				
3.1	Setiap vaksin diasingkan mengikut jenis dan bekas vaksin dilabelkan				
	i. Menggunakan bekas simpanan berlubang				
	ii. Vaksin tidak menyentuh plet dibelakang peti				
	iii. Pencair vaksin disimpan dibahagian bawah dalam peti sejuk				
	iv. Vaksin disusun FEFO (First Expiry , First Out)				
	v. Vaksin tidak luput tarikh atau rosak (vaksin yang luput tarikh atau rosak hendaklah dikeluarkan dari peti sejuk)				
	vi. Setiap barisan vaksin mempunyai ruangan 1-2 cm				
	vii. Ruang kosong di pintu peti sejuk ditempatkanbotol berisi air				
	viii. Tiada vaksin diletakkan di ruang paling bawah di peti sejuk atau di sisi pintu				
3.2	Pelarut bagi vaksin kering tidak ditempatkan di ruang dingin beku				
4	**Penjagaan *cold box***				
4.1	Menggunakan *cold box* dan ais pak yang mencukupi untuk stok / pengunaan semasa sesi klinikal				
4.2	Pek ais disusun didalam *cold box*				
4.3	Terdapat Dial Thermometer untuk memantau suhu didalam *cold box* berada pada paras +2^{0}C hingga + 8^{0}C				
4.4	Vaksin tidak menyentuh ais pak				
4.5	Vaksin diletakkan didalam bakul berlubang				

Bil	Perkara	Ya	Tidak	Ulasan
4.6	Ais pak yang dikeluarkan dari tempat pembeku perlu didedahkan terlebih dahulu untuk mencapai suhu $0^{0}C$ sebelum dimasukkan didalam *cold box*			
5	Tindakan yang diambil apabila bekalan terputus(Melalui temubual dengan anggota bertugas)			
	i. Dapatkan maklumat dari TNB anggaran tempoh bekalan letrik terputus			
	ii. Menggunakan *cold box* untuk memindahkan vaksin			
	iii. Mempunyai Generator yang berfungsi			

APPENDIX D

INITIAL INTERVIEW GUIDE FOR NON-VACCINATING PARENTS

Non-vaccination for MMR – barriers, parental perception, needs

1. Perceptions towards measles and its vaccine
    a. Knowledge about measles
        i. Every child needs to get measles?
        ii. Measles is a mild disease?
    b. Perceptions towards MMR vaccination
        i. MMR associated with side effects and sickness
        ii. Vaccination is against belief or religion
    c. Past experience in getting the child vaccinated
        i. Long waits
        ii. Unaddressed queries and concerns
        iii. Interaction/communication with health providers
        iv. Pain and misery in the child resulting from injection
    d. Sources of information about measles and MMR vaccine
        i. stories shared by family and friends
        ii. information published online or in printed material
2. Barriers
    a. Access
        i. Physical: distance of health facilities offering immunization from home
        ii. Cost: transport, taking time off work
        iii. Convenience of hours
    b. Support
        i. Child care for other siblings
        ii. Unattended house work
3. Needs
    a. Access
        i. Service with convenient hours, outreach
    b. Education & information

APPENDIX E

FINAL INTERVIEW GUIDE FOR NON-VACCINATING PARENTS

Non-vaccination for MMR – barriers, parental perception, needs

1. Perception about measles and its vaccine
   a. Perceived danger of measles to children
   b. Perceived benefits and risks of measles vaccine compared to natural infection
2. Parents' experience with health services (including vaccination)
   a. Decision making process
      i. Parent's personality
      ii. Social network
   b. Previous encounters with health providers
      i. Antenatal and birth experiences
      ii. Trust in vaccine providers
3. Perceived barriers to vaccination services
4. Parents' needs regarding vaccination service
   a. Outreach and tracing
   b. Empowering the parents