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Pharmaceutical Policy in China

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Executive Summary

The Chinese pharmaceutical market is currently the second largest in the world, behind only the United States. The pharmaceutical sector is highly fragmented, with over 5000 domestic manufacturers in operation. Decision making is also highly fragmented, with provinces assuming regulatory and funding authority under a broader national framework. Significant variation in out-of-pocket payments and access to medicines is seen both across provinces and between urban and rural areas within China. Current challenges within the Chinese pharmaceutical sector include poor drug quality, weak protection of intellectual property, high levels of inappropriate prescribing, delayed access to innovative medicines and high out-of-pocket payments.

Over the past ten years, there have been a number of significant reforms within the Chinese pharmaceutical sector. Among other policy reforms, China has extended healthcare coverage to over 99% of the population, established an essential medicines list, implemented a zero mark-up policy in all primary care facilities and public hospitals, and has deregulated the pricing of off-patent medicines in order to bridge the gap between originator and generic products.

Recently, China announced their 13th Five Year plan which outlines six major tasks for the Chinese pharmaceutical sector:

1) Building a scientific and rational tiered medical service system
2) Implementing a scientific and effective modern hospital management system
3) Improving the efficiency of the universal basic medical insurance system
4) Streamlining the drug supply security system, that ensures full inventory and prioritizes use of essential medicines.
5) Establishing a stringent and streamlined regulatory system.
6) Carrying out reforms relevant to human resource capacity building and training, medical provision funding, and public health service infrastructure building.

As China continues to face fiscal challenges from an aging population and increases in non-communicable diseases, promoting efficiency within the pharmaceutical sector will become increasingly important. With the overall aim of establishing an overarching national pharmaceutical framework to help guide policy reform this report has 3-key objectives:

1) To undertake a mapping of the key trends and policy directions in China's health and pharmaceutical policy and benchmark these with similar trends from an international perspective;
2) To identify and propose several validated policy areas in China's health and pharmaceutical policy environment that merit in-depth research and analysis; and
3) To combine the above two objectives by highlighting the key international policy trends from which China could benefit

In order to map the key trends and policy directions in China's pharmaceutical system, an analytical framework was developed outlining the relationship between system- and micro-level policies and their role in promoting pharmaceutical policy objectives. Collectively, national pharmaceutical policy aims to promote several key objectives: access to medicines, quality of medicines, efficiency in resource allocation, and rational use of medicines, while maintaining a

budgetary constraint (macroeconomic efficiency). At the system level, key functions include: 1) gatekeeping through regulatory agencies and 2) budget setting through control of overall pharmaceutical expenditure. System level policies are critical for ensuring safety and efficacy of medicines entering the pharmaceutical system and for controlling macroeconomic efficiency to ensure the health system as a whole is sustainable. Micro-level policies can be broadly divided into supply-side policies, including pricing, reimbursement and procurement and demand-side policies that target either prescribers or patients including formularies, clinical guidelines, and cost sharing. Mapping of pharmaceutical policy and trends requires consideration of not only the direct impact of a policy on pharmaceutical policy objectives, but also on the relationship between system and micro-level policies in promoting those objectives.

This report relies on both secondary and primary data. An extensive literature review was performed via PubMed, Web of Science, and EconLit to identify peer-review literature assessing the impact of demand and supply side policies on one of the following research endpoints: access to medicines, quality of medicines, rational use of medicines, macroeconomic efficiency, or microeconomic efficiency. Peer review literature was supplemented with grey literature was retrieved from national and state level sources, social health insurance and private health insurance reports, and primary health care and hospital care reports. Primary data was collected through semi-structured interviews with experts and key opinion leaders in health pharmaceutical policy in China. Interviews were performed with the aim of corroborating and updating evidence from secondary data sources, to reveal major gaps in pharmaceutical policy, to offer insights on possible ways to address these gaps and to establish a list of policy initiatives moving forward.

A total of 151 articles/reports were included in the comprehensive literature review, fifty-two English sources and ninety-eight Chinese sources. A total of 13 semi-structured interviews were performed, included 8 leading academics in Chinese health and pharmaceutical policy, 1 person in a health policy-making position at a municipal government, 1 person in a pharmacy director position from a major hospital, 1 person in a marketing director position from a major pharmaceutical company, 1 person in a manager position at a hospital-based research centre, and 1 person in a regional director position at a health-promotion foundation. In addition, insights were also drawn upon through short and informal exchanges with 10 participants at a high-profile conference hosted by a top university in China.

On the supply-side, trends and policy reforms were discussed relating to drug innovation, drug approval, drug pricing, drug procurement, and health technology assessment. On the demand-side, trends and policy reforms were discussed relating to formularies, drug distribution, prospective payment models, generic substitution, clinical guidelines, disease specific initiatives, cost-sharing, and patient education.

Despite being the second largest pharmaceutical market in the world, China lags behind other countries in terms of drug innovation. Weak intellectual property protection and slow drug approval are key barriers to promotion of research and development. Relative to other regulatory agencies globally, China employs low number of technical reviews and has high median time for approval. Within the 13th FYP, China has indicated a priority will be to accelerate innovation and access to new drugs in the areas of oncology, major infectious diseases, nervous system and mental diseases, chronic disease, and orphan diseases. Monoclonal Antibodies (mAb), protein and peptide based biotech drugs, therapeutic vaccines, and biotherapeutics based on RNA, SELEX and CAR-T technologies are likely to be prioritised for accelerated access. Further, the State Council hopes to encourage local research and development by offering accelerated regulatory approval for domestically produced products.

The national medical products administration (formally the CFDA) is the regulatory agency for drug safety. Historically, NMPA standard for drug approval and regulation have been weak, leading to mistrust over domestically produced medicines. In 2016, China overhauled its equivalence testing process for generic medicines, by making regulations more closely aligned

with international standards. This reform requires all products approved prior to October 2007 to renew their license with a comparative study prior to 2018. A secondary aim of the reform was to clear all drug application backlogs. Despite stringent deadlines, the process was slower than intended. By April 2019 only 239 drugs out of the 685 listed on the Essential Medicines List had passed bio-equivalence tests. Beyond reforming generic drug approval, the NMPA has also introduced a priority review process to streamline approval innovative drugs for HIV/AIDS, cancer, major chronic diseases, orphan disease and for products with high potential economic impact. Further a new conditional approval process will provide early approval for products indicated for serious, life threatening conditions or for serious unmet medical needs on the basis of early or mid-stage clinical data.

All products on reimbursed drug lists within China, including generic products, off-patent originator products and in-patent medicines, are subject to pricing regulation at national and provincial level. The primary mechanism for pricing off-patent and generic medicines on the national reimbursed drugs list is provincial tendering. Provinces issue tenders for to manufacturers for the right supply a drug to healthcare facilities. The winning bid represents the reimbursement price for a product within that province. Historically, many provinces employed separate tenders for off-patent originator products and generic products, under the assumption that generic products were of lower products. Originator products were granted preferential pricing and maintained a price monopoly over generic products. Recently the State council reformed the provincial tendering process requiring that tenders are issued by molecule name, eliminating the possibility for preferential pricing. In-patent products are priced through direct negotiation at either national or provincial level although this process has not been formalized. Historically, new products had to wait upwards of 3 to 4 years for revisions to the NRDL before being eligible for reimbursement. A recent negotiations pilot at national level reached agreement on price for 36 out 44 products and these were subsequently added to the NRDL. However the process remains opaque and requires formalization. While progress has been made, China still requires a systematic approach to pricing and reimbursement of expensive and innovative medicines.

Provincial tendering sets the reimbursement price of medicines but is currently not directly linked to procurement. Hospitals procure products directly from manufacturers and wholesalers and often engage in secondary negotiation to obtain additional rebates. Meanwhile, provinces procure products directly from manufacturers for primary care facilities. While secondary negotiation lowers the effective cost of a medicine and provides hospitals with more revenue, concerns emerge that this creates distorted incentives overprescribe medicines with higher rebates. However the extent to which secondary negotiation contributes to inappropriate prescribing remains unclear. Recent pilots have explored joint procurement of medicines through cross-province/cross-municipality group purchasing organizations in order to achieve lower prices. One possible way forward is to issue tenders with a fixed commitment of procurement quantities in order to eliminate the possibility of secondary negotiations.

In October 2018, China established the National Pharmaceutical and Health Technology Assessment center. Currently, HTA is not formally utilized for decision making on the pricing and reimbursement of pharmaceutical products in China. Uses of HTA have been predominantly academic. The negotiation pilot in 2016 represented the first instance of dossier submission for the pricing and reimbursement of medicines, however no formal guidelines were available on evidence requirements, assessment criteria, and assessment timelines. Nevertheless, the establishment of national pharmaceutical and HTA center represent the first steps towards integrating HTA with decision making in China. The key challenge is to establish clear and specific pathways to include HTA as part of the policy-making process.

Following marketing authorization, products can be listed on two national formularies, the national reimbursed drug list (NRDL) or the Emergency Medicines List (EML). Provinces are able to modify the NRDL by up to 15% in order to establish their own provincial reimbursed drug lists (PRDL). Until recently, the NRDL was only updated every 3 to 4 years, and new drugs often had

to wait until a revision period to be added. Following the negotiation pilot, future adjustments to the list are likely to be more frequent and dynamic, although cost-containment will remain a long-term focal point for pharmaceutical policy. Advancements in gene-based therapies and cell technologies will pose significant challenges from a financing perspective. The essential medicines list (EML) was established as part of the 2009 health system reforms in an effort to achieve universal coverage in China. Drugs on the EML are fully reimbursed for all patients in China, and a zero mark-up policy is present to prevent hospital mark-ups. Historically, hospitals in China received significant parts of their revenue from drug sales and applied mark-ups of up to 15% on all pharmaceuticals. This contributed to China's high levels of inappropriate prescribing as hospitals overprescribed medicines in order to maximize revenue. The Essential Medicines List and zero mark-up policy resulted in significant reductions in inappropriate prescribing, and improved availability of essential medicines in primary health facilities. However, hospitals began to rely more heavily on other healthcare services to compensate for lost revenue and drug shortages of emergency medicines remains an issue.

Historically, the drug distribution and supply chain in China was extremely fragmented, with several layers of wholesalers applying mark-ups along the supply chain. This contributed to the relatively high price of medicines within China. In 2016, a "dual-invoice" policy was launched, limiting the number of distributors in the supply chain between manufacturer and hospital to one. Further, both the manufacturer and distributor are required to provide invoices reporting sale-prices. However, expert interviews suggest that this policy may do little to lower drug prices on its own. It does not address the fundamental issue that hospitals have an economic incentive to profit from drug sales, thus many demand under-the-table rebates for allowing drugs to enter the hospital.

Currently, health care facilities across China are reimbursed retrospectively for the services they provide, in what is typically referred to as a fee-for-service payment model. Insufficient government funding, has led medical departments to set specific revenue targets, thereby incentivizing doctors to overprovide health services. China has explored the use of prospective payment models such as capitation, global budget, or salary models in a number of pilot studies. By decoupling physician income from the services they provide, prospective payment systems discourage overprescribing. In general PPS systems successfully reduced expensive and unnecessary prescriptions. However, some evidence emerges of cost-shifting from low to high level services, suggesting that some physicians may be passing on expensive patients to higher level services. As part of the 2017 healthcare reform policy, the state council announced intentions to reform the basic medical insurance payment model to a prospective system however the timeline to implementation remains unclear. Differences in the way health care providers code diagnoses and in the electronic health record systems implemented across healthcare facilities pose a barrier to the introduction of a universal prospective payment system.

China has had generic substitution policy in place since 2007, however there has been very little enforcement of the policy, likely due to issues in trust over the quality of generic medicines. While physicians are required to prescribe by International Nonproprietary Name (INN) they typically indicate the desired brand name as well. Studies show that generic utilization is as low as 20-34% in some disease areas, resulting in a substantial loss of potential savings. While improvements in bioequivalence testing will help to improve the quality of domestically produced products, more targeted efforts will likely be needed to overcome public mistrust of generics.

Historically, the use of clinical guidelines in China has been highly variable. China is unique in its use of both Western medicine and traditional Chinese medicines. Guidelines must be able to help provider employ evidence based decision making across both types of medicines. The quality of Chinese guidelines is typically lower than those from other developed countries, with significantly fewer overall citations and fewer Cochrane review citations. Feedback from interviewees suggest many of these guidelines are based on consensus and lack scientific rigour. Adherence to guidelines generally is much lower among low-tier healthcare providers due to lack of awareness. Improvements in the quality and implementation of clinical guidelines in China will require a

coordinated and systematic approach. National standards should be established for guideline methodology, quality, and implementation in order to promote effective dissemination and adherence.

China has been successful in employing targeted disease specific initiatives to reducing inappropriate prescribing. Prior to 2010, percentage of prescriptions with antibiotic prescribed and levels of antibiotic polypharmacy were well above WHO recommended levels. In 2011, The Chinese government implemented a National Action Plan for Antibiotic Stewardship. Under the action plan, antibiotics were categorized and usage of controlled antibiotics was restricted to higher level hospitals. Chief administrators of hospitals were made accountable for patient outcomes and efficiency surrounding antibiotic use with penalties employed in cases of inappropriate prescribing. The plan was associated with significant reductions in total costs and volume of antibiotic use. Other targeted initiatives have taken poverty alleviation into consideration in an attempt to remove barriers in access to care and promote better disease management in patients with chronic conditions.

In the year 2000, only 15% of the population in China was covered under health insurance, and for most, utilisation of health services was often associated with catastrophic expenditure. As part of the 2009 healthcare reforms, the Chinese government committed an additional USD 124 billion in public spending over three years in order to expand population coverage, through one of the three main health insurance schemes, with the aim of covering 90% of premiums for poor families and 70% of premiums in wealthier coastal regions. Further, complimentary medical assistance programmes were established to cover the remaining out-of-pocket fees for particularly poor families. Expansions in coverage resulted in significant increases in the use of healthcare, particularly in in poor families. Despite increases in utilization, out-of-pocket payments remain high, as patients in the NCMS or URBMI still paid upwards of 50% of their costs for outpatient and inpatient services due to reimbursement ceilings.

One of the key contributing factors to irrational use of medicines in China is patient health literacy, particularly surrounding the use of antibiotics, injectable, and generic products Prevailing attitudes around these products are that antibiotics are a cure-all, that injectable have improved efficacy over orally administered drugs, and that generic products, particularly low-priced generic products, are inferior to branded medicines. While physicians are often in a position to prescribe appropriately, patient demand often influences prescribing behavior. Targeted health literacy programmes and patient education programmes are needed to overcome issues in inappropriate antibiotic use and the inefficiencies caused by poor generic utilization. Beyond improving appropriate prescribing, patient education can also play a critical role in management of chronic diseases by improving patient self-care and reducing acute exacerbations of disease.

Overall, China has made substantial progress in improving its health system in a short period of time; most notably, it has achieved near-universal coverage of health insurance, it has established the EML and it has lowered prices for these drugs. Nonetheless, many challenges still exist in the Chinese pharmaceutical sector, from R&D, to manufacturing, distribution, and dispensing of drugs on the supply side, and irrational prescription and use on the demand side. Based on the present review, current priority areas for reform include HTA and negotiations, pharmaceutical pricing, generic policy, healthcare provider payment models and healthcare financing and primary care.

First, as China faces growing fiscal pressure from an aging population and increases in non-communicable diseases, the use of health technology assessment is likely to play a critical role in the promotion of rational use of medicines. To this end, the piloted negotiation process requires formalization through legislation with clarity on submission processes and requirements, product eligibility, types of evidence considered, and evaluation processes and timelines. Second, While the goal may ultimately be to move towards an evidence-based system with HTA

and pricing negotiations for innovative and expensive products, external reference pricing can provide a reasonable stop-gap until capacity in this area is built. Improvements are also needed in the pricing system for originator and generic products which are largely undermined by poor utilization of generic products. Switching from a fixed percentage reimbursement rate model to a tiered-co-payment model with full reimbursement for generics (set based on internal reference pricing), will likely help to alleviate some of these issues. Third, despite recent reforms in regulatory approval of generic medicines, the process has been time-intensive and opaque. More resources are required to strengthen the review team, and improved coordination with regulatory authorities is needed. Improving local generic quality will not only improve utilization domestically, but will also provide greater opportunities in international markets. Fourth, despite implementation of the zero mark-up policy, rates of over-prescribing and inappropriate prescribing, particularly in the context of antibiotics and injections, remain high relative to WHO recommendations for low and middle income countries. Distorted financial incentives from a retrospective payment model plays a key role in inappropriate prescribing. Greater implementation of prospective payment systems throughout China may help to further reduce irrational prescribing, however careful monitoring is needed to ensure quality of services does not decline. Finally, problems persist in funding healthcare following the 2009 health reforms. Removal of income from mark-ups has not been adequately replaced through government subsidies. Increases in government subsidies and financing and strengthening of the weak rural healthcare system will also be required to address shortages in physician income structure. Boosting the primary care quality, particularly through training workforce and attracting talent to primary care institutions, will gradually change patients' perception of poor care quality associated with these healthcare facilities and encourage them to utilize community healthcare resources more efficiently.

List of abbreviations

AIDS	Acquired Immunodeficiency Syndrome
CAR-T	Chimeric Antigen Receptor T cell
CIF	Cost Insurance and Freight
CFDA	China Food and Drug Administration
CNIPA	China National Intellectual Property Administration
CDA	China Drug Administration
EML	Essential Medicines List
EMA	European Medicine Agency
FDA	Food and Drug Administration
FYP	Five Year Plan
HIV	Human Immunodeficiency Virus
INN	International Nonproprietary Name
mAB	Monoclonal Antibody
MHRSS	Ministry of Human Resources and Social Security
MIIT	Ministry of Industry and Information Technology
M&A	Mergers and Acquisitions
MoH	Ministry of Health
NEMP	National Essential Medicines Policy
NHC	National Health Commission
NHFPC	National Health and Family Planning Committee
NMPA	National Medical Products Administration
NRCMS	New Rural Cooperative Medical Scheme
NDRC	National Development Research Council
NRDL	National Reimbursed Drug List
OECD	Organisation of Economic Co-operation and Development
R&D	Research and Development
RNA	Ribonucleic Acid
SELEX	Systematic Evolutions of Ligands by Exponential Enrichment
SFDA	State Food and Drug Administration
SMIA	State Medical Insurance Administration
SAMR	State Administration for Market Regulation
TCM	Traditional Chinese Medicines
THE	Total Health Expenditure
UEBMI	Urban Employee Basic Medical Insurance
URBMI	Urban Resident Basic Medical Insurance
US	United States
ZMU	Zero mark-up

1. Introduction

This report provides an assessment of the current challenges and opportunities facing the Chinese pharmaceutical sector. The Chinese pharmaceutical market is the second largest in the world, behind only the United States. China routinely spends nearly 40% of their health expenditure on pharmaceuticals, which is substantially higher than the OECD average of 19%. The Chinese pharmaceutical sector is highly fragmented with over 5000 domestic manufacturers in operation. The top 5 pharmaceutical manufacturers within China account for less than 15% of the market, a value far below what is typically seen in developed countries (Mossialos et al. 2016). Pharmaceutical regulatory authority is also highly fragmented within China, as provinces are given authority to establish their own provincial reimbursed drugs list according to the national formulary and are responsible for drug pricing through provincial tenders. As result, significant variation is seen across provinces in terms of out-of-pocket payments and patient access to medicines (Huang et al. 2018).

There have been a number of significant pharmaceutical sector reforms in the past ten years following the pivotal 2009 heath care reforms. Over the past decade, and among other policy reforms, China has extended healthcare coverage to over 99% of the population, established an essential medicines list, implemented a zero mark-up policy in all primary care facilities and public hospitals, and has deregulated the pricing of off-patent medicines in order to bridge the gap between originator and generic products. Further, China has also reformed their regulatory system, by bringing bioequivalence requirements close to international standards and through introduction of an expedited approval pathway (Sun et al. 2018).

Currently, China is midway through their 13th Five Year Plan for Healthcare reform (2016-2020). The 13th Five Year Plan aims to promote fair access to basic medical services, to improve primary healthcare infrastructure, and to coordinate healthcare form of medical services, health insurance and the pharmaceutical sector (Multiple Ministries 2016). In pursuit of these goals, the plan outlines six major tasks:

1) Building a scientific and rational tiered medical service system
2) Implementing a scientific and effective modern hospital management system
3) Improving the efficiency of the universal basic medical insurance system
4) Streamlining the drug supply security system, that ensures full inventory and prioritizes use of essential medicines.
5) Establishing a stringent and streamlined regulatory system.
6) Carrying out reforms relevant to human resource capacity building and training, medical provision funding, and public health service infrastructure building.

Despite recent reforms, a number of outstanding issues remain within the Chinese pharmaceutical sector including poor drug quality, high levels of inappropriate prescribing, and high out-of-pocket payments for medicines. Further, new medicines have often faced substantial delays in regulatory approval due to application backlog and must often wait years for inclusion on the national reimbursed drug list, which historically has only been reviewed every 4 to 5 years (Mossialos et al. 2016, Sun et al. 2018).

