

## SUPPLY CHAIN OF IRON CHELATORS FOR THALASSAEMIA IN MALAYSIA: AN OVERVIEW FOR PROCESS OPTIMISATION

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### ABSTRACT

*Iron chelating therapy (ICT) drugs are prescribed to transfusion dependent thalassaemia (TDT) patients to prevent iron overload complications. The high number of TDT patients in Malaysia strained the public healthcare resources. This paper aims to provide an insight on existing supply chain management of ICT medicines in Malaysia and to explore ways for a more efficient system. A rapid review of literatures was conducted in electronic databases (PubMed, Emerald, Scopus and ScienceDirect) and other relevant Malaysian government documents. Supply of ICT to thalassaemia patients is publicly funded but much availability of oral ICT is restricted due to financial consideration. ICT in Malaysia is supplied through central procurement but purchasing and inventory management are decentralised to each hospital. Vendor-managed inventory system is an ideal option to the inventory management practice in Malaysian public healthcare facilities as it could provide better efficiency and reduces inventory management costs.*

**Keywords:** Thalassaemia, Iron chelating therapy, Supply chain, Vendor-managed inventory

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## INTRODUCTION

Thalassaemia, a complex blood disorder and the most inherited haemolytic anaemia. This chronic life-long condition can be classified into transfusion dependent thalassaemia (TDT) and non-transfusion dependent (NTDT). Globally, it is estimated that more than 300 million people are thalassaemia carriers (Viprakasit *et al.* 2009). As reported, 350,000 babies are born each year with haemoglobinopathies including thalassaemia (Weatherall *et al.* 2010). Iron chelating therapy (ICT) are prescribed to TDT patients, hamper the toxic effects of iron overload such as heart failure, diabetes, hypothyroidism and liver disease. The availability and accessibility to ICT has dramatically increased patient's survival and quality of life (Cappellini *et al.* 2014). In Malaysia, more than 72% of the 8,681 thalassaemia patients registered in Malaysia Thalassaemia Registry are TDT patients and this number is expected only to increase (Mohd Ibrahim 2019).

There are different types of ICT drugs available such as desferrioxamine (DFO), deferiprone (DFP) and deferasirox (DFX). Although DFO is widely used, it comes with issues, such as complicated mode of administration, long infusion hours and reliance on infusion pump. These prove to be challenging to patients' long-term compliance with reported high rate of missing doses (Lee *et al.* 2011). Alternatively, use of oral ICT such as DFP and DFX are particularly useful to counter these issues. Use of oral ICT showed better patients' satisfaction and reported quality of life (Chordiya *et al.* 2018).

Public healthcare in Malaysia provides a comprehensive medical service including preventive, diagnostic and curative care as well as monitoring that are accessible to all. Thalassaemia patients in Malaysia largely seeks treatment in public hospitals that are heavily funded by the government. Malaysian hospital are categorised into several levels starting with district hospitals with only visiting specialists, hospitals with resident specialists up to major hospitals with more than 15 specialties and sub-specialties (Jaafar *et al.* 2013). Studies have shown that Malaysia has one of the most well-established quality medical care from screening programme, counselling, curative care up to palliative care for thalassaemia patients (Azman *et al.* 2016). Thus, it is unsurprising that such huge provision places a strenuous economic burden on public healthcare system.

Increasing demand on finite healthcare resources also puts additional pressure to policymakers to find more efficient ways to deliver health services. One of important component of healthcare system is pharmaceutical supply chain (PSC). Supply chain is particularly complex and challenging in healthcare. Apart from being constrained by stringent regulations, supply chain in healthcare must ensure uninterrupted supply of medications or other supplies reaches patients (Uthayakumar and Priyan 2013; Bhakoo, Singh and Sohal 2012). Across the Organization for Economic Co-operation Development (OECD) countries, pharmaceutical expenditure accounts to almost 30% of total health spending (OECD Data 2018). Thus, PSC management has become one of essential government strategy in utilising development policies to achieve a country's economic and social goals (Ladipo, Sánchez and Sopher 2009). A study showed that inventory and the labour costs can take up almost a third of hospital budget (Oliveira and Nightingale 2007). Consequently, a robust supply chain management is vital as poor inventories is identified as one of major factor of inefficiencies.