Moving forward, an aging population and increase in the incidence of non-communicable disease will put increasing fiscal pressure on the Chinese healthcare system. Promoting efficiency within the pharmaceutical sector will undoubtedly become increasingly important as China continues to strive for equal access to effective medicines. Effective pharmaceutical reform will require concerted action across all stakeholders, including government, providers, patients and industry. An overarching national pharmaceutical framework could be very helpful in achieving coordinated reform.

With an overall aim of establishing an overarching national pharmaceutical framework, from both a supply- and demand-side, this report has 3 key objectives:

1) To undertake a mapping of the key trends and policy directions in China's health and pharmaceutical policy and benchmark these with similar trends from an international perspective;
2) To identify and propose several validated policy areas in China's health and pharmaceutical policy environment that merit in-depth research and analysis; and
3) To combine the above two objectives by highlighting the key international policy trends from which China could benefit.

2. Materials and Methods

2.1. Analytical Framework

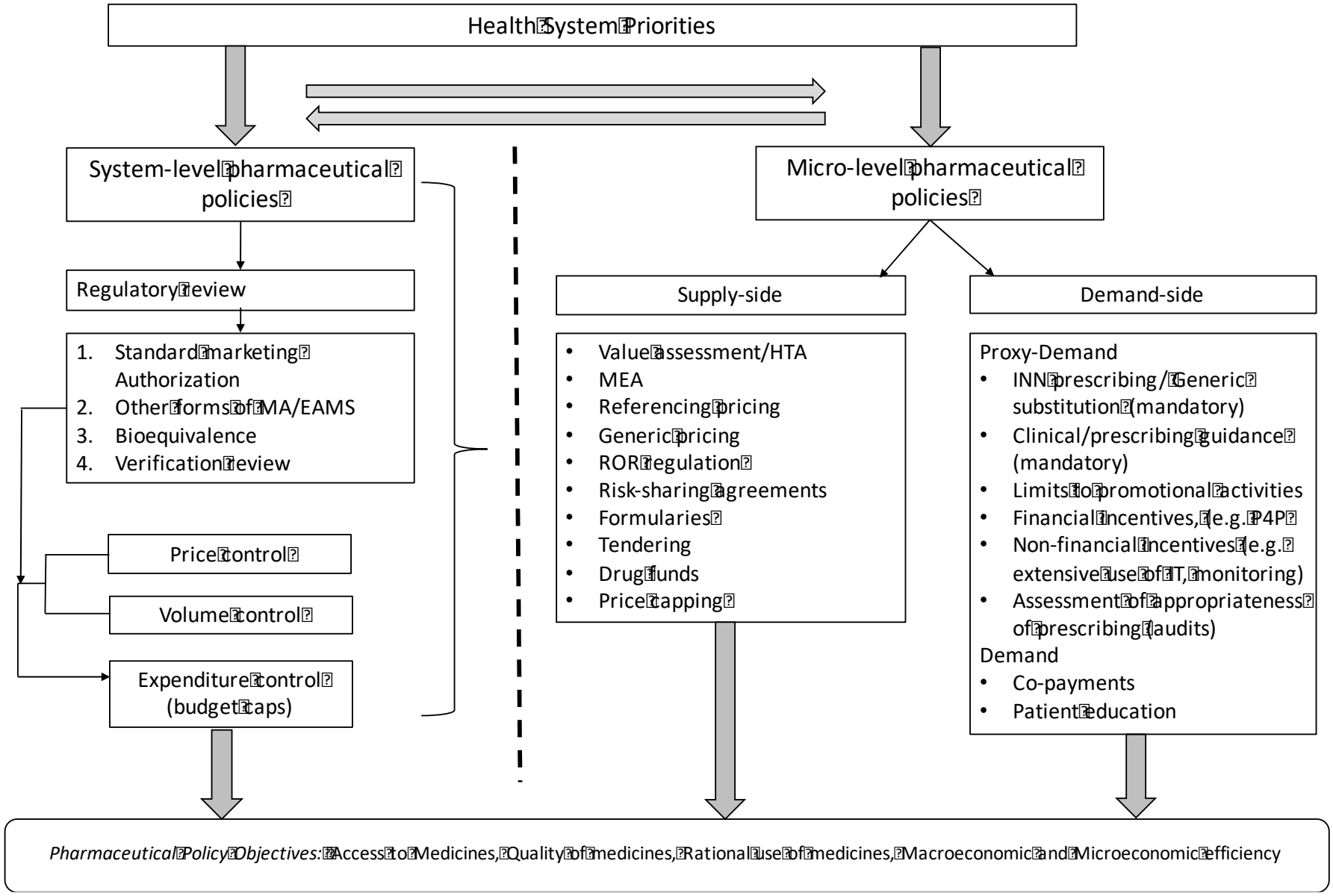
In order to map the key trends and policy directions in China's pharmaceutical system, an analytical framework was developed outlining the relationship between system- and micro-level policies. Collectively, national pharmaceutical policy aims at promoting several key objectives: access to medicines, quality of medicines, improving efficiency in resource allocation and rational use of medicines, whilst observing a budgetary constraint (macroeconomic efficiency). Access to medicines refers to the promotion of equitable access to a wide-range of essential medicines. Access is typically considered in terms of both affordability (e.g. levels of co-payments) and in terms of availability (e.g. inclusion on formularies). Beyond access, national pharmaceutical policy aims to ensure that medicines are safe, efficacious and produced with high quality. Finally, rational use of medicines aims to ensure efficient use of pharmaceutical resources and appropriate use of medicines (e.g. avoiding unnecessary and potentially harmful prescriptions). Improving efficiency in resource allocation is also an important policy goal and relates to the issue of value assessment for new medicines (and their use) as well as the likely trade-offs between using branded and generic medicines, where the latter exist.

At the system level, regulatory agencies serve as a gatekeeper to the pharmaceutical market, with important implications for both access to and quality of medicines. Through regulatory review and bioequivalence testing, standards are placed to ensure the efficacy and safety of medicines, prior to routine use within the pharmaceutical system. As a gatekeeper, regulatory agencies also dictate the timeliness of access to new medicines. Several regulatory agencies, such as the Food and Drug Administration (FDA) and the European Medicine Agency (EMA), employ Early Access to Medicines Schemes (EAMS) to accelerate the review time or development time for medicines that address an unmet medical need. Effective regulatory policy must balance the need to ensure quality of medicines with timely access.

System level pharmaceutical policy may also determine the total levels of pharmaceutical expenditure. While cost-containment is not a key pharmaceutical policy objective in its own right, it can play a key role in the macroeconomic efficiency of the health system as a whole. Unsustainable growth in pharmaceutical expenditure may divert resources away from other health system inputs, such as hospitals and doctors, to the detriment of patients who rely on these services. Many health systems apply budget caps to ensure that pharmaceutical expenditure is both sustainable and predictable. Pharmaceutical expenditure can be further controlled through micro-level policies that target either the price or volume of pharmaceuticals prescribed, including tendering, reference pricing, price cuts, financial incentives, generic substitution and use of co-payments. Broadly-speaking these policies can be divided into supply- and demand-side policies. Supply-side policies relate to the pricing, reimbursement and procurement of pharmaceuticals. Demand-side policies are further divided into (a) proxy-demand policies, which target prescribers through promoting appropriate prescribing, and the distribution chain, relating to the dispensing of medicines and the incentives that shape behaviour; and (b) demand policies, which target patients with the aim of encouraging appropriate use, including cost-sharing as a tool to shape behaviour.

Overall, mapping of pharmaceutical policy and trends requires careful consideration of the relationship between macro- and micro-level policies and of their role in promoting key pharmaceutical policy objectives. Assessment of both macro- and micro-level pharmaceutical policies aims to identify outstanding gaps and areas for future reform.

Figure 1. Analytical Framework



2.2. Secondary Data Collection

An extensive literature review was performed in order to supplement and update a 2016 LSE Health report on the Chinese pharmaceutical system (Mossialos et al. 2016). The following databases were searched for peer-reviewed literature: *PubMed (*search limited to papers including the keywords in title or abstract, use of subject heading (MSH) search); *Web of Science* (includes also published conference abstracts), and *EconLit*. Grey literature was retrieved from national and state level sources, social health insurance and private health insurance reports, and primary health care and hospital care reports. The literature review was limited to articles published between 01/01/2015 and 01/09/2018 and to articles published in either English or Chinese. Table 1 provides the research endpoints.

Combinations of the following terms were used to identify relevant studies or reports: "HTA" OR "Health Technology Assessment" OR "MEA" OR "Marketing Authorisation" OR "Bio-equivalence" OR "Bioequivalence" OR "Referencing Pricing" OR "Generic Pricing" OR "ROR Regulation" OR "Rate of Return Regulation" OR "Risk-sharing Agreements" OR "Formularies" OR "Tendering" OR "Drug Funds" OR "Price Capping" OR "Reimbursement Caps" OR "Drug Quality Regulation" OR "Price Controls" OR "Compassionate Use Programmes" OR " Early Access Programmes" OR " Priority Review" OR "Fast-track" OR "Traditional Chinese medicines" OR "Negotiations" "INN Prescribing" OR "Generic substitution" OR "generic prescribing" "clinical practice guidelines" OR "patient education" OR "marketing regulation" OR "promotional regulation" OR "financial incentives" OR "pay for performance" OR "co-payments" OR "non-financial incentives" OR "prescribing audits" OR "formulary management" OR "pharmacy remuneration" OR "pharmacy mark-ups" OR "cost-sharing" OR "e-prescribing" OR "IT for prescribing" OR "generic dispensing" AND "Pharmaceuticals" OR "Drugs" OR "Medicines" OR "Medicinal products" AND "China".

Table 1. Literature review endpoints

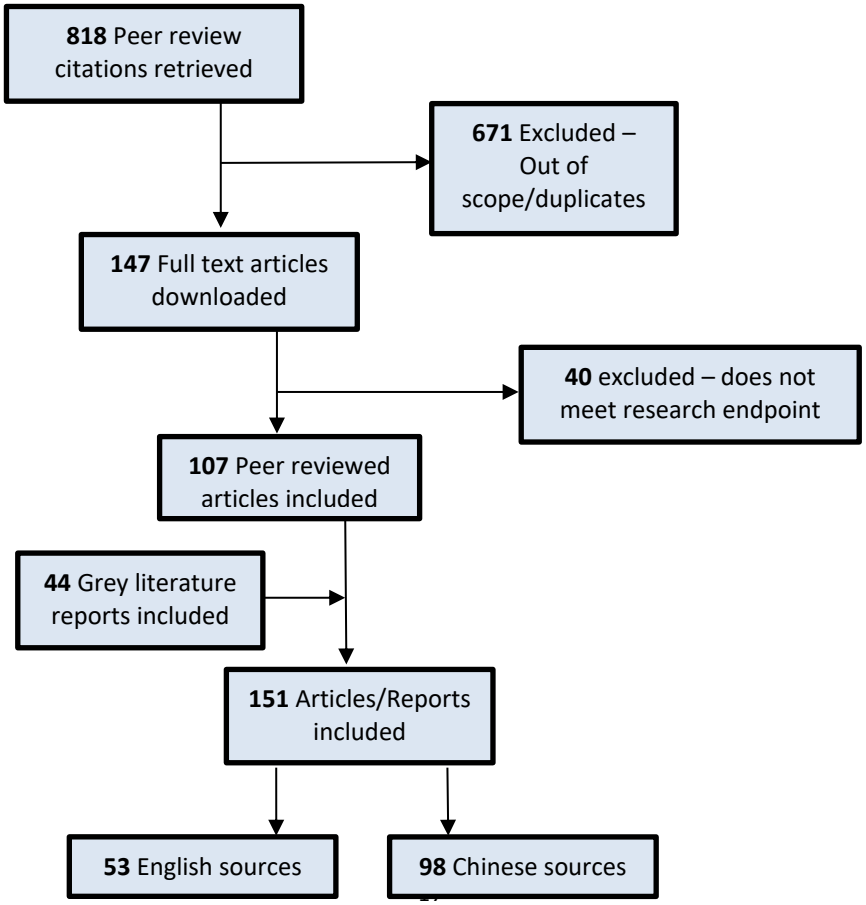
Research Endpoint	Description
Access to medicines	Access to medicines relates to both the availability and affordability of medicines. Studies outlining the implementation of policies which impact either the availability of medicines or affordability of medicines within China were included. Data was extracted on details of policy reform, impact on drug availability, impact on drug utilisation, and impact on out-of-pocket expenditure.
Quality of medicines	Quality of medicines refers to the provision of safe and efficacious medicines. Studies researching reforms to the standards of drug approval, drug manufacturing, and drug procurement within China were included. Data was extracted on details of policy reform and impact on drug quality.
Rational use of medicines	Rational use of medicines refers to the appropriate use of medicines. Studies relating to appropriate prescribing within China were included. Data was extracted on details of policy reform and impact on indicators of appropriate prescribing.

Macroeconomic efficiency/cost-containment	Macroeconomic efficiency relates to the ability of the pharmaceutical system to operate efficiently within the health system, subject to a budget constraint. Studies discussing reform relating to expenditure control within China were included. Data was extracted on details of policy reform, impact on pharmaceutical expenditure, and impact on health expenditure.
Microeconomic efficiency	Microeconomic efficiency refers to the efficient use of pharmaceutical resources. Studies discussing reforms on HTA, pricing and reimbursement of medicines, and generic policy within China were included in this endpoint. Data was extracted on details of policy reform, and impact on the drug price, drug volume, and health outcomes.

2.3. Results of Literature Review

Figure 2 outlines the total number of citations retrieved, excluded and included in the literature review. 817 peer-reviewed article citations were retrieved from PubMed, Web of Science, Google Scholar, and EconLit and reviewed for relevance to research endpoints. A total of 150 articles/reports were included: 106 from peer-reviewed literature and 44 from grey-literature.

Figure 2. Results of Comprehensive Literature Review on the Impact of Supply- and Demand-Side Pharmaceutical Policy in China



2.4. Primary data collection

The second stage of data collection involved obtaining primary data based on fieldwork in China. A series of semi-structured interviews were performed with stakeholders, experts and key opinion leaders (KOLs) in health and pharmaceutical policy in China, including leading academics on health and pharmaceutical policy, policy advisors in government think tanks, and stakeholders in leading hospitals and pharmaceutical companies.

The purpose of the primary data collection was fourfold. First, to corroborate and update existing evidence from the secondary data sources. Second, to reveal the major gaps in pharmaceutical policy and challenges for further reforms, as perceived by various stakeholders at different levels. To this end, interviewees were asked to provide evidence on key trends and priorities in Chinese health and pharmaceutical policy, including how international trends vs. carving its own pathway are likely to shape and impact future directions in Chinese pharmaceutical policy. Third to offer insights on ways to address these priorities in a sustainable manner. Finally, to establish a validated list of research activities and policy initiatives capable of addressing gaps in health and pharmaceutical policy in China.

The interviews were conducted in a semi-structured fashion. The questions broadly fall into five areas of pharmaceutical policy: drug approval, drug pricing and reimbursement, hospital management, primary health care, and health insurance. A questionnaire was constructed addressing recent policy initiatives, trends, gaps and challenges for future reform in these five domains. The questionnaire is found in Appendix A. Various combinations of questions were used according to the stakeholder's area of expertise. For instance, drug approval stakeholders were asked in-depth questions related to recent development in drug approval and major gaps in current standards, and related questions on drug pricing and reimbursement and health insurance, but not issues related to hospital management or primary health care.

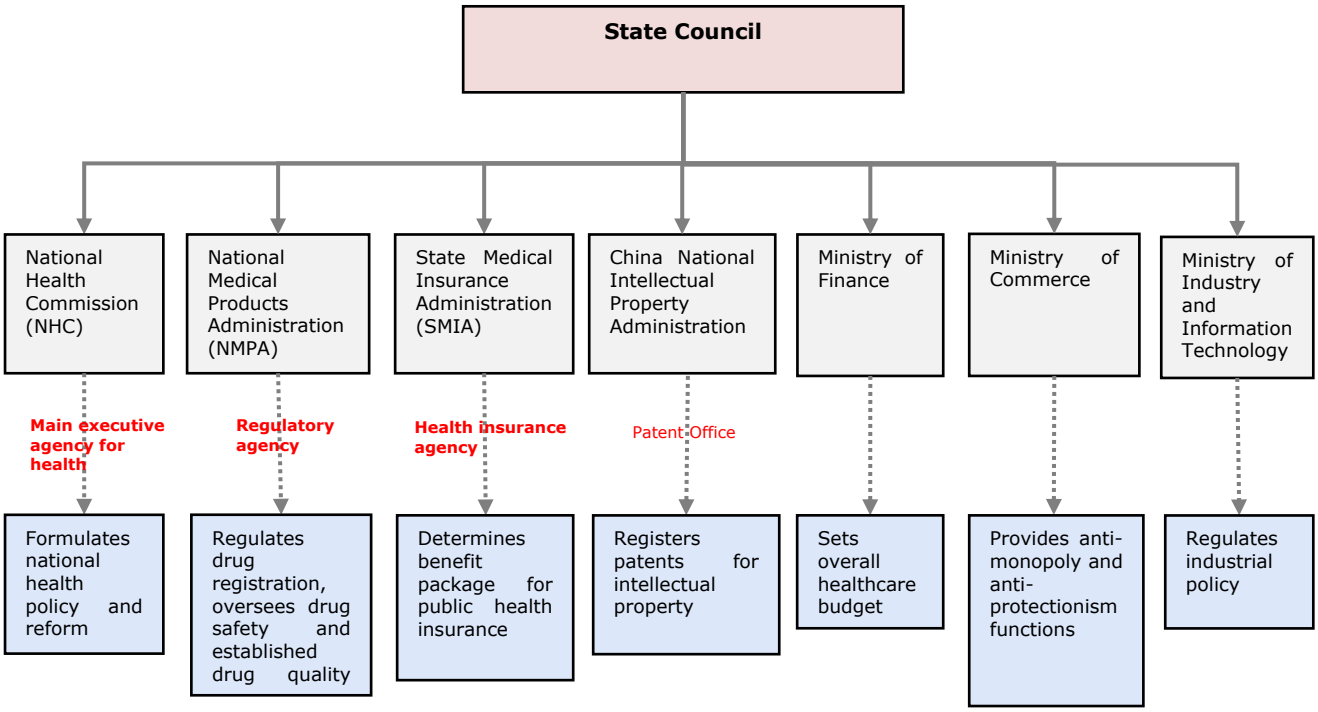
2.5. Summary of Interviews Performed

Primary data collection involved in-depth face-to-face formal interviews with 13 stakeholders from different backgrounds, each lasting 1-2 hours. Interviewees included 8 leading academics in Chinese health and pharmaceutical policy, 1 person in a health policy-making position at a municipal government, 1 person in a pharmacy director position from a major hospital, 1 person in a marketing director position from a major pharmaceutical company, 1 person in a manager position at a hospital-based research centre, and 1 person in a regional director position at a health-promotion foundation. In addition, insights were also drawn upon through short and informal exchanges with 10 participants at a high-profile conference hosted by a top university in China. These 10 conference participants included 5 people formerly or currently in government health policy positions at central, provincial, and peprfectual levels, and 5 academic experts in health and pharmaceutical policy.

3. Health System Governance and Pharmaceutical Regulatory Structure

Governance of the health system is led by the State Council, China's chief administrative authority, and responsibilities are delegated to several government ministries (IMS 2015; Mossialos et al. 2016; J. hwan Wang, Chen, and Tsai 2012; Zou et al. 2016). Figure 3 outlines the key government bodies within the healthcare sector and their respective functions.

Figure 3 Governance in the Chinese Healthcare System



On a horizontal dimension at the national level, the key government bodies involved in pharmaceutical policy are:

- National Health Commission (NHC): The NHC is China's main executive agency for its health system. It was established in March 2018, replacing the dismantled National Health and Family Planning Commission (NHFPC). Its main functions include formulating national health policies, coordinating and advancing healthcare reforms, overseeing disease prevention and treatment, ensuring the accessibility of health services, and monitoring the quality of health services. Its responsibilities directly related to pharmaceutical policies involve establishing national pharmaceutical policies and maintaining the national essential medicine list (EML).
- National Medical Products Administration (NMPA): NMPA is the regulatory agency for drug safety. It replaced the predecessor organisation - China Food and Drug Administration (CFDA) - in April 2018, as part of a national government restructure. CFDA was a stand-alone ministry-level agency directly led by the State Council, but now NMPA has become a sub-ministerial level subsidiary of a newly formed State Administration for Market Regulation (SAMR) which subsumes the responsibilities previously held by several bodies and oversees all manner of market controls. NMPA is responsible for overseeing drug

safety, ranging from formulating standards for medicine management, regulating drug registration, establishing quality standards, to drug quality supervision and inspections.

- State Medical Insurance Administration (SMIA): SMIA is responsible for formulating policies, plans, and standards on medical insurance, maternity insurance, and medical assistance, and ensuring their implementation. It was set up in 2018, taking over the health insurance responsibilities from the Ministry of Human Resources and Social Security (MHRSS) which oversaw the Urban Employee Basic Medical Insurance (UEBMI) and Urban Resident Basic Medical Insurance (URBMI), and NHFPC which oversaw the New Rural Cooperative Medical Scheme (NRCMS). In relevance to pharmaceutical policy, it is responsible for pharmaceutical pricing regulation, which prior to 2018 fell under the jurisdiction of National Development and Reform Commission (NDRC). It regulates the National Reimbursement Drug List (NRDL), health insurance payout standards, and tendering policies.

Several other government bodies provide support functions to the health system, including the Ministry of Finance, which drafts overall budgets and manages national government subsidies, the Ministry of Industry and Information Technology (MIIT), which makes industry policies, the Ministry of Commerce (MoC), which provides anti-monopoly and anti-protectionism functions, and the China National Intellectual Property Administration (CNIPA), which is the patent office in China.

On a vertical dimension of the governance structure, provincial agents also exert considerable influence on the making and implementation of pharmaceutical policies (Mossialos et al. 2016). Table 2 briefly summarizes the regulatory responsibilities at national and provincial levels for various pharmaceutical activities, from registration, to pricing, reimbursement, prescribing, distribution, and cost-sharing. For instance, while the SMIA maintains the NRDL, provinces have significant discretion in supplementing the list and deciding on the co-payments based on their needs and resources, leading to vast differences across provinces. Similarly, while SMIA provides national guidance for tendering and procurement, implementation is drastically different across provinces. Local protectionism is a major issue in a fragmented market where each province does its own tendering individually (Zou et al. 2016).

Table 2 – Regulatory responsibilities for pharmaceutical activities at national and provincial levels.

Pharmaceutical Activities	National authorities and responsibilities	Provincial responsibilities

Registration	NMPA responsible for drug licensing	Preliminary examination of drug applications and recommendation
Pricing	SMIA responsible for making tendering policies for off-patent drugs; directly negotiate for on-patent drugs	Implementing tendering of off-patent drugs in their jurisdictions
Reimbursement	SMIA maintains the NRDL	Supplement the NRDL
Prescribing	NHC develops clinical guidelines (through China Medical Association), monitors pharmaceutical use and clinical assessment	Implement policies
Distribution	NHC formulates distribution policies; NMPA supervises the distribution process	Implement policies
Cost sharing	SMIA sets co-payment guidelines	Adjust co-payments

4. Recent trends and Reforms in Supply-side Policies

4.1. Intellectual Property and Drug Innovation

China is the world's second largest pharmaceutical market, after the US. Its total sales amounted to $115 billion in 2015 (IMS 2015). This market is dominated by generic drugs with 95% of the approved biochemical drugs in China being generics. Investment in R&D is much lower compared to international standards, at less than 5% of total revenues (J. hwan Wang, Chen, and Tsai 2012). Between 2010 and 2016, the R&D intensity (R&D spending as proportion of revenue) of large- and medium-size pharmaceutical manufacturers has increased from 1.79% to 1.91% (Table 3).

Despite being the 2nd largest pharmaceutical market globally, China lags behind other countries in terms of drug innovation. Weak intellectual property (IP) protection is a major barrier to new drug development. China is still developing its intellectual property laws. China's patent law, enacted in 1985, specifically excluded pharmaceuticals at the beginning in an attempt to prevent monopolies in the pharmaceutical market. Patenting of compositions of matter was not allowed until 1993. Even where patent laws are in place, enforcement of patent protection can be difficult. Pfizer's Viagra was met with an 11-year legal battle over patent and trademark infringement with Chinese generic manufacturers. Weak IP protection has led pharmaceutical manufacturers to seek competitive advantage from administrative protection or market entry barriers instead of innovation. On the other hand, unlike India, to date China has not exercised compulsory licensing of patented drugs.

Table 3. Pharmaceutical industry revenue and R&D spending (2010-2016)

	Year						
	2010	2011	2012	2013	2014	2015	2016
Gross Industrial Revenue in billion RMB (in billion USD)	1,142 ($169)	1,448 ($224)	1,734 ($275)	2,048 ($331)	2,335 ($380)	2,573 ($413)	2,821 ($425)
Market share by LMM*	60.16 %	62.23 %	63.66 %	63.65 %	65.24 %	66.11 %	66.85 %
Revenue by LMM in billion RMB (in billion USD)	687 ($101)	901 ($140)	1,104 ($175)	1,304 ($211)	1,523 ($248)	1,701 ($273)	1,885 ($284)
R&D Spending by LMM in billion RMB (in billion USD)	12.26 ($1.81)	15.63 ($2.42)	21.49 ($3.40)	25.89 ($4.18)	28.97 ($4.72)	32.62 ($5.24)	35.99 ($5.42)
Ratio of R&D to revenue by LMM	1.79%	1.73%	1.95%	1.99%	1.90%	1.92%	1.91%

Source: China High-tech Industry Statistics Yearbook.
* LMM: Large- and medium-size manufacturers.

Historically, low levels of drug innovation are also caused by the weak regulatory system of pharmaceutical products and the redundant application of generic drugs without technical innovation. The pharmaceutical industry in China is considered highly fragmented with weak research and development and low product heterogeneity (Ni et al. 2017). For instance, drug approval often occurs after a change in name or a slight modification in formulation to avoid price ceilings or cuts. There is also a current backlog in new drug approvals as well as a three to

four-year time lag between drug registration in Europe and in China, due to the requirement of clinical trials by foreign pharmaceutical countries prior to their product launches (Ni et al. 2017)..

At its peak there was a backlog of 22,000 applications in 2015, which had been gradually lowered since, but there still was a significant number of 4,000 in 2017 (CFDA 2018). A number of historical reasons led to the backlogs, including a large number of duplicate generic applications (Mossialos et al. 2016), inaction of the authority, an opaque approval process, lack of well-defined guidelines, and an ineffective signaling channel. Relative to other regulatory agencies globally, China has long standard review timelines and median times for approval (Table 4). Relatively low levels of funding and low number of technical reviewers are likely to be contributing factors (Jain et al. 2017). NMPA in recent years had taken several measures to address the backlog issues, by increasing inspection resources, relaxing rules requiring performing clinical trials within China, clarifying and streamlining the approval process and bringing it in line with international standards and guidelines.

Table 4 – Budgets, product approvals, timelines, and fees of various regulatory authorities for new pharmaceutical products.

Regulatory authority	Budget for the fiscal years 2015/2016 (in US$ millions)*	Number of technical reviewers in 2016	Number of NDA submissions for new drugs in 2015/2016‡	Number of new therapeutic approvals in 2015/2016‡	Standard review timelines (days)	Median time for approval (days) in 2015	Fees per NDA in 2016 (in US$ thousands)*
European Medicines Agency (EMA)	340/342	~4,500§	61/68	39/27	210	422‖	316
US Food and Drug Administration (FDA)	1,194/1,230	~2,000	35/41	45/22	300	333‖	2,374
Pharmaceuticals and Medical Devices Agency (Japan)	246/241	~560	127/NA	42/48	365	311‖	274
Chinese Food and Drug Administration	199/250	~120¶	NA	72/31#	900	639	862
UK Medicines and Healthcare products Regulatory Agency (MHRA)	438/477	NA§	NA	146**/NA	210	230	120
Health Canada	84/108	~1,570	27/25	20/27	270	361	248
Swissmedic	115/108	~60	295	27/42	365	464	72
Central Drugs Standard Control Organization (India)	26/NA	~130	NA	17/22	270	523	1
Roszdravnadzor (Russia)	55/NA	NA	NA	NA	210	335	8
Health Sciences Authority (Singapore)	146/NA	~300	NA	61/72	295	409	62
Therapeutic Goods Administration (Australia)	104/NA	NA	43	27/NA	255‡‡	373	172
Brazilian Health Surveillance Agency	NA/NA	NA	NA	NA	730	834	69

NA, not available; NDA, new drug application. *Currency conversion rates are as of 22 May 2017. ‡Where possible, numbers are for NDAs for new therapeutics, such as new molecular entities approved by the US FDA's Center for Drug Evaluation and Research. Direct comparisons between regulatory authorities are not possible owing to differences in definitions; see Supplementary information S2 (box). §The EMA has a regulatory network with a pool of 4,500 scientific experts from member countries. MHRA experts are part of the EMA network. ‖Data from 2016. ¶Data from August 2015; by January 2017, this number had increased to ~300. #Excludes traditional Chinese medicines. **Data includes all decentralised (concerned member state and reference member state) product licenses. ‡‡Working days.

(Source: Jain et al. 2017)

Fundamentally, the pharmaceutical industry within China will likely need to become less fragmented in order to meet new regulatory standards. With over 5,000 different drug manufacturers and the top 5 holding less than 15% of market share, many companies are unlikely to abide to Good Manufacturing Practices essential for drug quality and safety (Mossialos et al. 2016). Within the 13th FYP the state council has declared it will support mergers and

acquisitions (M&A) of domestic manufactures with the aim of consolidating and concentrating the pharmaceutical industry (Multiple Ministries 2016).

The 13th FYP outlined several priorities for innovation and industrialisation of new drugs. Specifically, the plan proposes accelerated innovation and access to new drugs in areas of oncology, major infectious diseases, nervous system and mental diseases, chronic diseases, and orphan diseases. Specifically, monoclonal Antibodies (mAb), protein and peptide based biotech drugs, therapeutic vaccines, and biotherapeutics based on RNA, SELEX and CAR-T technologies should be prioritised for accelerated access. The 13th FYP also aims to improve the quality of traditional Chinese medicines (TCMs), through strengthened quality tracking from herbal origins and through new development of TCMs that address high clinical need. Further, the 13th FYP aims to further advance generic equivalence testing and to promote the development and use of biosimilar in China. Finally, the 13th FYP aims to improve the use of personalized medicine based on genomic data. Overall, the plan stipulates that between 2016 and 2020, economic growth will be driven by increased use of TCM, healthcare services, wearable health devices and genetic screening (Multiple Ministries 2016).

In terms of drug approval, the State Council hopes to incentivize greater use of domestically produced generics and innovative drugs and to reduce reliance on imported products. In order to achieve these goals, the 13th FYP proposes strategic measures including the introduction of Good Clinical Practice international standards, the implementation of explicit clinical evaluation platforms stratified by type of new drug, an increase in the capacity of drug review teams, and the optimisation of prioritisation and fast track schemes for new drug approval. In alignment with the State Council, the CFDA (now NMPA) introduced a number of reforms in the past three years, such as expediting approval for innovative drugs, introducing Bolar exception into law, and accepting overseas clinical trial data. Given the short period of time since the reforms, the impact of these policies on encouraging innovation remains to be seen.

Key messages and remaining gaps

- Weak intellectual property protection and slow drug approval processes in China have contributed to low levels of local research and development.
- Relative to other regulatory authorities, the NMPA has a low number of technical reviewers and long median review times for new drugs.
- As part of the 13th FYP, China lists several priorities for improvements in the innovation and industrialisation of new drugs. Specific focus is place on incentivizing greater use of domestically produced drugs.

4.2. Drug Approval

In 2016, the Chinese government issued the Pharmaceutical Industry Development Planning Guidelines, which outlined China's strategy for strengthening the pharmaceutical system between 2016 and 2020. One of the core development tasks in the planning guidelines was to improve product quality and safety (Multiple Ministries 2016). Historically, NMPA standards regarding drug approval and regulation have been weak, leading to mistrust over quality of domestically produced medicines. For instance, recent reports found that over 80% of clinical trial data submitted for drug registration were either fabricated, flawed or contained inadequate data (Woodhead 2016). Over the past decade, a number of reforms have been introduced with the aim of raising the standards for drug approval and improving drug quality. Table 5 outlines the current drug approval processes within China.

Table 5 – NMPA Drug Approval Processes

NMPA Approval processes	Type of Product	Evidence Requirements	Additional notes
New Drug	New product without overseas authorisation	Local Phase I, II, and III trials	Monitoring period of 5 years
	Modified innovative product without overseas authorisation (e.g. new formulation/new indication)	Local Phase I, II, and III trials	Monitoring period of 3-4 years
Imported Drug	New product approved and manufactured outside China	Local pharmacokinetic and phase III trial	N/A
	Generic product approved and manufactured outside China	Local Bioequivalence study	N/A
Generic Drug	Locally manufactured generic product with approval only outside China	Pharmacokinetics and Phase III trial	N/A
	Locally manufactured generic product already approved in China	Bioequivalence study	N/A
Priority Review	Innovative products not approved overseas, innovative products with plans for local manufacturing or global clinical trials in China, innovative drugs for HIV/AIDs, viral hepatitis, rare diseases, malignant tumours or paediatric indications	Local Phase I, II, and III trials	Additional consultation with Center for Drug Evaluation (CDE). Targeted review time of six months
	Newly launched generic products	Bioequivalence study	Additional consultation with Center for Drug Evaluation (CDE). Targeted review time of six months
Conditional Approval	Products indicated for serious life-threatening conditions or for significant unmet medical needs	Early or mid-stage clinical data	Defined risk management plan required and completion of clinical trials
	Orphan drugs	Trials with fewer trial subject numbers	Completion of clinical trials

Source: (Adapted from Wang and Davidson 2017)

4.2.1. Issues in Drug Quality

China is the second largest producer of counterfeit or substandard drugs worldwide (Pan et al. 2016). A series of scandals involving unsafe or impotent vaccines in recent years have prompted serious concerns about drug safety. The most recent incidence of impotent vaccines broke out in 2018, affecting over 200,000 children (The Lancet 2018; Yuan 2018). Drug safety surveillance is an area that needs major reform (Liu 2016; K. Zhang 2017).

> *"Historically drug approval was quite a mess. Many substandard drugs were approved. Some more advanced drugs, like cancer targeting agents, requires a lot of technological know-how so many small manufacturers were not able to make them. But more common medicines such as antibiotics, basically flooded the market, with dozens of manufacturers" producing the same drug of varying quality."* - Leading academic expert

Weak equivalence testing is another reason for low quality of drugs. Historically, there was no mandatory equivalence testing against the innovator drug as part of the generic drug approval system; only conformity with a weak standard was required. Feedback from expert interviews suggested that the first generic drugs would achieve about 80% efficacy of the originator, then and then the second generic drugs would achieve about 80% efficacy of the first generic drugs. Lack of stringent requirements had led to varying quality of generic drugs.

China started to overhaul the equivalence testing process in 2016, making the procedures for regulation more closely aligned with international standards (Zhen, Sun, and Dong 2018). Deadlines were set for already approved drugs to retroactively pass equivalence testing against the innovator drugs; drugs approved before October 2007 would have to pass the test by the end of 2018, with some exceptions to pass by the end of 2021. Failure to meet the deadline would risk revocation of registration licenses. Moreover, it was announced that for each drug, only the first three manufacturers that passed bioequivalence tests would be allowed in the procurement process; manufacturers that passed the tests later would in principle lose their market in centralized procurement. Prior to 2016, generic products were eligible for registration on the basis of a single in vitro comparative bioavailability study to demonstrate equivalence. A lack of clear equivalence assessment likely contributes to the poor perceptions of generic drugs, present in both doctors and patients. The 2016 reform requires that companies undertake comparative studies to maintain or renew their licenses. Originator drugs should be used as the comparator. Where comparators are not available, full scale clinical efficacy and safety trials should be conducted. Following submission of study results, development and production sites will be inspected, and three consecutive batches will be tested to control the quality of drug products. Generic products previously registered in Europe, U.S., or Japan, can apply to renew registration for the generic drug in China without conducting additional comparative studies.

In 2017, the State council issued a major reform policy document which provided further clarification for strengthening approval of generic products. This document stated that filing management for equivalence studies will be introduced. Separate regulations will allow qualifying medical institutions, academic institutions and private facilities to conduct equivalence tests. Substitution lists will be established for all originators. Under the new system central procurement of off-patent medicines will be restricted to products which have received equivalence certification. Exceptions are in place for molecules with less than three generic versions certified, in order to ensure supply remains sufficient. In these cases, priority for procurement should still be given to certified products, before non-certified versions are procured. Unfortunately, recent reports suggest that re-registration of generic products has been a slow

and opaque process lacking proper integration with regulatory authorities. Further reform is likely needed to continue improving the quality and perception of domestically produced products in China (J. Sun et al. 2018).

One of the key aims of the 2016 reform was to clear all drug backlogs and to ensure that all new applications from 2018 onwards are reviewed within a specified timeframe. Despite the stringent deadlines and strong incentives, progress was slower than intended. By the end of November 2018, only 90 out of 289 EML drugs have completed bioequivalence testing. On 28th December 2018, NMPA announced to abolish the 2018 deadlines and allowed drug manufacturers to apply for an extension of less than 5 years if it could be demonstrated that the drugs meet urgent clinical and market demand, although drugs passing tests earlier would be prioritized to be included in EML. As of April 2019, the NHC announced that 239 drugs out of 685 listed in the EML had passed bio-equivalence tests.

"CFDA asked pharmaceutical companies to assess the quality and authenticity their own submitted clinical trial data. 80% of applications were withdrawn by pharmaceutical companies and CROs (contract research organizations)." - Marketing expert at a pharmaceutical company

"The self-assessment requirement was basically an implicit warning, withdraw fake data without further implications, or go ahead and risking being punished. And we saw 80% withdrew." – Leading academic expert in pharmaceutical policy

Another issue in the process of drug approval is the quality and authenticity of data submitted by drug manufacturers. In 2015, CFDA required pharmaceutical companies to self-assess clinical trial data submitted in drug approval applications. By 2016, 1184 (over 80%) drug applications were withdrawn, for reasons ranging from incomplete data, data not subject to quality control, to fraudulent data.

Historically, China has also failed to properly distinguish between chemical products, produced synthetically, and biologics, which are derived from microorganisms, parasites, or animals. Only in 2015, has China implemented regulatory standards for the registration of biosimilars. These guidelines outlined the application process, classification and dossier requirements, referencing WHO and international guidelines.

4.2.2. International trade of Drugs

Weak regulatory approval systems have not only had negative consequences for industrialisation of medicines within China, but also at an international level where concerns over quality have limited China's ability to compete in generic exports. Given China's manufacturing capacity, closer alignment with international standards may improve international perception of Chinese products. The 13th FYP, has set a target for at least 100 pharmaceutical formulation manufacturers to gain international accreditation in developed countries (e.g. USA, EU) by 2020 (B. Huang et al. 2017; Multiple Ministries 2016).

Given drug approval lag, many patients have turned to illegal importation of drugs in order to obtain treatment. Doctors are placed in an ethical dilemma when patients ask about treatment options that are not currently available in China. This is particularly significant in the case of

Hepatitis C Virus (HCV), which has seen the development of substantial innovation in recent years through the development of direct-acting antiretroviral agents (DAAs). Until recently, China, despite having the highest number of HCV cases worldwide, did not have DAAs available to patients whose only reimbursed option is the far less effective interferon-alpha. As a result, many patients elected to purchase DAAs in generic form from other countries or areas. Unfortunately, the quality of these products is not always ensured, and this process creates additional legal and ethical issues. Further drug-drug interactions are also another potential issue as patients often take interferon-alpha or other drugs concurrently (Han and Liu 2016).

4.2.3. Expedited approval of innovative drugs

Other attempts to reduce the drug approval backlog beyond the 2016 reform include the implementation of the 'Special Review and Approval scheme' in 2009, which allowed for fast-tracking of new chemical entities for serious conditions such as HIV, AIDS, and cancer. The NMPA has recently promised to reform the priority review process to further streamline approval of innovative drugs for HIV/AIDS, cancer, major chronic diseases, orphan disease and for products with high potential economic impact. While it remains unclear how this will be operationalised and how this may impact approval of non-eligible products, these initiatives signal a clear priority to promote access to medicines for serious diseases (Mossialos et al. 2016). Within the Chinese 13th Five Year Plan (FYP) for Biotech Sector development (NDRC 2016b), which was recently issued by the NDRC, the State Council reiterated these objectives, outlining additional plans to accelerate evaluation and approval of urgently needed drugs and medical devices. Under the new conditional approval process, products indicated for serious, life threatening conditions or for serious unmet medical needs can be approved on the basis of early or mid-stage clinical data predictive of a clinical benefit with conditions for additional evidence development (Wang and Davidson 2017).

4.2.4. Reforms in Drug Monitoring

Beyond reforms in drug approval, China is actively building capacity in drug monitoring and review. In October 2018, NHC announced timelines to establish a comprehensive clinical assessment system. By 2020, China plans to set up 100 assessment centres, to provide evidence on clinical effectiveness of key medicines. The assessments are also envisaged to provide support for adjustments to the EML and for establishing clinical guidelines. A key challenge in this area is to establish clear and specific pathways for this evidence to be included in policy decisions. Another challenge is to build a standardized framework for assessment methods, to ensure comparativeness of evidence. The latter point is a particularly challenging task for TCMs.