More studies must be conducted to evaluate the current PSC and procurement system and identify the root causes for any inefficiency in order to improve (Baboli *et al.* 2011). World Health Organization (WHO) (2015) National Medicine Policy (NMP) provides a sound foundation for any PSC. The four basic pillars to make up WHO PSC framework specifically are product selection, procurement, distribution and use. Procurement encompasses the process of enumerating supplies, selection of procurement method, to

management of contracts and tenders. Distribution includes stock control and inventory management. Various strategies have been outlined globally to attain the goal of NMP and pharmaceutical supply systems in providing the vital medicines and supplies to public with efficient costs. Improving supply chain and procurement system can also avoid shortages of supply that eventually lead to disruption treatment and effect to health outcomes (WHO 2015).

Although the supply of ICT is fully subsidised in Malaysia, it is unfortunate that there is still a considerable number of patients not on ICT (George 2001). Budget constraint, patient's compliance and accessibility particularly in rural area are some of the causes (Viprakasit *et al.* 2009). In any field including healthcare, efficiency and good governance in procurement are key to cost reduction and increase in productivity (Baghdadi-Sabeti and Serhan 2010).

A robust PSC management is vital as that leads to wastage and interruptions of supplies. In Malaysia, frequent medicine stock-outs oftentimes cause public dissatisfaction and ultimately cause disturbance in healthcare service delivery (Nasuruddin 2017). This paper aims to discuss on existing supply chain management of ICT in Malaysia and to explore ways for a more efficient and resource-saving measures to improve the current system.

This paper aims to address the following questions: (1) What is the current practice of PSC in Malaysia? and (2) Which pharmaceutical supply chain model type best fit for thalassaemia treatment in Malaysia? The approach to answer these questions would be by reviewing existing literatures, extracting the experiences of the countries implementations by looking at both strengths and weaknesses.

## **METHODS**

### **Search Process and Criteria**

The search strategy framework was developed based on the ECLIPSE model (Wildridge and Bell 2002). Search protocol was developed by Authors 1 and 2. The protocol was not registered externally. We searched databases that include PubMed, Emerald and Scopus. There were no limiters placed on the document type and study design. Additional searches were also conducted based on review of bibliographies from the publications. Google Scholar search engine was also used to find articles related to the included publications.

### **Study Selection and Eligibility Criteria**

After search was conducted, all records retrieved were exported to Endnote (version X7) software. All titles were reviewed for relevance and articles with irrelevant titles were sensibly removed. Abstracts and when appropriate, full articles were evaluated to determine the applicability to this review. Searches was generally conducted in general manner to give the overview on PSC particularly the procurement and inventory system but later was narrowed down to better describe local Malaysian practice.

Electronic databases including PubMed, Emerald, Scopus and ScienceDirect were searched for related literatures with keywords (procurement OR purchasing OR supply) AND (decentraliz\* OR centraliz\*) AND (drug\* OR medicine\* OR pharmaceutical\* OR healthcare) AND (public OR government) AND (inventory management OR inventory model OR inventory management model). Searches were also conducted for grey

literatures like Malaysia government reports and local standard operating procedures as well as in Google Scholar. This is because of the lack of academic publication describing Malaysia pharmaceutical supply chain.

## Data Analysis

Many of references included in this review does not use experimental design, therefore, statistical pooling of data could not be conducted. Alternately, data extracted for this review were summarised qualitatively to answer the objective of this paper.

## RESULTS

The literature search yielded a total of 5,133 articles. After eliminating duplicates with Endnote and also manually, 4,957 articles were screened by titles and abstract. From this, 4,880 articles were excluded from review due to irrelevancy. Full texts of 77 articles were then reviewed to evaluate relevance. Later, 26 articles fulfil the inclusion and exclusion criteria and thus, included in this review. It is interesting to note the lack of local Malaysian related publication related to this topic. Only three literatures are available describing the nature of healthcare system and pharmaceutical supply chain in Malaysia with two of those are government reports.

From all the articles reviewed, 21 described the procurement method, where one is a systematic review discussing specifically on cost effect of procurement (Seidman and Atun 2017) and eight are review papers (Huff-Rousselle 2012; Homedes and Ugalde 2006; Rob *et al.* 2002; Sorte Junior 2012; Barber *et al.*, 2013; Millington and Bhardwaj 2017; Yip and Hanson 2009; Kastanioti *et al.* 2013). Six of the articles report original data adopting qualitative or mixed method in their studies (Tsofa *et al.* 2017; Bossert, Bowser and Amenyah 2007; Chaudhury *et al.* 2005; Magadzire *et al.* 2017; Iqbal, Geer and Dar 2016; Frumence *et al.* 2014). The remaining eight reviewed and analysed existing documents (Baldi and Vannoni 2015; Chokshi *et al.* 2015; Selvaraj *et al.* 2014; Yang, Huang and Liu 2017; Li *et al.* 2013; He *et al.* 2018; Callea *et al.* 2017; Sharma and Gupta 2014).