> *"CDE (Center for Drug Evaluation) has enlarged its team from 120 evaluation staff to about 600. This is a major boost in capacity, although better training is needed for personnel. Building a well-trained professional team, with great capacity to deal with increasing demand of drug approval and evaluation, is still one of the major challenges facing NEMA."* - Government policy advisor

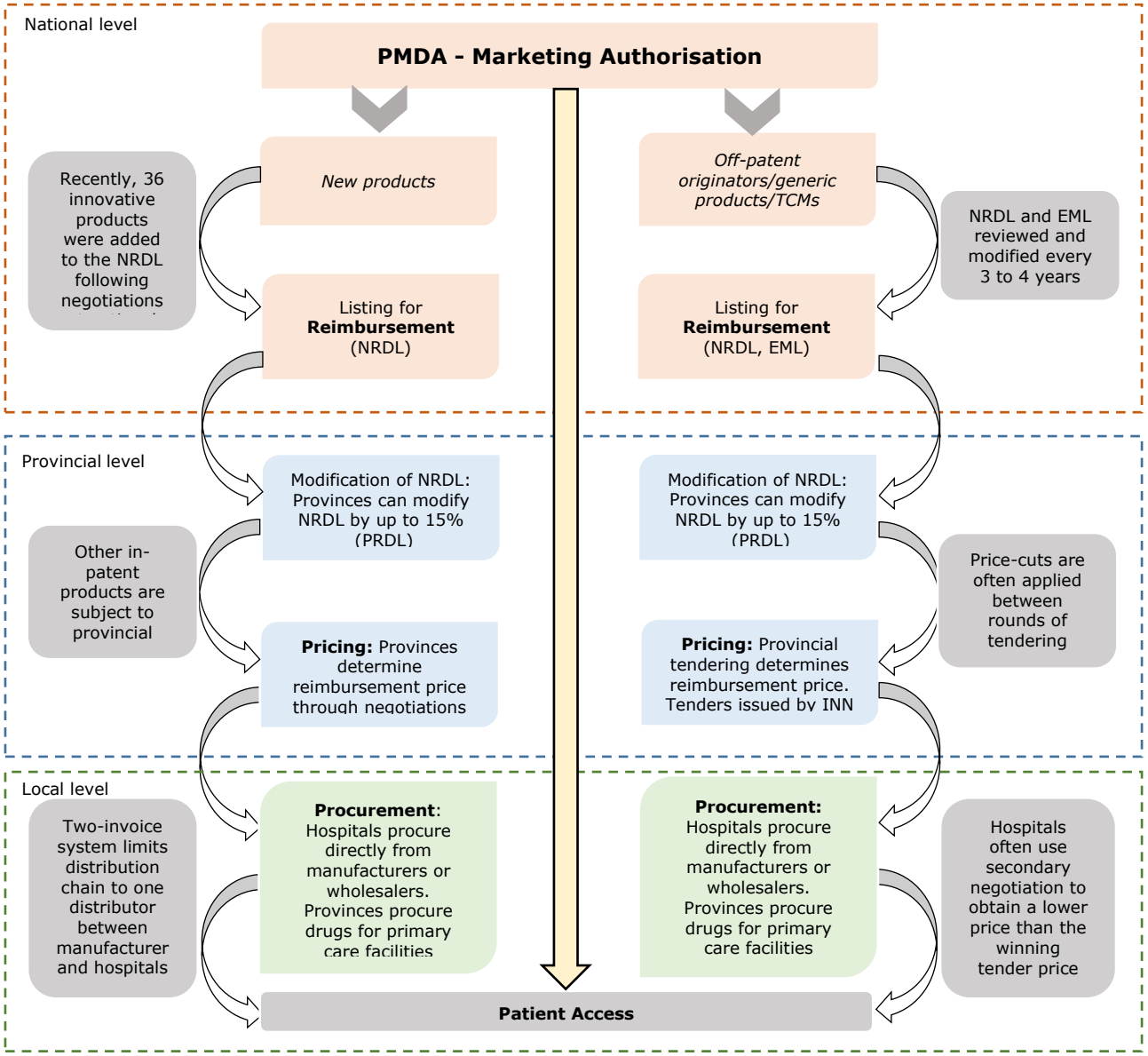
Key messages and remaining gaps

- China has taken an important step to improve the quality of domestically produced generic products through amendments of the Drug Registration Regulation, which moved them closer to international standards. However, the review process for re-registration of new generics has been inefficient and opaque.
- Drug registration is still subject to significant backlog, and China still lags behind other countries in terms of approval of new medicines.
- Systematic monitoring and reviewing of drugs post-approval needs to become an integral part of pharmaceutical policy.

4.3. Drug Pricing

All products on reimbursed drug lists within China, including generic products, off-patent originator products and in-patent medicines, are subject to pricing regulation at national and provincial level. Following marketing authorisation, drugs can be made available for reimbursement through one of two national drug lists, the Essential Medicines List (EML) or the National Reimbursed Drugs List (NRDL) (Figure 4). Additionally, each province has a Provincial Reimbursed Drug List (PRDL), which is based on the NRDL. Provinces can modify the NRDL by up to 15% with the addition or subtraction of authorised products, provided they are not on the essential medicines list (For more information on the use of formularies in China see section 5.1).

Figure 4 – Patient Access Pathway for Medicines in China



Historically, China's drug pricing policy has been criticized for producing a large gap in price levels between off-patent originators and generics, and for lacking a clear and transparent mechanism for pricing in-patent products. Recent pricing reforms within China have attempted to create a more unified system for pricing generic and off-patent originator products, in addition to establishing guidelines for state-regulated pricing of in-patent products. The following sections provide an overview pricing policies for generic, off-patent originator and in-patent products respectively. Table 6 at the end of the section provides a summary of the various pharmaceutical pricing policies used within the Chinese healthcare system.

> *"Because some generic drugs are low in quality, the medical insurances cover both originators and generics of the same molecule. This wouldn't happen if generics are of the same quality as originators. Many patients don't trust the quality of generics; they would choose originators as long as they can afford it. At hospitals, particularly at higher-tier hospitals, the majority of doctors would recommend originators to patients."* - Leading academic expert

4.3.1. Tendering – Generic and off-patent originator products

Prior to 2015, the price of generic products on either the national reimbursed drug list or provincial reimbursed drug lists within China were regulated through price ceilings based on cost-plus pricing, provincial tendering, and price cutting (Table 5). At national level, the NDRC set a maximum retail price based on a cost-plus pricing methodology for both locally produced products and for imported products on the National Reimbursed Drug List. For locally manufactured products, the maximum retail price was calculated based on an addition of production costs, a capped level of promotional expenses, a VAT of 17%, a profit margin ranging from 15-50%, and hospital mark-up. For imported products, maximum retail price was calculated based on the cost insurance and freight (CIF) price, a duty of 4-6%, a VAT of 17%, landing costs of up to 2%, a profit margin ranging from 15-50%, and hospital mark-up.

At provincial level, all products on the EML and many of the products on the PRDL were subject to a tendering process to determine actual retail price, whereby various manufacturers submit bids for the right to supply healthcare facilities within the province (Table 5). The government mandates that hospitals purchase a minimum of 80% of their drugs from winning tender lists. In this context the maximum retail price set by the NRDC would serve as the starting bid. For PRDC specific products Provincial Development and Reform Committees would set the starting price (Hsiao, Li, and Zhang 2015)(Yip and Hsiao 2015). The method of tendering varies across provinces, with differences seen in the qualification criteria and number of possible winners (Zou et al. 2016; Man et al. 2016). Most provinces employ some variation of the Anhui Province's "two-envelope" system, with separate envelopes for drug quality and drug pricing. Further, some provinces have separate tenders for generic and originator products for the same molecule, under the assumption that the products vary based on quality (McTiernan 2014). Several criticisms to the tendering process have emerged. While tendering has successfully lowered prices of EML medicines (Z. Wang et al. 2015), many provinces place priority on price over quality, leading to generic firms lowering quality in order to undercut prices and win bids (Development Research Center of the State Council 2015). Further, awarding tenders to single companies has the potential to create monopolies and drug shortages if winning companies face supply issues (Barber et al. 2013; X. Li 2016).

The maximum retail price of generic products was also subject to periodic price cuts. These price cuts were determined predominantly by the bidding price through provincial tendering, although the NRDC conducted cost surveys every two years which also factored in. In principle, the price cuts would not lower the maximum retail price beyond the average bid prices plus hospital mark-up.

Despite years of utilising price ceilings and price cuts, a substantial body of evidence emerged suggesting these policies were ineffective at reducing drug costs. In May 2014, the NDRC issued a notice which abolished the use of drug price ceilings for generic products, in an attempt to help close the gap between generic and off-patent originator products. However, price cutting in subsequent rounds of tendering is still a common practice across many provinces. In order to ensure companies did not engage in price fixing under this new system, the NRDC also issued a notice on enhancing the supervision of drug market pricing activities, with a focus on monitoring for excessive price jumps and anti-competitive behaviour. Manufacturers found to be engaged in price fixing could be banned from the public tendering process for up to two years. Surprisingly, following the abolition of price cutting in 2015 the utilisation of generic products rose slightly, although it is unclear if this is a result of higher generic prices or if other targeted policies played a role. Despite a slight increase in the use of generics, there is still a clear preference for higher priced branded products (J. Sun et al. 2018). Given removal of price cutting policies, the state council also issued a notice on improving centralized bidding and procurement of drugs in 2015. Here, the state council outlined that provincial tendering would become the primary mechanism for pricing off-patent products on the NRDL. This notice addresses several issues of tendering by drug quality with the aim of creating a more transparent and unified system (Mossialos et al. 2016). Further reform took place in 2018, through a State Council notice which requires tendering to take place by generic name, thereby assuming equivalence between generic and off-patent originator products (State Council 2018).

> *"Now a unified information system is in place. All provincial prices must be reported to central government health administrations or health insurance authorities. So there is a trend of a common market within the whole China. Provincial prices are converging. But there is also a side effect, in that there is too much emphasis on getting the lowest price. This is not healthy. One consequence is shortage of drugs. The government's countermeasure is to establish a list of essential drugs and designate the supply to a small number of manufacturers. Manufacturers are willing to accept low prices because the volumes in the national market are huge, which makes low prices sustainable."* - Leading academic expert

Like generic products, off-patent originators within China were subject to cost-plus pricing at national level, provincial tendering, and price cuts prior to 2015 (Table 5). While the NDRC would set a maximum retail price, local governments were able to adjust this price for originator products considered to be of greater quality than the generic versions. This product would receive a pricing privilege. Further, the two-envelope system of tendering and provincial practices of creating different tiers within tenders for generic products and off-patent originators led to pricing monopolies for off-patent originator products. Originator products would be procured at a higher winning bid price, while generic products faced stiffer competition and therefore lower prices. (Mossialos et al. 2016). The NDRC attempted to reduce this gap, through

price cuts based on the price gap over generic products, manufacturer costs, expense levels and average bidding prices.

In theory, drugs with larger gaps between originator and generic versions would receive larger price cuts. In practice, these price cuts were largely ineffective at reducing the gap between originator and generic products (Mossialos et al. 2016). As a result, the use of price ceiling and preferential pricing was abolished in 2015. As a replacement for nationally set price ceilings, the NDRC implemented an internal reference pricing system for generic and off-patent originators with high levels of competition. This system places a cap on the level of reimbursement for these products. At the time of announcement in 2015, no details were provided on the methodology for determining the reimbursement level. In principle, regulations for setting reimbursement caps will be set at national level, while provincial level governments will set the levels. In theory, implementing a reimbursement cap allows hospitals to negotiate below the cap with manufacturers in order to lower costs. Through revisions of reimbursement caps based hospital procurement prices, this process will gradually put price pressure on pharmaceutical companies. Caps will be set according to generic names, eliminating the possibility for a preferential pricing of off-patent originators.

"You would expect prices to drop shortly after patents expire. But you don't see that. Off-patent drug still command high prices, and they are not short of demand." - Academic expert in pharmaceutical policy

Finally, reforms in the provincial tendering process and in equivalence testing will likely help to bridge the gap between the quality and price of generic and off-patent originator products. Under the most recent state council guidance, provinces are now required to issue tenders according to molecule name and cannot differentiate between originator and generic products (State Council 2018). In principle, this should promote greater use and procurement of generic products.

4.3.2. Negotiations - In-patent products

"Current pricing mechanism for innovative drugs are mainly done through pricing negotiations. We have seen three batches of such negotiations. The first attempt was led by NHFPC, where they succeeded in negotiating prices for three drugs out of an intended five. But there was an issue at the regional levels. Health administrative authorities were not the payers. Health insurance funds were the payers. Now after three batches of pricing negotiations, it is increasingly clear that health insurance funds should lead the negotiations. Once prices are negotiated, the drugs can be immediately included in the health insurance reimbursement lists." - Government policy advisor

In-patent products are priced based on negotiation by the State Administration for Medical Insurance (SAMI - formerly this was the NDRC's responsibility), although this process is not formalised. Recently, the Chinese government implemented a negotiation pilot in an attempt to reach an acceptable agreement on the price of 44 high priced, but innovative medicines. Agreement was successfully reached for 36 of 44 medicines. Prior to the pilot, pricing negotiations took place between NHFPC, local governments and manufacturers, but the negotiations were small in scope and most of the process was closed from pharmaceutical suppliers. Guidance issued by the NHFPC indicates that a selection of in-patent products will be

eligible for national negotiations, while others will proceed through provincial negotiation, although it remains unclear how these products will be differentiated in the future (Figure 4).

> *"I was recently at a WHO conference. One notion they tried to promote was fairness pricing, not low pricing. Fairness pricing is about sustainable development of the industry, not going bankrupt. I think this notion is now gradually accepted by the Chinese government. It should be about a reasonable price, not necessarily the lowest price. This is one of the positive developments recently."* - Leading academic expert

The role of negotiations in the pricing and reimbursement of medicines was further discussed in the 13th FYP (Multiple Ministries 2016). Specifically, the plan states that selected patented and exclusively-produced drug products will be subject to negotiations at national level, with the number of products increasing gradually over time. Priority review status, patent life and pharmaco-economics should be key considerations in the negotiation process. Other patented medicines, or off-patent medicines with low levels of competition, are priced through provincial negotiation, although the details of the process are unclear (Multiple Ministries 2016). The process remains opaque and requires formalisation. Clarity must be given on the assessment of medicines in terms of the submission process, types of evidence considered, evaluation criteria and assessment timelines.

> *"The two main criteria for deciding what drugs should be included in the negation list, are high price and high volume. Those are the main concerns for the general public. These two factors lead to affordability issues on a large scale so we try to work on that." - Government policy stakeholder*

4.3.3. Reference Pricing

> *"For innovative drugs reference pricing is used, although it's not specified which countries form the reference basis. The main countries that drug manufacturers include in their dossier include US, UK, Germany, France, Australia, New Zealand, South Korea, and Japan. Taiwan and Hong Kong are sometimes included as well. So, although we don't have an official country basket, drug manufacturers have to report their prices in a number of countries mentioned before. On average, price negotiations reduced the prices by 44% for the second batch, and 54% for the third batch."* – Leading academic expert

In 2012, the NDRC conducted a pricing survey in order to explore potential applications of external reference pricing within the Chinese system. The survey applied to both in-patent and off-patent products. A basket of 9 countries was included: the USA, Canada, UK, Germany, France, Japan, Korea, Taiwan, Hong Kong, and the manufacturer's country (Table 5). Data was collected on both the retail and reimbursed price. As a rule, the price of the identical strength/pack size was submitted, unless unavailable whereby alternative prices would be provided. In 2015, the NDRC issued guidance for the implementation of external reference pricing. Multinational corporations were required to provide information on drug prices in their home country as well as prices in the European countries, the USA, and additional markets in Asia and Africa. In theory, reference pricing would be used to inform the starting bid for provincial tenders for off-patent products and would be used as a starting point in negotiations for in-patent products (Mossialos et al. 2016). Within the 13th FYP, the State Council reiterated

these objectives, outlining plans to accelerate evaluation and approval of urgently needed drugs and medical devices (NDRC 2016b).

Evidence from expert interviews suggests that while external reference pricing is in use, there is currently no systematic standards for cross-country referencing. On the other hand, at the regional level, prices across provinces are increasingly more transparent, which leads to procurers often demanding the lowest available price in other provinces. While this may help form converging prices across provinces, it cannot be ignored that in the presence of market fragmentation, each province has a market of its own size. Larger markets can absorb high volumes which could lead to production efficiency and lower costs and in consequence lower prices; smaller markets may need to take into account higher unit-costs during price negotiation due to low volumes of demand.

Table 6 – Summary of Pharmaceutical Pricing Policies in China

Pricing Policy	Scope	Description	Effect
Price ceilings (cost-plus pricing)	Used to set maximum retail prices of products on National Reimbursed Drug List (Abolished in 2014)	Price ceiling set based on production costs + capped promotional expenses + 17% VAT + 15-50% profit margin +hospital mark-up. Imported products calculated based on CIF price, duty, VAT, landing costs, profit margins, and hospital mark-up.	Failed to adequately control overall drug spending. Physicians evaded price ceilings by switching to more expensive products or by increasing volume of prescriptions.
Price-cuts	Applied to maximum retail prices periodically as cost-containment measure	Fixed reduction in maximum retail price of a product, based on cost-surveys of average retail price. Applied between rounds of tendering.	Lowered prices of targeted drugs by 15-20% on average, but failed to control overall drug spending.
Tendering	Primary pricing mechanism for generic and off-patent medicines. Applied provincially	Tenders issued provincially for the supply of a molecule. Tenders are issued by International Non-proprietary Names (INN). Manufacturers submit bids based on maximum retail price. Hospitals are required to procure 80% of products from winning tender lists.	Successful at lowering drug prices by 25-50%. Historically emphasized price over quality and contributed to both low quality of generic medicines and off-patent originator price monopolies.
Negotiations	Primary pricing mechanism for in-patent products. Applied nationally and provincially.	Conducted by State Administration for Medical Insurance (SAMI - at national level) or by Provincial Development Reform Committees (PDRC - at provincial level).	Agreements reached for 36 out of 44 products in negotiations pilot. Products added to NRDL.
Secondary Negotiations	Between hospitals and manufacturers/wholesalers.	Informal negotiations during drug procurement between hospitals and manufacturers/ wholesalers. Actual drug volume is specified and hospitals often obtain a lower price than the listed tender winning price.	Provides additional profits to hospitals and lowers the effective price of products. May create incentives to overprescribe drugs with high profit margins.

External Reference Pricing	Informally used for innovative products	International price data is included in submission dossier for innovative products. No formal guidelines are in place and there is currently no systematic standard for cross-country referencing. Most manufacturers include data from US, UK, Germany, France, Australia, New Zealand, South Korea, and Japan.	N/A

(Source: the Authors)

Key messages and remaining gaps

- Pricing for generics and off-patent originators takes place primarily through provincial tendering, following abolishment of national price ceiling and price cutting policies. While no formal system has been established for pricing in-patent products, a select number of products have proceeded through negotiations at state level. In practice, other products are priced through negotiations at provincial level.

- Implementation of tendering varies considerably across regions. In some regions, price is valued over drug quality, incentivizing companies to lower quality in order to undercut prices. Separate tenders are frequently issued for generic and originator products which perpetuates pricing monopolies.

- The negotiation process remains opaque and requires formalisation. Clarity must be given on the assessment of medicines in terms of the submission process, types of evidence considered, evaluation criteria and assessment timelines. Clarity is required on how managed entry agreements can be used within the negotiation process to help facilitate agreements.

- External reference pricing has only been implemented recently and the impact thus far remains unclear. More clarity is needed on how external reference pricing has been operationalised. It is unclear how the starting bid price is set for products which are ineligible for external reference pricing.

4.4. Drug Procurement

The drug tendering process within China is not directly linked to the procurement of medicines. Procurement of pharmaceuticals occurs in separate processes for hospitals and primary care facilities. While pharmaceuticals for primary health facilities are procured at provincial level, hospitals procure their products directly from manufacturers. Following a provincial tender, hospitals are required to deal directly with manufacturers or wholesalers in order to procure drugs. Prior to 2015, this process often involved secondary negotiation, whereby a hospital would agree on drug volumes and negotiate and procure products at a lower price than the winning tender price. This practice occurred only in some provinces, while others required procurement at the winning bid price. Opinions on the use of secondary negotiation were mixed. Some thought that added competition at the local level would help drive down prices and produce a more efficient system. However, secondary negotiation has the potential to undermine the zero mark-up policy, as hospitals are able to produce a profit margin between the tender price and secondary price. This may create incentives to overprescribe products with the largest margin to maximize hospital revenue. In response to concerns regarding secondary negotiation, the NHFPC issued a notice on implementing and improving centralized bidding and procurement of drugs. This notice requires hospitals to acquire 80% of their medications from the list of products that underwent provincial tendering and requires that drug sales do not exceed 25-30% of total hospital revenue (NHFPC 2015).

Recently, as part of the 13th FYP, the State Council outlined plans to continue to enhance the nationwide pharmaceutical distribution network in order to cover both urban and rural areas. As part of this process a national drug information public service platform will be established to publicize information on price and quality (Multiple Ministries 2016).

In 2017, the State Council issued a major reform policy with implications on drug procurement. Specifically, the policy aims to improve the procurement of high quality generic products. Under the 2017 reforms, provinces are unable to procure products that have yet to pass equivalence review if three or more generic products for an originator have done so. In cases where less than three generic products have passed equivalence studies, the products having passed review should still be preferred (State Council 2017).