Six of the articles focuses on procurement methods. Various methods and systems of pharmaceutical supply system exists, such as centralised and decentralised systems, and each system has its own advantages and disadvantages. It is found that centralised procurement has the best potential to be cost-saving by means of economies of scale and increased purchasing power, and centralised tendering (Seidman and Atun 2017). This is also evident in countries like China, Guatemala, India and Italy (Yip and Hanson 2009; Chokshi *et al.* 2015; Bossert, Bowser and Amenyah 2007; Baldi and Vannoni 2015). With economies of scale, centralised procurement was able to purchase drugs or medical supplies at reduced price as procurer would have higher purchasing power and stronger negotiating power, better efficiency in purchasing flow as all are done by a systematic centralised unit. Apart from reduction of drug or medical supply's prices, operation costs and expenses can also be decreased (Kastanioti *et al.* 2013).

Search also yielded articles describing inventory management models in PSC. Five common models applied in PSC includes central medical stores (CMS), autonomous supply agency (ASA), direct delivery system, primary distributor system and primarily private system (Mustaffa and Potter 2009; Cachon and Fisher 2000). Primarily private system is where private pharmacies supplies medicines to patients in public sector. Both CMS and ASA models use centralised bulk purchasing, however, they differ in regards of distribution. In CMS, pharmaceuticals are distributed by a centralised body whereas in

ASA, there is separate autonomous or semi-autonomous supply agency. In direct delivery system, selection of supplier and prices are determined by government through tenders, but medicines are supplied directly to each facility by suppliers. In primary distributor system, there is separate contract negotiation with supplier and different primary distributors (Embrey 2013; Uthayakumar and Priyan 2013; Cachon and Fisher 2000).

Several inventory systems that are widely used in healthcare include Just-In-Time (JIT), stockless, Vendor-Managed Inventory (VMI) and Co-Managed Inventory (CMI) (Wilson, Cunningham and Westbrook 1992). Stockless system refers to having zero inventory on site. JIT and stockless approaches, both representing 'pull' inventory system, are first undertaken to lessen the supply chain costs and upgrade the customer service (Kowalski 1986). VMI/CMI are based on the principle of stockless system, whereby, the task of controlling stock is transferred to supplier while ordering process remain automated. The supplier in VMI will fully assume the role of determining inventory replenishment for the hospital while it is a joint responsibility in CMI.

## DISCUSSION

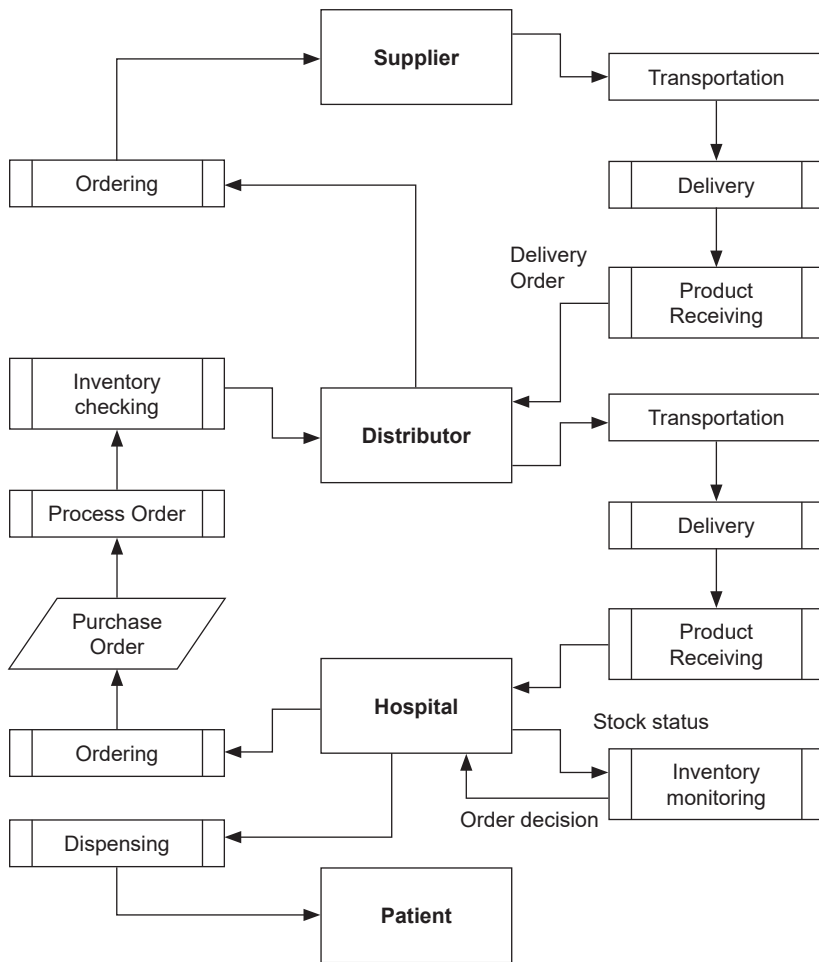
Malaysian public hospitals are generally categorised into specialists and non-specialists. Specialist hospitals are further divided into state, major and minor hospitals as shown in Table 1. Specialist hospitals have more comprehensive infrastructure, bigger manpower and more funding as compared to non-specialist hospitals. Among the specialist hospitals, state hospitals become the referral centre as they have more subspecialty services. In practice, the clinical management of thalassaemia patient and prescription of ICT is reviewed by haematology sub-specialist, resident or visiting depending on the treatment setting (Jaafar *et al.* 2013).