Increasingly, China will also aim to promote inter-regional procurement of medicines. The 2017 health care reforms encourage both medical institutions and regions to collaborate in the procurement of medicines. Public hospitals will be able to purchase products directly from provincial centralized drug purchase platforms. Joint procurement of medicines will likely play a key role in strengthening China's capacity and ability to engage in price negotiations at both central and provincial level (State Council 2017).

> *"A principle in existing drug procurement is to establish a "procurement platform under the sun", in the sense that pricing information is transparent and shared online. From the perspective of the procurement body, If I see a drug listed for a certain price at another province, I'll ask for the same price if not lower. But the volume is never specified. This puts a lot of pressure on drug manufacturers. In practice, some manufacturers are not even considering lowering prices for large provincial markets, as they fear other smaller markets see the low price at this province and demand the same."* – Expert from health-promotion foundation

There have already been some pilots of cross-municipality or cross-province group purchasing organizations (GPOs). One prominent example, the 4+7 procurement group overseen by the SMIA, organizes pharmaceutical procurement for the four directly-controlled municipalities (Beijing, Shanghai, Tianjin, and Chongqing) plus seven other large cities (Shenyang, Dalian, Guangzhou, Shenzhen, Xiamen, Chengdu, and Xi'an) (See Figure 5)

The commitment of procurement quantities is an improvement of the pricing process. Under most current mechanisms, the tendering process sets a ceiling price, but does not specify the quantity of procurement. This essentially leads to a secondary market, where pharmaceutical manufacturers end up in second round of negotiations with hospitals for their medicines to enter the hospital pharmacies, resulting in either lowering the prices or giving rebates to hospitals. This means the tender bid prices are not binding, and actual prices are set in the secondary market. With the committed quantity, manufacturers do not have to spend extra resources to make sure they get orders from hospitals after the tendering process. Interviews with KOLs posit that quantity commitment will be a direction of future reforms to the pricing mechanism.

Figure 5. Group Purchasing Organization Case Study

Case Study – Cross Province Group Purchasing Organizations (GPO) Pilot	
Description	Pilot study for joint procurement of medicines across 11 municipalities in the Chinese pharmaceutical market. The GPO is overseen by the National Medical Insurance Administration (SMIA).
Municipalities involved:	4+7 Procurement group: four directly-controlled municipalities (Beijing, Shanghai, Tianjin, and Chongqing) plus seven other large cities (Shenyang, Dalian, Guangzhou, Shenzhen, Xiamen, Chengdu, and Xi'an). Collectively these 11 cities constitute 25% of the Chinese pharmaceutical market.
Drugs involved	31 drugs listed in tendering process, with fixed intended quantities. Quantities represented 30-50% of procurement volumes in included hospitals.
Results	Sharp drop in listed drug prices. Over two thirds of products had a drop of over 30%, with the largest drop exceeding 90%.

Another critical issue from the tendering process is that procurers focus heavily on prices, and less on quality. Due to the lack of quality standards historically, different versions of the same generic drug vary substantially in quality. In reality, the emphasis on low price means usually the lowest bid wins, which is inevitably associated with lower quality. Tiered tendering by quality addressed this issue to some extent, by issuing a separate tender for higher quality products, but this system lacks a scientific approach, leads to greater market fragmentation and leads to more fierce secondary negotiations. As discussed above, incorporating a requirement to pass bioequivalence tests as a prerequisite into the tendering process is a promising development for addressing quality issues. Under the new development, only manufacturers that have passed the bioequivalence tests are allowed to submit bids; further, for each medicine there is a limit on the number of bidders to be allowed, which means manufacturers passing bioequivalence later will be driven out of the market. While manufacturers race to pass the bioequivalence tests before the deadline in December 2018, there is no empirical evidence yet as to whether the drugs that have passed these tests are indeed of good quality standards.

Key messages and remaining gaps

- Health facilities frequently engage in secondary negotiation. This process remains opaque and it is unclear how large the difference is between the tender price and the secondary price. This could create distorted incentives for hospitals to overprescribe products with the largest profit margin and undermine the aim of the zero mark-up policy.

- While the NHFPC has issued notices aiming to address issues in secondary negotiation, it remains unclear what steps have been taken and how this issue varies across provinces. Quantity commitment is a promising avenue for avoiding secondary negotiations, but it remains to be seen whether this can be implemented on a large scale.

- Emphasis on lowering prices without stringent regulatory requirements has contributed to drug quality issues. The pricing process needs to strike the right balance between price and quality.

4.5. HTA

Despite the 2009 health reforms, there are still significant challenges in China regarding pharmaceutical policy from a supply-side policy perspective. Since 2016, the National Health and Family Planning Commission (NHFPC) has issued policies to guide and strengthen the implementation and use of HTA in China (Y. Chen et al. 2018). However, the use of HTA has not yet been formalised and current uses have been predominantly academic. Whilst policy makers are aware of HTA, it is not mandatory to utilise or implement it on a national scale. Therefore it is not fully embedded in the policy making process (Y. Chen et al. 2018). When HTA is conducted, there are large gaps between the understanding and integration between HTA itself, knowledge translation and policy-making (Wei et al. 2017). For instance, in a qualitative study interviewing both HTA researchers and policy makers, HTA researchers believed that their research was high-quality and relevant for policy-making, but policy-makers do not use evidence-based approaches when making health decisions (Wei et al. 2017). In contrast, policy-makers believed their decisions are largely evidence-based, but the HTA research is of low quality. This research indicates that the alignment between research and decision making needs to be improved in order to provide higher quality research as well as more informed decisions. Thus, insufficient communication between stakeholders is a key barrier in the HTA process in addition to inadequate policy support and funding. Beyond stakeholder engagement, the institutionalisation of HTA is a second conducive factor for strengthening HTA systems (MacQuilkan et al. 2018). The establishment of the National Pharmaceutical and Health Technology Assessment Center in October 2018 was one of the first steps towards integrating HTA into policy.

Recently, a pricing negotiations pilot within China represented the first instance of evaluating evidence dossiers submitted by manufacturers. While the pilot was associated with some success through the listing of products on the NRDL (see section 4.4), criticism emerged surrounding the evaluation process which lacked clear guidelines on evidence requirements, assessment criteria, and assessment timelines (Hong Li et al. 2018). Interviews with KOLs also confirm these assessments.

> *"HTA has had some positive effects. But I don't think a large country like China can build an HTA system like NICE. It's just some individual cases at the moment. For instance, pharmaceutical economists are involved in some pricing negotiations. They can make suggestions; drug manufacturers also present some evidence based on HTA. But it's impossible to exclude certain drugs based on HTA evidence. Maybe one or two, but that's the size of it. But I do have to say HTA as a concept is more and more widely accepted by pharmaceutical companies and government. This is for sure…Overall, HTA may serve in an advisory role; health administrations and health insurance authorities make the final call."*
> - Leading academic expert

Beyond utilizing HTA for the purposes of informing price negotiations, China has also indicated interest in using HTA to help guide reimbursement decisions. The 13th FYP outlined plans for consolidating and improving the essential drug system. In this context, China intends to explore how clinical and economic evidence can be used in the selection of essential drugs.

The key challenge in this area is to find clear and specific pathways to include HTA as part of the policy-making process. While this will be a long-term process, policy makers could start with

clarifying the requirements of evidence they would like to see as the basis of policy decisions. An open and transparent process would help form correct expectations and guide pharmaceutical manufacturers towards utilizing HTA to their own benefit.

Key messages and remaining gaps

- While the establishment of guidelines intending to strengthen the use of HTA in China is a positive step, HTA is still rarely used in decision making for the pricing and reimbursement of medicines. Without a formalised and integrated HTA system, China lacks a clear value framework for the pricing and reimbursement of medicines. As a result, it remains unclear if national health system priorities translate to decision making in the pharmaceutical sector.

- The key challenge is to establish clear and specific pathways to include HTA as part of the policy-making process.

5. Recent Trends and Reforms in Demand-side Policies

Over the past two decades demand-side policy reforms have been implemented both at state level and at regional/county level, with the aim of reducing inappropriate prescribing, improving microeconomic efficiency and improving quality of care (Mao et al. 2015). Demand-side policies can be subdivided into proxy-demand side policies which target health care providers, and demand-side policies which target patients.

5.1. Proxy-demand side policies

5.1.1. Formularies

A. National Reimbursement Drug List (NDRL)

The Chinese national reimbursed drug list (NRDL) was formally established in 2000. There have been 3 updates to the formulary: one in 2004, one in 2009, and another between the end of 2016 and February 2017. Following the most recent update, there are 2,535 medicines in the NRDL (1297 western, and 1238 are TCMs). The 2017 update added 339 new medicines to the formulary. A specific focus was placed on areas of serious disease, paediatric medications, medications for work-related accidents, and TCMs. Despite the update, several expensive but innovative products are excluded from the formulary. Historically, many in-patent products have been subject to free pricing and excluded from the NRDL, which is only updated every three or four years. Newly approved products that have missed the update window often had to wait years before their product was eligible for reimbursement. Non-reimbursed drugs are typically priced freely by manufacturers. Patients were required to bear the full cost of these products.

Recently, the Chinese government implemented a negotiation pilot in an attempt to reach an acceptable agreement on the price of 44 high priced, but innovative medicines. Prior to the pilot, pricing negotiations took place between NHFPC, local governments and manufacturers, but the negotiations were small in scope and most of the process was closed from pharmaceutical suppliers. The pilot introduced the concept of submitting evidence dossiers for the first time. Overall, an agreement was reached for 36 out of 44 medicines that entered the pilot. The negotiated products were added to the NRDL without provincial modification (Li et al. 2018).

The inclusion of high-priced innovative drugs indicates a recognition of value-based healthcare concept. There is a gentle shift from solely focusing on driving down healthcare costs towards addressing unmet needs. Meanwhile, this also reflects that political and public advocacy is a key factor that shapes pharmaceutical policy decisions. The addition of these drugs is partly incident-driven, e.g. the blockbuster movie Dying to Survive has had an impact in pushing some cancer drugs into the NRDL list. Future adjustments to the list are likely more frequent and dynamic, to reflect changing disease burdens and public health focus. That said, cost containment would remain a long-term focal point for pharmaceutical and health insurance policies. Listed medicines would face pressure from health insurance authorities to lower prices, as a tradeoff for gaining access to a large market.

As the pipeline of emerging technologies such as personalized medicines continues to grow, it is likely to present a number of challenges from a financing perspective. China is moving very fast in this direction for a number of areas. For instance, there has been advancement in gene-based precision medicine in China. But this area is mainly funded by pharma companies, and there is no clear indication of including these new technologies in the reimbursement list because of their high costs, as cost containment remains a priority policy focus in future. Recent incidents such as the gene-edited babies probably also means government will be more cautious with sponsoring such technologies. On the other hand, China's vast market size is an important driving factor of these technologies. There are now examples where drugs are first marketed in China before they marketed in neighboring countries such as South Korea. Overall, while emerging technologies are growing fast in China, inclusion of these technologies into the public health insurance system has a long way to go. High costs and questions surrounding the extent to which these technologies address pressing unmet needs are the major obstacles for these technologies to enter the health insurance system.

B. Provincial Reimbursement Drug List (PRDL)

Each province has a Provincial Reimbursed Drug List (PRDL), which is based on the NRDL. Provinces can modify the NRDL by up to 15% with the addition or subtraction of authorised products, provided they are not on the essential medicines list. The NRDL is divided into class A drugs, considered to be effective, essential, and relatively cheap and class B drugs, considered to be less effective. Class A drugs must be fully reimbursed, while class B drugs have varying level of co-payments. PRDLs must include all class A drugs, but can adjust up to 15% of class B drugs to suit local needs. While important recognize variations in need across provinces, concerns have been raised that PRDLs contribute to variations in drug coverage across China. Until recently, this was also caused in part by variations in urban and rural health insurance schemes. Introduction of a merged health insurance scheme is likely to alleviate these issues. (Mossialos et al. 2016)

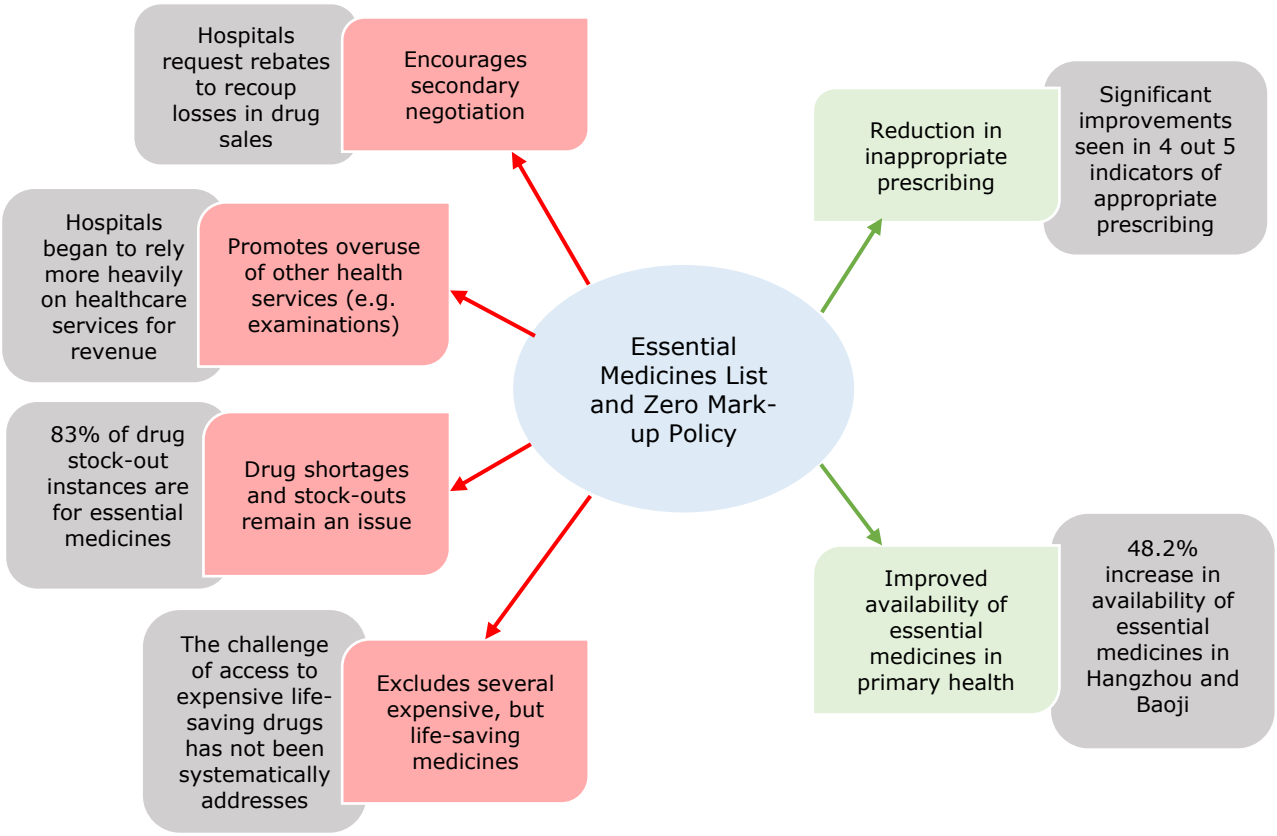
C. Emergency Medicines List (EML)

One of the most fundamental reforms in proxy-demand side policy was the establishment of the National Essential Medicines Programme (NEMP), as part of the 2009 health system reforms. The NEMP regulates drug production, pricing, procurement, and prescribing. One of the first reforms as part of the NEMP was the establishment of an essential drug list for primary care providers (including community health centres, village clinics and township hospitals). The list initially contained 307 drugs, but provinces are able to modify the list based on local disease burden and socioeconomic status. The list is eligible for updates every 3 years. Procurement of drugs on the essential medicines list occurs through tendering at provincial level, based on bid prices capped centrally (Yun Gong 2016) . As part of the NEMP, drugs on the EML are subject to a zero mark-up policy, which prevents health care providers and dispensers from increasing the price beyond the winning bid in the procurement process. In theory, preventing mark-ups on essential medicines would remove distorted financial incentives to over-prescribing pharmaceuticals as a source of funding in health care facilities. By then end of 2011, 98.8% of primary care institutions were implementing the NEMP (Hsiao, Li, and Zhang 2015). Increasingly since 2009, the zero mark-up policy has also been implemented in public secondary and tertiary

hospitals for both drugs on the essential medicines list and for the drugs on the national reimbursed drugs list (NRDL) (Tian et al. 2016; Zesheng Sun, Wang, and Barnes 2016; W. Y. Zhang et al. 2015; T. Zhang, Graham, and White 2018). Initially, elimination of margins on drug sales in hospitals took place in 100 trial site cities. In 2016, the state council announced plans to expand hospital reform to 200 cities by the end of the year, with the aim of eventually completely eliminating hospital drug sales margins (State Council 2016). In 2017, the NHFPC announced that all public hospitals have abandoned drug sale margins (People's Daily 2017).

Evidence on the ability of the National Essential Medicines List and Zero Mark-up Policy to reduce irrational prescribing, improve access to medicines and improve efficiency is mixed (Figure 6). Appropriateness of prescribing is assessed based on 5 indicators: average number of drugs prescribed per prescription, percentage of prescriptions with antibiotics prescribed, percentage of prescriptions with injections prescribed, percentage of prescriptions with two or more antibiotics prescribed and average expenditure per prescription (WHO 1993) . Early assessments found that the NEMP resulted in statistically significant reductions in each indicator except for the percentage of prescriptions with injection (Honglin Li et al. 2016) However, absolute values remained high for all indicators and well above WHO recommended levels (Yun Gong 2016; Q. Yao et al. 2015). A review of irrational prescribing in China reports that, as of 2015, the original goals of the 2009 reforms have not been achieved. Differences in inappropriate prescribing are seen across rural and urban areas and among different levels of hospitals, with higher levels seen in rural areas. Further, the overuse of injections remains a key challenge in terms of irrational prescribing (Mao et al. 2015).

Figure 6 – Effects of Essential Medicines List and Zero Mark-up policy



Beyond irrational prescribing, other unintended consequences of these policies saw hospitals resort to demanding rebates from pharmaceutical manufacturers in secondary price negotiations and raising revenues from unnecessary examinations, to compensate for the loss of revenue from drug sales. As government subsidies only contribute about 10% of public hospital revenues, and generally government compensation for loss of drug sales revenue is inadequate, hospitals have an economic incentive to seek revenues from other avenues. A positive effect of these policies on the healthcare workforce, is that healthcare services (e.g. consultations) are compensated better, an improvement from the historically low payment standards for the workforce. On the negative side, unnecessary examinations lead to waste of healthcare resources. The key challenge for policy makers is to provide correct incentives for healthcare providers with the right compensation, to guide their behaviors towards more efficient use of healthcare resources.

> "Drug sale was a major source of hospital revenues. After zero markup policy, hospitals had to rely on more healthcare services. Services like consultations are seeing their prices increase, but it's not enough yet. So now a lot of revenues are coming from examinations. An overuse of examinations. If you want to have a CT scan at a developed country, there is usually a long waiting list; in China, it's available everywhere. It's very convenient, yes, you can get the results even within the same day; but often it's also a waste of resources. *– Expert at a hospital-based research centre*

In terms of access to medicines, the NEMP appears to have made some progress in terms of expanding coverage; however, patients still face significant barriers in access due to high levels of out-of-pocket expenditure. In a study of primary health facilities in Hangzhou and Baoji, the EML resulted in a 48.2% increase in the availability of essential medicines, and patients generally reported that their medicines needs were met. However, out of pocket payments were still substantial for medicines outside of the list and medicines costs still accounted for a major part of patient's annual health expenditure (over 40% of THE in 2010) (Y. Huang et al. 2018). Drug shortages and stock-outs also remain an issue. An investigation in 2010 reports that, of 284 medicines found to be out-of-stock in at least one facility throughout various levels of health care, 83% were on the EML. A later report in 2015, found that out of the 780 medicines on the NRDL, 357 medicines were out-of-stock. In particular, these reports suggested a poor buffering and alert capacity of inventory control systems currently used through health facilities in China (J. Sun et al. 2018). Finally, several expensive but potentially life-saving drugs remain outside of the EML. Although recent negotiation pilot programmes successfully added 36 of 44 medicines evaluated into the NRDL, the problem of access to innovative and expensive life-saving drugs has not been systematically addressed within China (Hong Li et al. 2018).