**Table 1:** Public hospital types in Ministry of Health Malaysia

Type		Specialty services
Specialists	State	<ul style="list-style-type: none"> <li>Act as referral centres</li> <li>Have at least 15 resident specialist and subspecialty services</li> </ul>
	Major	<ul style="list-style-type: none"> <li>Hospitals with multiple specialties also at least 15 resident specialist services</li> </ul>
	Minor	<ul style="list-style-type: none"> <li>Minimum of 8 basic specialist services (general medicine, general surgery, paediatrics, orthopaedics, obstetrics &amp; gynaecology and anaesthesiology)</li> </ul>
Non-Specialist	District hospitals	<ul style="list-style-type: none"> <li>No resident specialists but have visiting specialists in regular sessions</li> <li>Complex cases with be referred to specialist hospitals for further management</li> </ul>

PSC in Malaysian public hospitals functions at three different levels (Figure 1). Level 1 consists of the manufacturer or supplier, level 2 the wholesaler or distributor and the third level includes the provider supplying medicines to patients (Malaysia Competition Commission 2017). The Ministry of Health Pharmaceutical Services Programme (PSP) manages pharmaceuticals procurement in public hospitals. Pharmaceuticals are purchased

through national central tender and concessions, where procurement is centralised or through local purchasing using quotations for items of small volumes consumption. All central tenders are negotiated by the Procurement and Privatisation Division under PSP. Decentralisation occurs further downstream in the PSC where local health establishments or smaller hospitals, also called autonomy centre (AC), will autonomously purchase and manage inventory of the pharmaceuticals with allocated funds from ministry (Jaafar *et al.* 2013).