While the NEMP has placed some control on public expenditure of medicines, total pharmaceutical expenditure and total health expenditure within China have continued to exceed GDP growth since 2009. At the macroeconomic level, the NEMP has not achieved the desired reductions in pharmaceutical expenditure as the distorted consumer and provider incentives have not fundamentally changed, despite some marginal improvements in rational prescribing. At the microeconomic level, preferences for injectables and for higher priced branded medicines remain an issue, limiting potential efficiency gains from cheaper oral products or generic products. The latter likely stems from the perceived poor quality of domestically produced generic products (J. Sun et al. 2018; W. Zeng et al. 2015; J. Zeng et al. 2015). Further, while drug revenue has decreased as a result of the ZMU, use of inpatient care has increased

substantially, indicating that health care providers have sought new forms of revenue (Yu and Xu 2015; Zheng et al. 2015; Yun Gong 2016; J. Huang et al. 2015; Wu, He, and Mao 2016; Dai et al. 2015; H. Yi et al. 2015; Xi. Yi et al. 2018; Zhuolin Sun, Ding, and Li 2017; H. Tan et al. 2016)

Studies reflecting on the NEMP also highlighted a correlation between levels of medical training and rational prescribing, suggesting enhanced training of health care professionals as a priority for future reform (Yun Gong 2016). Further, years of over-prescribing have distorted physician and patient expectations around prescribing leading to widespread perceptions that antibiotics are 'cure all' and that injections have increased efficacy compared to orally administered drugs. (Yun Gong 2016). Overall, there are nine influential factors that contribute towards irrational prescribing: 1) provider's lack of knowledge, 2) patient's lack of knowledge, 3) poor quality of health services, 4) human resources issues at health facilities, 5) pressure from heavy patient load, 6) pressure from patients demand, 7) economic incentive and profits from prescribing medicines, 8) insurance status of patients, and 9) lack of effective control and regulatory mechanisms on medicines use (Mao et al. 2015).Finally, the implementation of the NEMS and zero mark-up policy has fundamentally changed village doctor roles. In order to compensate loss of income, the Chinese government began to pay doctors to implement public health activities and to provide other services covered by social insurance. Despite these changes, village doctors have reported inconsistency in payments, a substantial decrease in income and an overall decrease in satisfaction resulting from the NEMS and the zero mark-up policy (S. Zhang et al. 2015).

In the most recent round of reforms, the State Council issued further guidance on the essential drugs list, stipulating that the NHFPS conducts an evaluation of clinical drug consumption of essential medicines within public hospitals. By 2020, the essential medicines list should be expanded to provide greater coverage of clinical pathways and should be implemented in all level II or greater hospitals.[1] However, the specific criteria guiding this assessment remain unclear (State Council 2017).

Key messages and remaining gaps

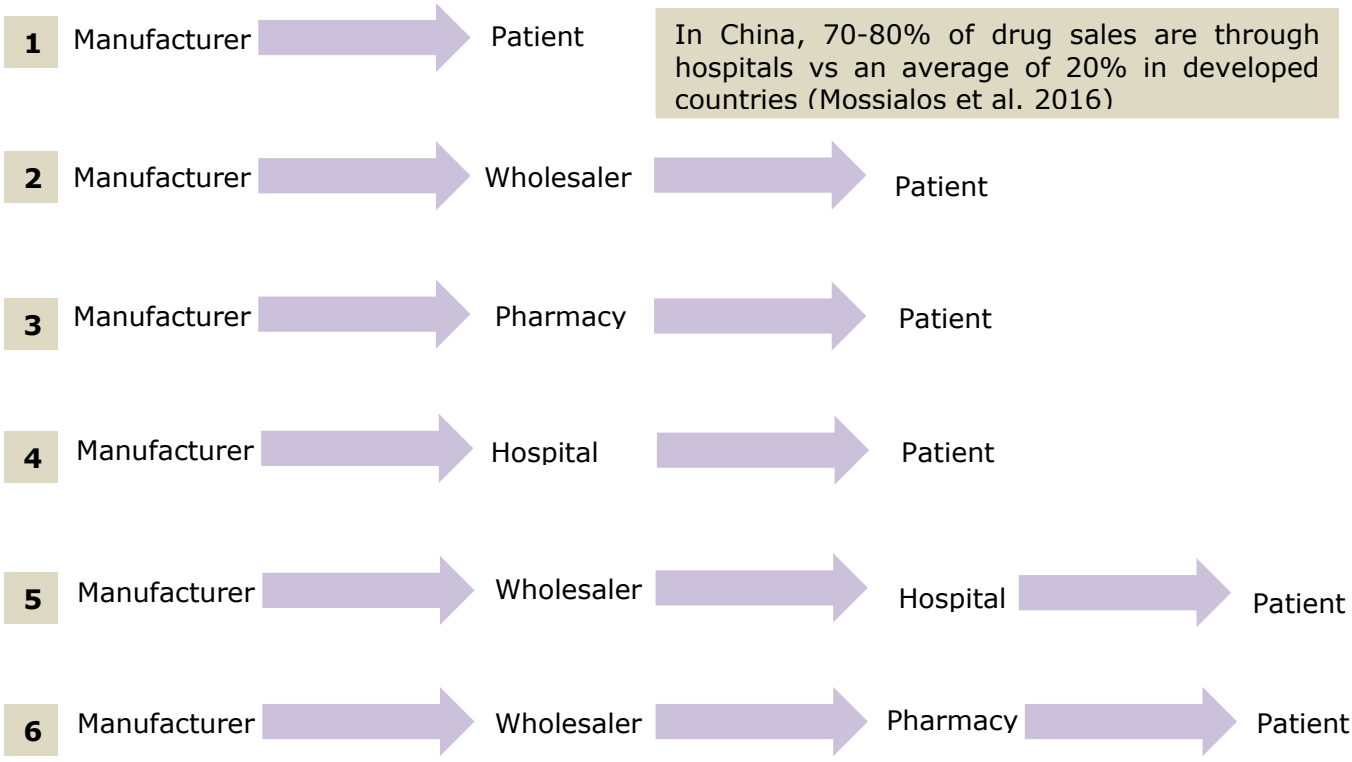
- Until recently, new products had to wait up to 3 or 4 years for addition to the NRDL. The process of adding new products to the NRDL requires formalization
- Emerging technologies, such as personalised medicine, are growing fast in China, but high costs and needs-based concerns are the major obstacles for them to enter the public health insurance system.
- The zero-mark-up policy has removed a substantial portion of health facility revenues, and government subsidies have not adequately compensated for this loss. Consequently, utilisation of other fee-for-service health services and unnecessary examinations have increased.
- The key challenge is for policy to provide the right incentives to guide healthcare providers and practitioners towards rational and efficient use of healthcare resources.

[1] *Within China, hospitals care classified within a three tiered system, based on the institutions ability to provide medical care and conduct medical research. Scoring is based on a number of factors including human and physical resources, type and number of departments, and teaching and research capabilities. The highest tier is reserved for tertiary hospitals considered to be domestic leaders in medical care with international influence (Mossialos et al. 2016).*

5.1.2. Drug Distribution and Supply Chain

Historically, the supply side of the pharmaceutical market featured a large number of small manufacturers and many layers of the wholesale distributors, both of which inevitably lead to low economies of scale and higher distribution costs. Pharmaceutical products go through several middle-man distributors from the manufacturer to reach hospitals and pharmacies. Fragmentation in manufacturing and distribution has led to insufficient regulatory oversight, low drug quality, and high drug prices (J. Hu and Mossialos 2016). In principle, patients had several potential access routes to pharmaceutical products. Manufacturers could sell directly to patients, through a pharmacy to patients, through a wholesaler to patients, through a wholesaler to hospitals to patients, or through a wholesaler to pharmacy to patients (Figure 7). Along the way, distributors would add mark-ups to products, contributing to the high price of medicines within China. Recently, the Development Research Center of the State Council reported that patients pay upwards of 10 times the ex-factory price of medicines due to mark-ups throughout the distribution chain, while IMS estimates the increase in price to be 52% (IMS 2015).

Figure 7 – Drug Distribution Chains in the Chinese Pharmaceutical Sector



Two Invoice Policy

- Limits number of distributors between manufacturers and hospitals to one.
- Both Manufacturer and Distributor required to provide invoices

In 2016, the 'two-invoice' policy was launched with the aim of reducing the number of middle-men and mark-ups within the drug distribution chain. Under the 'two-invoice' policy, the number of distributors between manufacturers and hospitals is limited to one. Further, both manufacturers and distributors are required to provide invoices reporting the sale price, thereby improving transparency within the distribution system. Exceptions are granted for exclusive

distributors of imported drugs, for emergency circumstances, distribution of specially administered drugs (e.g. anaesthetics) and for distribution to hospitals in remote or rural areas. Hospitals are required to obtain invoices from both the drug manufacturer and the distributor making both the ex-factory price and profit margins fully transparent to hospitals. Manufacturers found to be non-compliant may be banned from future provincial bidding events and blacklisted from procurement practices. The system was initially launched as a pilot, with the aim of implementing it in all public hospitals by the end of 2018 (Multiple Ministries 2018).

More recently, and as part of the 2017 major health reform, the State Council identified further reform of the drug distribution system as a key priority. A focus was placed on improving urban and rural distribution networks through consolidation of pharmaceutical distributors. M&As of pharmaceutical distributors will help to integrate warehouse and transportation resources. Further, the state council reiterated the aim of fully implementing the "two invoice" policy by 2018 (State Council 2017).

While there is little empirical evidence on the consequences of the dual-invoice system from peer-review literature, expert interviews suggest that this policy may do little to lower drug prices on its own. It does not address the fundamental issue that hospitals have an economic incentive to profit from drug sales, thus many demand under-the-table rebates for allowing drugs to enter the hospital. Against this background, many distributors are in fact sales agents for pharmaceutical manufacturers, who are seeking economic rents for their connections with hospitals. The dual-invoice policy is a reform on nominal factors. While it could drive many small-scale middle-man distributors out of business, the economic interest links between pharmaceutical manufacturers and hospitals remain. Pharmaceutical manufacturers are likely to raise the ex-factory prices to absorb the profits previously earned by distributors through markups, instead of outsourcing this process to distributors.

That said, the dual-invoice system is likely to push the pharmaceutical market towards a more concentrated structure, as well as having some positive effects on alleviating local protection issues. It will help develop regional and national distribution centres that are more specialised in distribution rather than promoting pharmaceutical products. Under these circumstances, the distribution process would be more transparent, and regulation of the distribution would be made easier.

Key messages and remaining gaps

- Historically, China's drug distribution chain was fragmented and characterised by high mark-ups. In 2016, China launched a 'dual-invoice' system pilot to reduce the number of distributors between manufacturers and hospitals and to provide greater transparency to the drug distribution chain. The system is expected to be implemented across all public hospitals by the end of 2018 and will need to be monitored closely to assess its impact.
- While the dual-invoice policy could change the existing distribution structure and help develop large-scale regional and national distributors, it would do little to reduce prices. The remaining gap would be to address the issue that hospitals have the economic incentive to profit from drug sales.

5.1.3. Prospective payment systems (PPS)

A number of studies attribute China's history of overprescribing to the payment models and financial incentives that dictate health care providers income at all levels of health care facilities (S. Zhang et al. 2015; Yang et al. 2016; Mao et al. 2015; Y. Gong et al. 2016). Prior to 2009, healthcare providers were able to mark-up the price of pharmaceuticals and as a result derive a significant portion of their income from pharmaceutical sales. The 2009 reform attempted to decouple physician income from drug sales by eliminating drug mark-ups and in return providing additional government funding and higher payments for other health services. Despite additional government funding, many health facilities reported a substantial decrease in revenue following the 2009 healthcare reforms. Further, given the insufficient government subsidy to account for lost revenue, health care providers have looked for other means of compensating for their loss of income, resulting in a doubling of inpatient services use (H. Yi et al. 2015).

Currently, health care facilities across China are reimbursed retrospectively for the services they provide, in what is typically referred to as a fee-for-service payment model. Insufficient government funding has led medical departments to set specific revenue targets, thereby incentivizing doctors to overprovide health services (Yang 2016). Alternatively, governments may wish to structure healthcare payments based on a prospective system, whereby all revenue is fixed prior to the provision of services. This may be done on a per-patient basis through capitation models where healthcare providers are payed a fixed amount for each patient they see, through global budgets where the total budget for a healthcare facility is fixed, or through salaries where physicians are paid a fixed amount either monthly or annually, independent of services provided. In theory, these three payment models decouple physician income from the services they provide. However, if structured incorrectly, prospective payment systems can incentivize cost-shifting or cream skimming, whereby physicians only choose to treat less expensive patients and shift expensive patients to other health facilities, in an attempt to lower costs. Many prospective payment models therefore include performance bonuses to further incentivize rational provider behaviour (S. Y. Tan and Melendez-Torres 2018).

While a comprehensive pay for performance model has not been implemented across China yet, several prospective payment system (PPS) pilots have taken place over the past few decades. Table 7 summarises the results of these initiatives.

Table 7. Overview of PPS pilots in China

Type of Prospective Payment Model	Scope	Details	Key results
Capitated budget and pay for performance	Township and village health centres- Two mountainous counties in Ningxia province, 28 towns, 266	Comparison between FFS and capitated budget in terms of rates of antibiotic prescription, total expenditure per visit and drug expenditure per visit, outpatient visit volumes, patient satisfaction, and	PPS resulted in decreases in total cost per admission but had an insignificant effect on drug cost/technology procedures. There was a tendency for cost shifting from low to high level

	villages (from 2009-2012)	time devoted to tasks that were incentivised and not incentivised by the intervention.	facilities. No change was seen in patient volume. There was a decrease in % of antibiotic prescription per prescription.
Capitated global budget	6 hospitals in Haikou (from 1995-1997)	Global budget determined based on historical data with risk adjustment. Outcome measures were expenditure on expensive drugs per inpatient admission, expenditure on high technology procedures per inpatient admission, and expenditure on standard inpatient bed charges per inpatient visit.	Introduction of PPS did not significantly change total cost per admission but did decrease drug cost per admission. Interestingly there was an increase in % of expensive diagnostics and of expensive unnecessary drug prescriptions.
Capitated budget and pay for performance	Two counties in Shandong province, 29 THCs in both counties (from 2011 to 2012)	Budget set based on population size. Comparison between FFS and capitated budget for out-of-pocket expenditure per prescription, polypharmacy indicator, and cost of consultation	PPS resulted in a decrease in % of expensive/unnecessary drug prescriptions but not significant change in other outcome measures.
Salary and pay for performance	Two rural townships (Fengshan and Machang) in Guizhou province, China (From 2002 to 2006)	Outcome measures included utilisation (number of outpatient doctor visits at village, township and county level health facilities), cost (spending on out-patient services at each of the three levels, and prescription behaviour among village doctors (% hormone prescription, % intravenous injection, % of combining use of three antibiotics during one visit, average expense per visit, average drug expense per visit, and average treatment expense per visit	PPS resulted in a decrease in total cost per admission in village health centres, but an increase in total cost in THC. There was also a decrease in total drug cost per admission. The PPS also resulted in a tendency for cost shifting from low to high level facilities.
Capitation	URBMI enrolees in Changde city, Hunan province (from 2008-2010)	Budget set based on historical data and risk adjusted. Outcome measures include inpatient medical expenditure, out of pocket expenditure, OOP expenditure as a share of total inpatient medical	PPS did not significantly change total cost per admission or drug cost per admission. Cost shifting tendency was present from patients with poor health to patients with good

		expenditure, drug to total expenditure, treatment effect, patient satisfaction.	health. Decrease in length of stay

Source: (S. Y. Tan and Melendez-Torres 2018).

While the results of PPS pilots were mixed, some general trends emerge. PPS implementation in China successfully reduced total costs per admission and specifically drug cost per admission. However, some of these costs are being shifted from lower levels of health facilities to higher levels. While it is unclear what impact this cost shifting has on patient outcomes, quality assurance mechanism and clinical guidance are likely needed alongside these payment models to ensure that patients with poor prognosis are still receiving adequate care (S. Y. Tan and Melendez-Torres 2018).

Beyond capitation, salary, and global budget PPS, hospitals can also bundle payment by disease area through Diagnosis-Related Group systems (DRG). DRG systems classify hospital cases in to specific diagnosis-related groups with fixed levels of reimbursement. The fee reimbursed for each case is fixed regardless of costs incurred. Interviewees suggest that wisespread implementation of a DRG-based system is limited by poor linkage and sharing of patient data across healthcare facilities. Hospitals typically have independent electronic health record systems. Often hospitals may not recognize test results brought by patients that were provided by another hospital. Further, provider code diagnoses in different ways, creating a barrier to implementation of a universal DRG-system.

> *"There are a mix of different payment methods at present. Some are paid for by day, for instance, nursing homes. Dialysis is paid for by person-times. Others are paid for by cases. But overall, it is the simplest to have global budget control, from the perspective of health insurance funds. The budget is set based on some historical numbers; anything over the budget is not paid by insurance or shared by the hospital and insurance. DRG pilots have been going on for three years. The pilots varied a lot across regions. It is still a trial at this stage. Wide implementation nationwide is going to take some time, or nearly impossible. Government is still advocating a mix of different payment methods."* - Leading academic expert

As part of the 2017 healthcare reform policy, the State Council once again highlighted the de-linkage of hospital funding from drug sales as a priority. The 2017 reforms reiterate that prescriptions must be made by generic name, and have stipulated that local health and family planning departments set healthcare expenditure growth targets. In this context, medical institutions will be provided with targets linked to government subsidies and performance evaluation in order to help control irrational growth. Further, the State Council intends to reform the basic medical insurance payment model to a prospective system, with funding fixed at disease level and supplemented with capitation schemes, thereby delinking hospital revenue from drug and diagnostic use. However, the specific details and timeline for implementation of this reform remain unclear (State Council 2017).

Key messages and remaining gaps

- The current fee-for-service model of reimbursement in China likely incentivises over-prescribing and over-utilisation of health services. Targeted policies such as the zero-mark-up have led to cost-shifting from pharmaceuticals to other health services and overall health expenditure in China continues to rise.
- The use of prospective payment models has been explored in several contexts with mixed results. Applying a prospective payment model such as global budgeting or capitation, generally reduces total cost per admission and drug cost per admission. However, some evidence reports that PPS incentivises cost-shifting which raises concerns about the quality of care.
- Differences in electronic health record systems represent a significant barrier to implementation of a universal DRG-payment model.
- Providing the right incentives is key to the design of payment systems.

5.1.4. Generic Substitution

In 2007, the prescription management ordinance was introduced which indicated that all prescriptions must be made by International Nonproprietary Name (INN). However, it appears there has been very little enforcement of this regulation as physicians typically prescribe by INN and simultaneously indicate the desired manufacturer or brand name. Further a disconnect is present between the prescription management ordinance and hospital IT systems which tend to list products according to brand name (Wenjie Zeng et al. 2015).

"A lot of this is down to habit. It's difficult to change physicians' prescribing habits---they've been using brand names for years. And often the hospital IT system doesn't facilitate prescribing by generic names in its supposed sense. There would be two or three brand names listed under each generic name, and then the system would require the physician to select one. They would have to let the pharmacy know in this way which brand name was prescribed. " – Pharmacy Director at a hospital

Prescribing by brand name, when equivalent generics are available, represents a substantial source of inefficiency. One study, which investigated the use of branded vs generic versions of proton pump inhibitors, reported that total expenditure could have been reduced by 84%

between 2004 and 2012 with improved generic substitution (Wenjie Zeng et al. 2015). Substantial loss of potential savings are also noted for prescriptions of statins, angiotensin inhibitors and TCMs, where generic utilisation levels range between 20 and 34% of total utilisation (W. Zeng et al. 2015). Fundamentally, the difficulty of enforcement of prescribing by brand name comes from a number of sources: 1) different brand name drugs under the same generic name are, at least perceptually, of different quality; 2) physicians may receive financial incentives from drug manufacturers to disproportionately prescribe certain brand names; 3) pharmacies do not have the autonomy of choosing from substitute generics.

In addition to poor enforcement of the prescription management ordinance, poor perceptions of the quality of generic medicines also presents a barrier to improved utilisation of generics. While reforms in equivalence regulation will help to address this issue, a long history of poor generic quality and misconceptions that higher priced products are associated with greater efficacy remain (J. Sun et al. 2018). Strengthening the use of generic medicines in China, particularly for essential medicines, is a key goal of the 13th FYP (NDRC 2016b). Recently, the NDRC issued a Departmental Work Plan of the Opinions for Promotion of Healthy Development of the Pharmaceutical Industry. This notice reiterates that healthcare professionals are required to write prescriptions using only generic drug names (NDRC 2016a).

Key messages and remaining gaps

- Health care providers have largely circumvented the prescription management ordinance implemented in 2007, which requires prescribing by INN.
- Poor perceptions about the quality of generic products remain across both healthcare providers and patients. As a result, overall utilisation of generic products remains low.
- It is too early to determine what the impact of the 2016 amendments to the Drug Registration Regulation will be, as the review process for re-registration is on-going.

5.1.5. Clinical guidelines

In 2015, the NHFPC established the National Center for Medical Service Administration. Once of the key functions of this agency is to promote quality of care and to greater use of clinical guidelines. The agency is currently working in collaboration with the WHO Collaborating Centre for Guideline Implementation and Knowledge Translation. Historically, the use of clinical guidelines in China has been highly variable. China is unique in its use of both Western medicine and traditional Chinese medicines. Guidelines must be able to help provider employ evidence based decision making across both types of medicines. With appropriate implementation and uptake, clinical guidelines can help reduce variability of care across settings (Chen 2018).

The publication of clinical guidelines has increased annually in China, from less than 50 in 2010 to over 120 in 2016. However, the quality of Chinese guidelines is typically lower than those from other developed countries, with significantly fewer overall citations and fewer Cochrane review citations. (Yu and Xu 2015; Zheng et al. 2015; Yun Gong 2016; J. Huang et al. 2015; Wu, He, and Mao 2016; Dai et al. 2015; Xi. Yi et al. 2018; Zhuolin Sun, Ding, and Li 2017; H. Tan et al. 2016). Evidence on dissemination, implementation and adherence to guidelines in China is extremely limited. One study showed adherence rates to guidelines on TCMs was approximately 50%, while another showed adherence rates of 20-40% for the treatment of gout (Liu et al. 2017, Sheng et al. 2014). Feedback from interviewees suggest many of these guidelines are based on consensus and lack scientific rigour. Adherence to guidelines generally is much lower among low-tier healthcare providers due to lack of awareness. Access is another major issue among these practitioners.

Improvements in the quality and implementation of clinical guidelines in China will require a coordinated and systematic approach. Existing guidelines should be comprehensively reviewed before developing new guidelines. Guidelines should be tailored to local needs, recognising that diagnostic criteria and treatments used in Western countries may not apply perfectly within China. National standards should be established for guideline methodology, quality, and implementation in order to promote effective dissemination and adherence. Finally, enhanced international communication and collaboration will play a key role in sharing best-practices and promoting the development and use of high quality guidelines (Chen 2018).

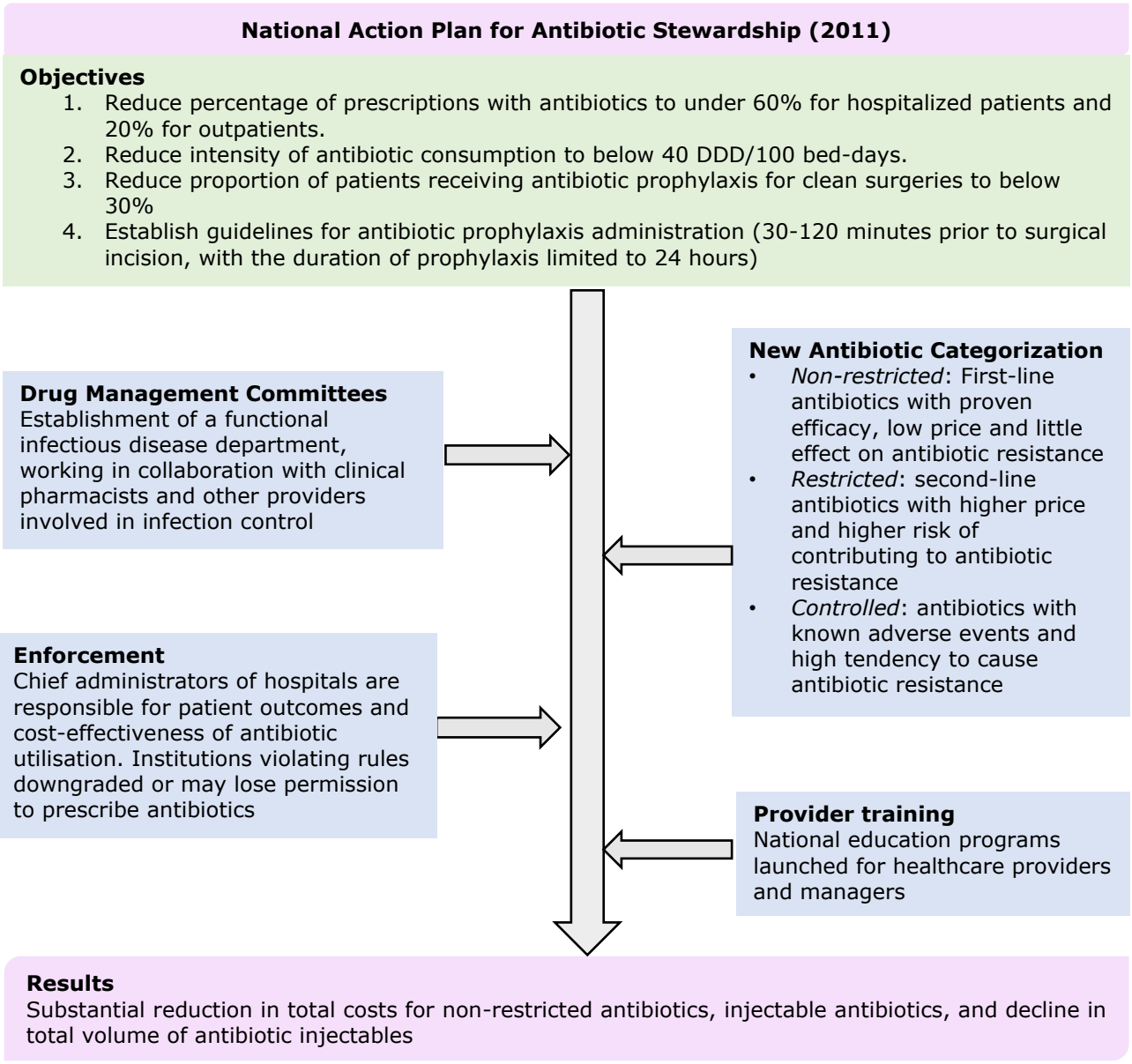
Key messages and remaining gaps

- Both the availability and adherence clinical guidelines is highly variable within China. Guidelines often lack scientific rigour, which limits their implementation.
- A formalised national guideline system is needed to improve the use of clinical guidelines in China. The establishment of the National Center for Medical Service Administration is a positive step, but it's impact thus far is unclear.

5.1.6. Disease Specific Initiatives

While the zero mark-up policy has only had marginal impacts on levels of inappropriate prescribing, more targeted initiatives may have been more successful. In 2011, the Chinese government implemented a National Action Plan for Antibiotic Stewardship providing both administrative and professional strategies for guiding antibiotic prescriptions (Figure 8). Under the action plan, antibiotics are categorized under three groups: 1) non-restricted, 2) restricted, and 3) controlled. Health workers in village clinics are only permitted to provide non-restricted antibiotics, and must obtain approval from county health bureaux for intravenous infusions. Restricted antibiotics, and controlled antibiotics are limited to secondary and tertiary hospitals. Clinical guidelines were issued on the clinical conditions and evidence required to justify antibiotic use. Prescriptions are audited on a regular basis according to these guidelines. Institutions violating rules may be downgraded or may be required to dismiss managers, or medical practitioners may lose permission to prescribe antibiotics (Tang et al. 2018; Bao et al. 2015).

Figure 8 – Case Study – National Action Plan for Antibiotic Stewardship



(Source: The authors, adapted from Tang et al. 2018 & Bao et al. 2015)

The national action plan for antibiotic stewardship was associated with a statistically significant reduction in total costs for non-restricted oral antibiotics and for injectable antibiotics, as well as a decline in the total volume of antibiotic injectables between 2011 and 2013 (Tang et al. 2018; Bao et al. 2015). However, some challenges remain as many health facilities lack the laboratory equipment to properly follow guidelines, forcing physicians to prescribe according to experience. Further, lack of inpatient beds and overcrowding also contributes to inappropriate prescribing. Enforcement issues are noted at all levels of care (T. Zhang, Graham, and White 2018).

Some pharmaceutical policies in this area are conditioned by higher-level policies. For instance, poverty alleviation has been a policy focus in a broad context. Reflected in pharmaceutical policy, this results in some disease-specific initiatives that target socio-economically disadvantaged individuals. For instance, in 2017, NHC set up a hypertension management office at the National

Center for Cardiovascular Diseases. The objectives are to establish hypertension clinical guidelines for primary care institutions, building capacity for hypertension management at primary care levels, and monitor prescribing at these institutions. One specific task of this office is to estimate the cost of free hypertensive drugs dispensed to poor individuals in rural areas, coupled with prescription audits, regular monitoring and tracking of these patients. Strengthening China's weak primary care system is a long-term task, and would require a system of such policies to build capacity and improve its professional abilities.

Key messages and remaining gaps

- The Chinese government has made appropriate prescribing and use of antibiotics a key national health priority. Historically, levels of antibiotic prescribing in China were well above WHO recommended levels, and China has faced significant global criticism for their contribution towards antibiotic resistance.

- The National action plan for antibiotic stewardship provided several key administrative and professional strategies for guiding the prescription and use of antibiotics. The plan was associated with a significant improvement in antibiotic prescribing. However, some primary health facilities lacked equipment to properly follow guidelines, and enforcement was inconsistent across all levels of care.

5.2. Demand-side policies

5.2.1. Cost-sharing

> *"The health reforms paid a lot of attention to prices, but not on volumes. In practice, there is a lot of unreasonable use, a waste of health resources. This is a major reason why drug expenditures in China remain so high."* - Leading academic expert

Demand-side policies aim to influence patient behaviour and encourage rational use of health services. In the year 2000, only 15% of the population in China was covered under health insurance, and for most, utilisation of health services was often associated with catastrophic expenditure (Hsiao, Li, and Zhang 2015). Until recently, there have been three key health insurance plans which have operated to provide universal coverage to the Chinese population. The UEBMI insurance plan was first established in 1998 for urban formally employed residents, the NCMS was subsequently established in 2003 to provide rudimentary coverage for rural populations, and, in 2007, the URBMI was established for urban residents without formal education (Chai et al. 2018, 201). Since their inception, all three schemes have gone through significant changes in terms of their size, number of services covered, and percentage of costs covered (Kaplan et al. 2017). In particular, as part of the 2009 healthcare reforms, the Chinese government committed an additional USD 124 billion in public spending over three years in order to expand population coverage, through one of the three schemes, to over 90%. Target subsidies were set for both urban and rural residents not currently covered, with the aim of close 90% of premiums for poorer areas in Western China, and up 70% in wealthier coastal regions. Between 2009 and 2011, the premium paid by governments rose from 80 RMB to 200 RMB. Further, complimentary medical assistance programmes were established to cover the remaining out-of-pocket fees for particularly poor families. In order to encourage enrolment, targets were set for village and community leaders as part of their performance measurement for future promotion (Hsiao, Li, and Zhang 2015). Prior to 2009, the NCMS and URBMI only covered inpatient services. In an effort to strengthen the primary care system, coverage for outpatient services through the NCMS and URBMI were gradually expanded.

By the end of 2011, over 95% of the population in China was covered through one of the three insurance schemes. However, patients in the NCMS or URBMI still paid upwards of 50% of their costs for outpatient and inpatient services as reimbursement ceilings are present across all patients. Further, significant disparities existed in the amount of funding and coverage between the urban UEBMI scheme and the URBMI and NCMS schemes. In an attempt to provide a unified coverage and to improve risk and fund pooling, the Chinese government has recently announced it intends to merge the three insurance programmes (Kaplan et al. 2017).

While patient co-payments remain high, expansion of coverage as part of the 2009 healthcare reforms have resulted in a significant increase in the use of health care, particularly amongst poor populations. However, health utilisation has also increased in urban areas, and OOP spending has also been reported to have increased in these regions (Hsiao, Li, and Zhang 2015).

Key messages and remaining gaps

- China has taken significant strides towards universal health coverage following the 2009 reforms, and the utilisation of health services has increased substantially, particularly in rural areas.
- Cost-sharing remains high and the package of services reimbursed is limited. The ability of health insurance to promote access to medicines is limited by the implementation of reimbursement ceilings.
- Disparities remain across provinces, and across urban and rural residents. It is too early to determine what impact merging the three health insurance plans will have on reducing these disparities. Additional work is needed to determine how levels of cost-sharing vary across regions and the extent to which current levels of cost-sharing discourage the use of health services, particularly in vulnerable populations.

5.2.2. Patient education

One of the key contributing factors to irrational use of medicines in China is patient health literacy, particularly surrounding the use of antibiotics, injectable, and generic products (Mao et al. 2015; J. Sun et al. 2018; Dyar et al. 2018; H. Chen et al. 2018). Prevailing attitudes around these products are that antibiotics are a cure-all, that injectable have improved efficacy over orally administered drugs, and that generic products, particularly low-priced generic products, are inferior to branded medicines. While physicians are often in a position to prescribe appropriately, patient demand often influences prescribing behaviour. In particular, primary care doctors are more likely to acquiesce to patient demands, given competition across primary care facilities and the risk of losing patients to other practices (J. Sun et al. 2018). Overall, these perceptions contribute to a substantial source of inefficiency in the Chinese pharmaceutical sector (W. Zeng et al. 2015; J. Zeng et al. 2015). No studies were identified that evaluated the impact of a targeted patient education programme for improving rational use of antibiotic, generic, or injectable medicines. As such, the ability of patient education programmes to change perceptions and improve the rational use of medicines in the Chinese context remains unclear.

Beyond irrational use of medicines, patient education also plays a key role in the management of chronic diseases. In this context, patient education programmes often aim to limit acute exacerbations of the diseases. From an efficiency standpoint, this plays a critical role as avoidable acute exacerbations often result in extended hospital stays or use of outpatient services. In a pilot of a digital health coaching programme, patients reported statistically significant improvement in quality of life through participation in health coaching and a reduction in health services use. Some variability was noted across disease areas, with Rheumatoid Arthritis patients reporting the highest improvements (Burton et al. 2018).

Key messages and remaining gaps

- Poor patient health literacy has been a key contributor towards issues of inappropriate use of medicines in China. Based on the evidence collected, it is unclear how the issue of patient health literacy is being addressed within China.
- Patient education can play a key role in managing chronic diseases, improving patient outcomes and reducing avoidable costs from acute exacerbations.

Because of the 2009 reforms, China has made substantial progress in improving its health system in a short period of time; most notably, it has achieved near-universal coverage of health insurance, it has established the EML and it has lowered prices for these drugs. Nonetheless, many challenges still exist in the Chinese pharmaceutical sector, from R&D, to manufacturing, distribution, and dispensing of drugs on the supply side, and irrational prescription and use on the demand side.

5.3. HTA and negotiations

Currently, HTA application is fragmented, sporadic and not fully embedded in the policy making process in China. While decision makers are aware of HTA, it is not mandatory. Recent reforms and changes to the national reimbursed drug list (NRDL) in 2016/2017 suggest that China is eager to move towards a more evidence-based pricing and reimbursement system. In 2016/2017, as part of the most recent update of the NRDL, The Ministry of Human Resources and Social Security (MOHRSS) employed an evidence-based, value-driven approach (previously the approach was passive without scientific input). Specifically, focus was placed on areas of serious disease, paediatric medications, medications for work-related accidents, and TCMs. Despite the update, several expensive but innovative and potentially life-saving products are excluded from the formulary, thereby restricting access for patients able to pay out-of-pocket. As a result, the central government initiated a pilot project in 2017, whereby pharmaceutical companies were invited to submit evidence dossiers in order to inform a subsequent price negotiation. Agreements were reached for 36 out of 44 high-priced innovative medicines, and these were subsequently added to the NRDL. In order to continue to promote rational use of medicines, this process will need to be formalized through legislation, with clarity on submission processes and requirements, product eligibility, types of evidence considered, and evaluation processes and timelines. In October 2018, China established National Pharmaceutical and Health Technology Assessment Center, however it remains unclear how HTA will be integrated in the decision making process. Interviews with key opinion leaders suggest the HTA will likely play more of an advisory role to begin with and will be taken into consideration as part of the price negotiation process. This role will need to be explicitly defined, along with clear guidelines for the HTA scope and evaluation criteria.

5.4. Pharmaceutical pricing

Despite recent successes with the negotiation pilot, improvements are still needed in pharmaceutical pricing for both originator and generic products. Medicine expenditure in public hospitals has been controlled since 2009, with price cutting, zero mark-up policies and dual invoicing featuring as key cost-containment initiatives. While implementation of these initiatives has continued to grow, these efforts are largely undermined by poor utilisation of generic products. Prior to 2015, generic products were subject to extensive price ceilings and cuts, while at the same time suffering from quality issues, resulting in originator products maintaining price monopolies after loss of market exclusivity. Abolishment of price ceilings in 2015 has helped alleviate this somewhat, but under-utilisation of generics remains an issue. While tendering helps to drive down prices, the current model of reimbursement fails to adequately promote generic use. Switching from a fixed percentage reimbursement rate model to a tiered-co-payment model with full reimbursement for generics (set based on internal reference pricing), will likely help to

alleviate some of these issues. Specific drug approval and pricing policy measures also need to be in place to ensure generic drugs are of good quality. In terms of in-patent products, while the goal may ultimately be to move towards an evidence-based system with HTA and pricing negotiations for innovative and expensive products, external reference pricing can provide a reasonable stop-gap until capacity in this area is built.

5.5. Generic policy

Poor utilisation of generic products is a significant source of inefficiency in the Chinese health system. Reforms to the Drug Registration Regulation in 2016, require all generic firms to re-ensure the interchangeability of their products, moving closer towards international standards. This is intended not only to improve the perception of generic drugs in health care providers and patients within China, but also internationally given the large number of domestic generic manufacturers. Evidence from literature suggests that this process has been time-intensive and opaque. More resources are required to strengthen the review team, and improved coordination with regulatory authorities is needed. Overcoming widespread perceptions that generic products are inferior to branded products will require additional initiatives targeting both healthcare professionals and patients through training workshops, public awareness campaigns and other patient education initiatives. Once the quality of generics is confirmed, INN prescribing or mandatory generic substitution should be considered.

5.6. Healthcare provider payment models (PPS)

PPS are the most direct ways to providing incentives to guide provider behaviors. Currently, China still operates predominantly on a retrospective fee-for-service payment model. While implementation of the zero mark-up policy has helped to reduce the incentive to overprescribe medicines, rates of over-prescribing and inappropriate prescribing, particularly in the context of antibiotics and injections, remain high relative to WHO recommendations for low and middle income countries. In particular, levels of inappropriate prescribing tend to be higher in primary care where patients have greater choice and ability to move practices, resulting in a tendency for physicians to be more compliant with patient demands. Further, rates of inappropriate prescribing are lower in healthcare professionals with higher levels of training. Evidence from literature suggests that prospective payment models, such as salary, capitation, and global budgets, can help to reduce over-prescribing and improve rational use of medicines. Several pilots have been carried out within China involving the implementation of prospective payment models in both in-patient and out-patient settings. Recent policy reforms point to a case-based payment system, but the system may be oversimplified, and new problems emerge as to "gaming the system", such as reducing the length of patient stays, increasing readmissions, and admitting outpatients who do not need to be hospitalized. While the results have been variable, in general PPS reduced health expenditures on both the supply and demand side, as well as length of stay and readmission rates. By providing the correct incentives, PPS generally improved service quality outcomes by reducing the likelihood or percentage of physicians prescribing unnecessary drugs or diagnostic procedures. Greater implementation of PPS throughout China may help to further reduce irrational prescribing, however careful monitoring is needed to ensure quality of services does not decline. Future effort in this area should focus

on refining the specifics of payment methods with better data. In addition, initiatives that aim to improve health literacy in both health care professionals and patients are also required.

5.7. Healthcare financing and primary care

One of the key priorities of the 2009 health reforms was to improve equitable access to medicines. This priority has been reiterated in the 13th FYP. While near universal coverage has been achieved, the extent of coverage varied considerably from urban to rural settings. Of the three health insurance programmes (UEBMI, URBMI, and NCMS), levels of coverage were considerably lower for NCMS. In order to provide a more unified coverage, China announced plans to merge the three programmes, however it still too early to determine if this will help to alleviate access issues in rural settings. The enactment of the EML policy since 2009 has in general improved access to essential medicines. It requires all primary healthcare facilities to stock and sell essential drugs. But implementation is faced with great challenges, and marked inefficiencies still exist in distributing essential drugs to patients. Many primary care institutions still do not have an adequate stock of essential drugs: a national-scale survey in 2016 found that 8% of primary care facilities do not stock any anti-hypertensive drugs, especially in poor rural areas (Su et al. 2017). Moreover, only 33% stock low-cost high-value anti-hypertensive drugs. There is much to be done on extending the coverage of essential drugs, improving drug procurement and distribution, and lowering financial burdens on patients, to ensure equitable access to essential medicines (Q. Yao et al. 2014; Guan et al. 2015). In addition, problems persist in funding healthcare following the 2009 health reforms. Removal of income from mark-ups has not been adequately replaced through government subsidies. In particular, village doctors have reported loss of income and increased dissatisfaction with work. Reports have emerged that doctors are secretly implementing mark-ups to supplement their income. While unification of health insurance programmes may help improve access to medicines in rural settings, increases in government subsidies and financing and strengthening of the weak rural healthcare system will also be required to address shortages in physician income structure. Boosting the primary care quality, particularly through training workforce and attracting talent to primary care institutions, will gradually change patients' perception of poor care quality associated with these healthcare facilities and encourage them to utilize community healthcare resources more efficiently.

6. References

Bao, Lidao, Rui Peng, Yi Wang, Ruilian Ma, Xianhua Ren, Wenbin Meng, Fusheng Sun, et al. 2015. "Significant Reduction of Antibiotic Consumption and Patients' Costs after an Action Plan in China, 2010–2014." *PLOS ONE* 10 (3): e0118868. https://doi.org/10.1371/journal.pone.0118868.

Barber, Sarah L., Baobin Huang, Budiono Santoso, Richard Laing, Valerie Paris, and Chunfu Wu. 2013. "The Reform of the Essential Medicines System in China: A Comprehensive Approach to Universal Coverage." *Journal of Global Health* 3 (1). https://doi.org/10.7189/jogh.03.010303.