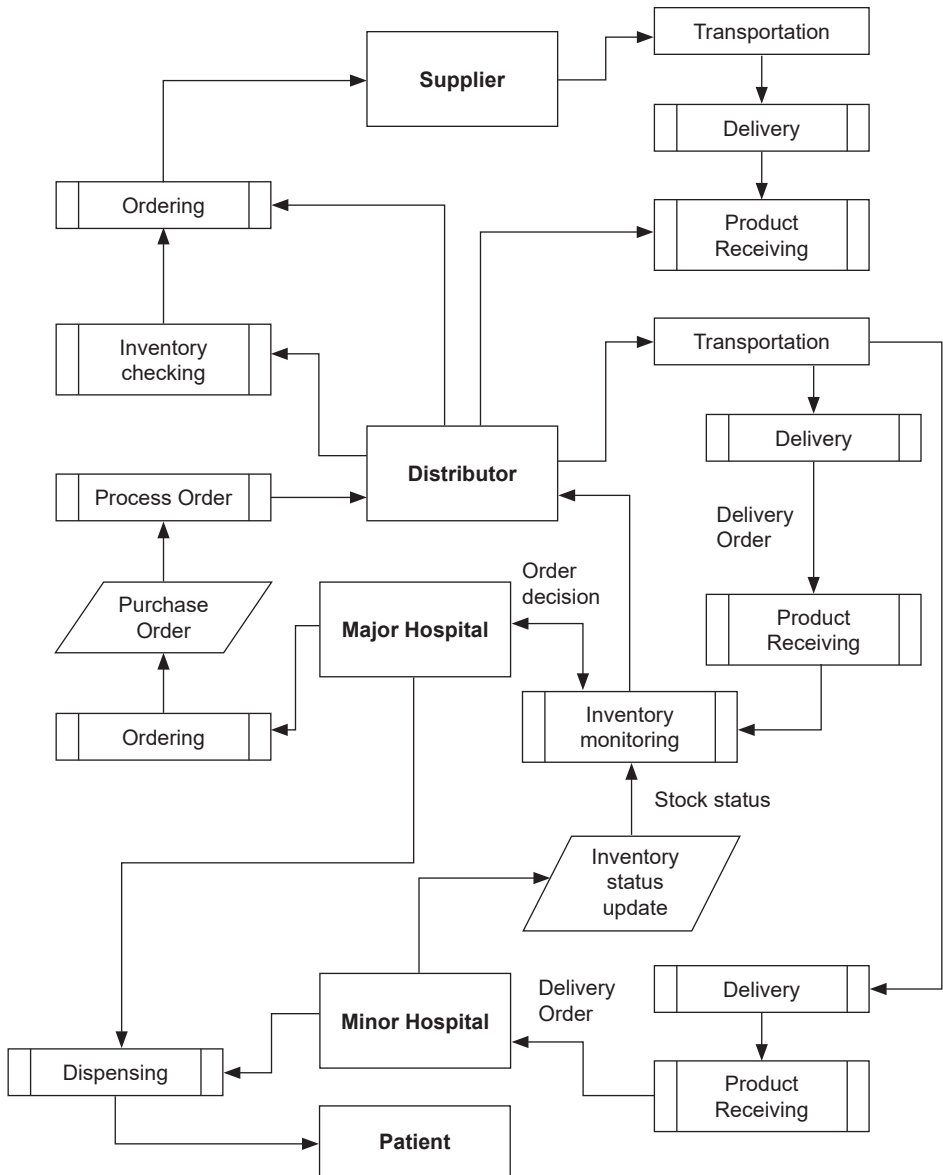
**Figure 1:** Flow chart of current supply management of ICT medicines in Malaysia.

Three types of ICT are available in Malaysia, namely DFO, DFP and DFX. All three types of ICT available in Malaysia are procured through centralised procurement either central tender or concession. This is advantageous as economies of scale is exploited by centralised procurement. The bulk purchasing also reduces operational costs and the need for administrative activities. Decentralisation of purchasing and inventory

management requires each AC to have sufficient financing, equipped with adequate skilled personnel and suitable storage facilities for inventories when in fact most AC lacks these. In short, procurement of all ICT is centralised at ministerial level, however each hospital purchases ICT autonomously according to their self-usage. Once purchased by each health facility, inventory will then be self-managed at site of the facility.

VMI/CMI has potential to be applied as it brings about several benefits such as it will reduce the administrative tasks and costs at the hospital. Less amount of inventory will be advantageous to smaller hospitals having already numerous other types of inventory in stock. VMI/CMI also showed to improve information reliability and reduce error (Kim 2005; Cachon and Fisher 2000). As aforementioned, VMI/CMI are based on the principle of stockless system, the major difference is, the transfer of stock control is moved to the supplier while ordering process would remain automated (Mustaffa and Potter 2009). This collaboration by the reduction of inventory level and lessen order cycle and fill rates (Cachon and Fisher, 2000). VMI implementation, however, may be hindered by lack of trust in information sharing between hospital and supplier.

VMI/CMI would be suitable in setting for procurement and distribution of ICT for thalassaemia in Malaysia. Potential new flow integrating VMI/CMI in the current PSC is illustrated in Figure 2. Apart from thalassaemia being a chronic life-long condition, the fact that Malaysia has such substantial number of thalassaemic across the country makes VMI/CMI a distinct option to be implemented locally. Ideally, purchasing of ICT should be done by state hospitals as they have more comprehensively skilled manpower for IM and greater fund allocation. Smaller hospitals instead, would only be required to inform the state hospitals on its ICT usage and therefore receive ICT when needed as per usage directly from supplier. This system also allows for automated replenishment of ICTs in public hospitals without the need of managing inventory and further strain the budget allocation for smaller hospitals.



**Figure 2:** Flow chart of newly proposed VMI for supply management of ICT medicines in Malaysia.



## CONCLUSION

The ICT in Malaysia is supplied through central procurement but purchasing and inventory management are decentralised to each hospital. VMI could be implemented for more efficient and resource-saving measures in supply chain of the ICT.

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