Burton, S., U. Srivastava, D. Patel, and M. Rasulnia. 2018. "Impact of Digital Remote Health Coaching for Patients with Chronic Conditions on Quality-Adjusted Life-Years." *Value in Health* 21 (May): S109. https://doi.org/10.1016/j.jval.2018.04.739.

CFDA. 2018. "2017 Annual report on drug reviews." China Food and Drug Administration (CFDA).

Chai, Jian, Limin Xing, Youhong Zhou, Shuo Li, K. K. Lai, and Shouyang Wang. 2018. "Impact of Healthcare Insurance on Medical Expense in China: New Evidence from Meta-Analysis." *Soft Computing* 22 (16): 5201–13. https://doi.org/10.1007/s00500-017-2928-5.

Chen, H., C. O. L. Ung, P. Chi, J. Wu, D. Tang, and H. Hu. 2018. "Consumers' Perceptions About Pharmaceutical Care Provided by Community Pharmacists in China in Relation to Over-the-Counter Drugs: A Qualitative Study." *Inquiry* 55 (December): 46958018793292. https://doi.org/10.1177/0046958018793292.

Chen Yaolong, Wang Chen, Shang Hongcai, YangKehu, Norris Susan L. Clinical practice guidelines in China BMJ 2018; 360 :j5158

Chen, Yingyao, Yao He, Xunyouzhi Chi, Yan Wei, and Lizheng Shi. 2018. "Development of Health Technology Assessment in China: New Challenges." *BioScience Trends* 12 (2): 102–8. https://doi.org/10.5582/bst.2018.01038.

Dai, Lingfang, Yichuan Zheng, Weiqing Xu, Feng Xu, Limin Zhang, and Yuelin Xie. 2015. "Qu Xian Gongli Yiyuan Shishi Yaopin Lingchalu Zhengce Hou de Buchang Moshi Tantao 区县公立医院实施药品零差率政策后的补偿模式探讨 [Discussions on Compensation Models for District/County-Level Public Hospitals after the Implementation of the Zero Markup Policy]." *Zhongguo Weisheng Ziyuan 中国卫生资源 [China Health Resources]*, no. 4: 305–8.

Dyar, O. J., J. Yin, L. Ding, K. Wikander, T. Zhang, C. Sun, Y. Wang, C. Greko, Q. Sun, and C. Stalsby Lundborg. 2018. "Antibiotic Use in People and Pigs: A One Health Survey of Rural Residents' Knowledge, Attitudes and Practices in Shandong Province, China." *J Antimicrob Chemother*, July. https://doi.org/10.1093/jac/dky240.

Gong, Y., C. Yang, X. Yin, M. Zhu, H. Yang, Y. Wang, Y. Li, et al. 2016. "The Effect of Essential Medicines Programme on Rational Use of Medicines in China." *Health Policy Plan* 31 (1): 21–27. https://doi.org/10.1093/heapol/czv008.

Gong, Yun. 2016. "Quxiao yaopin jiacheng zhengce dui gongli yiyuan de yingxiang ji duice 取消药品加成政策对公立医院的影响及对策 [the impact of zero markup policy on public hospitals and countermeasures]." *Zhongguo shichang 中国市场 [China Market]* 10: 217–18.

Guan, Xiaodong, Baomin Wang, Xiaoxiong Xin, Zhigang Guo, Cheng Han, and Luwen Shi. 2015. "Mianfei Yongyao Zhengce Dui Cujin Zhongguo Yaopin Gongping Keji de Qishi 免费用药政策对促进中国药品公平可及的启示 [Free Medicine Policy: Lessons for Improving Equity and Accessibility of Pharmaceuticals in China]." *Zhongguo Weisheng Zhengce Yanjiu 中国卫生政策研究 [Chinese Journal of Health Policy]* 8 (2): 54–59.

Han, Q. Y., and Z. W. Liu. 2016. "Current Treatment of Chronic Hepatitis C in China: Dilemma and Potential Problems." *World J Gastroenterol* 22 (19): 4615–18. https://doi.org/10.3748/wjg.v22.i19.4615.

Hsiao, William, Mingqiang Li, and Shufang Zhang. 2015. "Universal Health Coverage: The Case of China." Working Paper 2014–15. UNRISD Working Paper. https://www.econstor.eu/handle/10419/148725.

Hu, Jia, and Elias Mossialos. 2016. "Pharmaceutical Pricing and Reimbursement in China: When the Whole Is Less than the Sum of Its Parts." *Health Policy* 120 (5): 519–34. https://doi.org/10.1016/j.healthpol.2016.03.014.

Hu, Shanlian. 2017. "Yaopin Gouxiao 'Liangpiaozhi' Zhengce de Lilun He Shijian 药品购销'两票制'政策的理论和实践 [Theory and Applications of the Two-Invoice Drug Procurement Policy]." *Weisheng Jingji Yanjiu 卫生经济研究 [Health Economics Research]* 0 (4): 8–10.

Huang, B., S. L. Barber, M. Xu, and S. Cheng. 2017. "Make up a Missed Lesson-New Policy to Ensure the Interchangeability of Generic Drugs in China." *Pharmacol Res Perspect* 5 (3): e00318. https://doi.org/10.1002/prp2.318.

Huang, Jizhi, Helang Huang, Xuan Zhou, Jianming Zhou, and Lei Wu. 2015. "Jiangxisheng xianji gongli yiyuan quxiao yaopin jiacheng zhengce libi fenxi 江西省县级公立医院取消药品加成政策利弊分析 [The analysis of advantages and disdavantages of zero markup policy in county-level hospitals in Jiangxi Province]." *Zhongguo Weisheng Shiye Guanli 中国卫生事业管理 [China Health Management]* 32 (6): 433–36.

Huang, Y., Y. Jiang, L. Zhang, W. Mao, J. F. M. van Boven, M. J. Postma, and W. Chen. 2018. "Availability, Use, and Affordability of Medicines in Urban China under Universal Health Coverage: An Empirical Study in Hangzhou and Baoji." *BMC Health Serv Res* 18 (1): 218. https://doi.org/10.1186/s12913-018-2993-1.

IMS. 2015. "Global Medicines Use in 2020." Institute for Healthcare Informatics.

Jain, A. B., Mollet, A., & Szucs, T. D. (2017). Regulatory watch: Structural and procedural characteristics of international regulatory authorities.

Kaplan, W. A., P. G. Ashigbie, M. I. Brooks, and V. J. Wirtz. 2017. "Comparison of Medicines Management Strategies in Insurance Schemes in Middle-Income Countries: Four Case Studies." *J Pharm Policy Pract* 10: 17. https://doi.org/10.1186/s40545-017-0105-y.

Li, Hong, Gordon G. Liu, Jing Wu, Jiu-Hong Wu, Chao-Hui Dong, and Shan-Lian Hu. 2018. "Recent Pricing Negotiations on Innovative Medicines Pilot in China: Experiences, Implications, and Suggestions." *Value in Health Regional Issues* 15 (May): 133–37. https://doi.org/10.1016/j.vhri.2018.01.009.

Li, Honglin, Enwu Long, Qing Shen, Hua Yang, Fei Wang, and Li Wu. 2016. "Guojia Yaowu Zhengce Dui Mou Xianji Gongli Yiyuan Jiben Yaowu Shiyong de Yingxiang 国家药物政策对某县级公立医院基本药物使用的影响 [The Impact of National Pharmaceutical Policy on Essential Medicine Use at a County-Level Public Hospital]." *Zhongguo Yaofang 中国药房 [China Pharmacy]* 27 (30): 4181–83.

Li, Xiaobin. 2016. "Yaopin Jizhong Caigou Zhengce Shishi Xiangguanfang Boyi de Nanti Yu Duice 药品集中采购政策实施相关方博弈的难题与对策 [Challenges in the Implementation of Centralised Drug Procurement Policy and Solutions]." *Zhonghua Yiyuan Guanli Zazhi 中华医院管理杂志 [Journal of Chinese Hospital Management]* 32 (7): 518–21.

Liu M, Zhang C, Zha Q, et a. A national survey of Chinese medicine doctors and clinical practice guidelines in China. BMC Complement Altern Med2017;17:451. doi:doi:10.1186/s12906-017-1946-2pmid:28877689

Liu, Shuomin. 2016. "Wanshan Woguo Yaopin Jiandu Guanli Tixi de Jiangxi: Jiyu Shandong Wenti Yimiao Shijian de Sikao 完善我国药品监督管理体系的建议——基于山东'问题疫苗'事件的思考 [Recommendations for Improving China's Pharmaceutical Surveilance System: Deliberation Based on the Shandong Substand Vaccines Incident]." *Xiandai Jingji Xinxi 现代经济信息 [Modern Economy Information]* 16. http://www.cnki.com.cn/Article/CJFDTotal-XDJZ201614024.htm.

MacQuilkan, Kim, Peter Baker, Laura Downey, Francis Ruiz, Kalipso Chalkidou, Shankar Prinja, Kun Zhao, Thomas Wilkinson, Amanda Glassman, and Karen Hofman. 2018. "Strengthening Health Technology Assessment Systems in the Global South: A Comparative Analysis of the HTA Journeys of China, India and South Africa." *Global Health Action* 11 (1): 1527556. https://doi.org/10.1080/16549716.2018.1527556.

Man, Chunxia, Xiaodong Guan, Wujie Zou, Zhigang Guo, Lili Ma, Yi Lu, and Luwen Shi. 2016. "Woguo Gesheng Yaopin Jizhong Zhaobiao Caigou Zhengce Fenxi He Sikao 我国各省药品集中招标采购政策分析和思考 [An Analysis of Centralised Pharmaceutical Procurement and Tendering Policies across Provinces in China]." *Zhongguo Weisheng Zhengce Yanjiu 中国卫生政策研究 [Chinese Journal of Health Policy]* 9 (7): 53–59.

Mao, Wenhui, Huyen Vu, Zening Xie, Wen Chen, and Shenglan Tang. 2015. "Systematic Review on Irrational Use of Medicines in China and Vietnam." *PLoS ONE* 10 (3). https://doi.org/10.1371/journal.pone.0117710.

McTiernan, R. 2014. "Au Revoir to Anhui: China's Shape-Shifting Tenders." *CPB Review* 85: 20–25.

Mossialos, Elias, Yanfeng Ge, Jia Hu, and Liejun Wang. 2016. *Pharmaceutical Policy in China: Challenges and Opportunities for Reform*. World Health Organization (WHO).

Multiple Ministries. 2016. "Yiyao gongye fazhan guihua zhinan 医药工业发展规划指南 [Pharmaceutical Industry Development Plan under the 13th Five Year Plan]." Ministry of Industry and Information Technology (MIIT) of China.

———. 2018. "Guanyu Gonggu Pochu Yi Yao Yang Yi Chengguo Chixu Shenhua Gongli Yiyuan Gaige de Tongzhi 关于巩固破除以药补医成果持续深化公立医院综合改革的通知 [Notice on Consolidating the Results and Further Implementing Public Hospital Reforms]." National Health and Family Planning Commission. http://www.nhfpc.gov.cn/tigs/s3581/201803/cf5b6ff7f55b4bc1a0d244f236008b32.shtml.

NDRC. 2016a. "Guanyu Cujin Yiyao Chanye Jiankang Fazhan de Zhidao Yijian Zhongdian Gongzuo Bumen Fengong Fang'an 关于促进医药产业健康发展的指导意见重点工作部门分工方案 [Departmental Work Plan of the Opinions for Promotion of Healthy Development of the Pharmaceutical Industry]." National Development and Reform Commisson (NDRC). http://www.ndrc.gov.cn/gzdt/201607/t20160725_812036.html.

———. 2016b. "'Shisan Wu' Shengwu Chanye Fazhan Guihua '十三五'生物产业发展规划 [13th Five-Year Plan for Biotech Sector Development]." National Development and Reform Commisson (NDRC).

NHFPC. 2015. "Guojia Weisheng Jishengwei Guanyu Luoshi Wanshan Gongli Yiyuan Jizhong Caigou Gongzuo Zhidao Yijian de Tongzhi 国家卫生计生委关于落实完善公立医院药品集中采购工作指导意见的通知 [Notice on Improving Implementation of Drug Procurement for Public Hospitals]." National Health and Family Planning Commission. http://www.nhfpc.gov.cn/yaozs/s3573/201506/36a74780403d4eed96ca93b665620941.shtml.

Ni, Jingyun, Junrui Zhao, Carolina Oi Lam Ung, Yuanjia Hu, Hao Hu, and Yitao Wang. 2017. "Obstacles and Opportunities in Chinese Pharmaceutical Innovation." *Globalization and Health* 13 (1): 21. https://doi.org/10.1186/s12992-017-0244-6.

Pan, Hui, Hongjun Luo, Shuru Chen, and William Ba-Thein. 2016. "Pharmacopoeial Quality of Antimicrobial Drugs in Southern China." *The Lancet Global Health* 4 (5): e300–302. https://doi.org/10.1016/S2214-109X(16)00049-8.

People's Daily. 2017. "Suoyou Gongli Yiyuan Quxiao Yaopin Jiacheng 所有公立医院取消药品加成 [All Public Hospitals Have Abolished Drug Markups]." *People's Daily*, December 11, 2017. http://paper.people.com.cn/rmrb/html/2017-12/11/nw.D110000renmrb_20171211_2-13.htm.

Sheng F, Zeng X, Fang W Adherence to treatment recommendations of gout: a patient survey in China. Arthritis Rheumatol2014;66:S76-7

State Council. 2016. "Shenhua Yiyao Weisheng Tizhi Gaige 2016 Nian Zhongdian Gongzuo Renwu 深化医药卫生体制改革 2016 年重点工作任务 [Major Tasks of 2016 for Deepening Pharmaceutical and Health System Reform]." The State Council of China. http://www.gov.cn/zhengce/content/2016-04/26/content_5068131.htm.

———. 2017. "Guowuyuan Bangongting Guanyu Jinyibu Gaige Wanshan Yaopin Shengchan Liutong Shiyong Zhengce de Ruogan Yijian 国务院办公厅关于进一步改革完善药品生产流通使用政策的若干意见 [Opinions for Further Reform and Improvement of Pharmaceutical Manufacturing, Distribution, and Application]." State Council of China. http://www.gov.cn/zhengce/content/2017-02/09/content_5166743.htm.

———. 2018. "Guowuyuan bangongting guanyu gaige wanshan fangzhiyao gongying baozhang ji shiyong zhengce de yijian 国务院办公厅关于改革完善仿制药供应保障及使用政策的意见[Opinions on Reform and Improvement of Generic Drug Security and Supply]." The State Council of China. http://www.gov.cn/zhengce/content/2018-04/03/content_5279546.htm.

Su, Meng, Qiuli Zhang, Xueke Bai, Chaoqun Wu, Yetong Li, Elias Mossialos, George A. Mensah, et al. 2017. "Availability, Cost, and Prescription Patterns of Antihypertensive Medications in Primary Health Care in China: A Nationwide Cross-Sectional Survey." *The Lancet* 390 (10112): 2559–68. https://doi.org/10.1016/S0140-6736(17)32476-5.

Sun, J., C. J. Hu, M. Stuntz, H. Hogerzeil, and Y. Liu. 2018. "A Review of Promoting Access to Medicines in China - Problems and Recommendations." *BMC Health Serv Res* 18 (1): 125. https://doi.org/10.1186/s12913-018-2875-6.

Sun, Zesheng, Shuhong Wang, and Stephen R. Barnes. 2016. "Understanding Congestion in China's Medical Market: An Incentive Structure Perspective." *Health Policy and Planning* 31 (3): 390–403. https://doi.org/10.1093/heapol/czv062.

Sun, Zhuolin, Ju Ding, and Naling Li. 2017. "Guangdongsheng Xianji Gongli Yiyuan Quxiao Yaopin Jiacheng Zhengce Hou de Yingxiang Yu Duice 广东省县级公立医院取消药品加成政策后的影响及对策研究 [The Impact of and Countermeasures to the Zero Markup Policy in County-Level Public Hospitals in Guangdong Province]." *Zhongguo Yiyao Daobao 中国医药导报 [China Pharmaceutical Herald]* 14 (9): 129–32.

Tan, Huawei, Guang Yang, Weihua Yan, Xian Liu, Wanhui Zheng, Yun Zhang, Xiaoling Zhu, and Peilin Zhang. 2016. "Woguo Xianji Gongli Yiyuan Quxiao Yaopin Jiacheng Buchang Zhengce 我国县级公立医院取消药品加成补偿政策的合理性研究 [Rationality of the Zero Markup Policy for County-Level Public Hospitals in China]." *Zhongguo Yaofang 中国药房 [China Pharmacy]* 27 (10): 1301–4.

Tan, S. Y., and G. J. Melendez-Torres. 2018. "Do Prospective Payment Systems (PPSs) Lead to Desirable Providers' Incentives and Patients' Outcomes? A Systematic Review of Evidence from Developing Countries." *Health Policy Plan* 33 (1): 137–53. https://doi.org/10.1093/heapol/czx151.

Tang, Yuqing, Chaojie Liu, Zinan Zhang, and Xinping Zhang. 2018. "Effects of Prescription Restrictive Interventions on Antibiotic Procurement in Primary Care Settings: A Controlled Interrupted Time Series Study in China." *Cost Effectiveness and Resource Allocation* 16 (1): 1. https://doi.org/10.1186/s12962-018-0086-y.

The Lancet. 2018. "Vaccine Scandal and Confidence Crisis in China." *The Lancet* 392 (10145): 360. https://doi.org/10.1016/S0140-6736(18)31695-7.

Tian, W., J. Yuan, D. Yang, and L. Zhang. 2016. "Descriptive Analysis on the Impacts of Universal Zero-Markup Drug Policy on a Chinese Urban Tertiary Hospital." *PLoS One* 11 (9): e0162795. https://doi.org/10.1371/journal.pone.0162795.

Wang, Jenn hwan, Tsung-Yuan Chen, and Ching-Jung Tsai. 2012. "In Search of an Innovative State: The Development of the Biopharmaceutical Industry in Taiwan, South Korea and China." *Development and Change* 43 (2): 481–503. https://doi.org/10.1111/j.1467-7660.2012.01769.x.

Wang, Zhonghai, Zongfu Mao, Tao Li, and Wenjuan Du. 2015. "Yaopin Jizhong Caigou Zhengce Gaige Shidian Xiaoguo Pingxi 药品集中采购政策改革试点效果评析——以福建省三明市为例 [Assessment of a Centralised Drug Procurement Pilot: The Case of Sanming, Fujian]." *Zhongguo Weisheng Zhengce Yanjiu 中国卫生政策研究 [Chinese Journal of Health Policy]* 8 (1): 21–26.

Wei, Yan, Raymond W. Pong, Lizheng Shi, Jian Ming, Meng Tang, Yiwei Mao, Wenbin Liu, and Yingyao Chen. 2017. "Perceptions of Health Technology Assessment Knowledge Translation in China: A Qualitative Study on HTA Researchers and Policy-Makers." *International Journal of Healthcare Technology and Management* 16 (1/2): 44. https://doi.org/10.1504/IJHTM.2017.087599.

WHO. 1993. "How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators."

Woodhead, Michael. 2016. "80% of China's Clinical Trial Data Are Fraudulent, Investigation Finds." https://doi.org/10.1136/bmj.i5396.

Wu, Jingxian, Rongxin He, and Ying Mao. 2016. "Shaanxisheng chengshi gongli yiyuan quxiao yaopin jiacheng zhengcexing kuisun cesuan 陕西省城市公立医院取消药品加成政策性亏损测算 [Zero markup policy: estimation of loss at urban public hospitals in Shaanxi Province]." *Zhongguo Weisheng Jingji 中国卫生经济 [China Health Economy]* 35 (04): 11–13.

Yang, Wei. 2016. "How Does the Pharmaceutical Industry Influence Prescription? A Qualitative Study of Provider Payment Incentives and Drug Remunerations in Hospitals in Shanghai." *Health Economics, Policy, and Law* 11 (4): 379–95. https://doi.org/10.1017/S1744133116000086.

Yang, Wei, Alex Jingwei He, Lijie Fang, and Elias Mossialos. 2016. "Financing Institutional Long-Term Care for the Elderly in China: A Policy Evaluation of New Models." *Health Policy and Planning* 31 (10): 1391–1401. https://doi.org/10.1093/heapol/czw081.

Yao, Qiang, Chaojie Liu, J. Adamm Ferrier, Zhiyong Liu, and Ju Sun. 2015. "Urban-Rural Inequality Regarding Drug Prescriptions in Primary Care Facilities – a Pre-Post Comparison of the National Essential Medicines Scheme of China." *International Journal for Equity in Health* 14 (1): 58. https://doi.org/10.1186/s12939-015-0186-7.

Yao, Qiang, Fei Luo, Luyang He, Shanquan Chen, Lan Yao, and Zhiyong Liu. 2014. "Yaopin Kejixing Shijiao Xia Guojia Jiben Yaowu Zhidu Shishi Xiaoguo Pingjia 药品可及性视角下国家基本药物制度实施效果评价 [Assessment of the Impact of the National Essential Medicine System from a Drug Accessibility Perspective]." *Zhongguo Yiyuan Guanli 中国医院管理 [China Hospital Management]*, no. 3: 60–62.

Yao, Xuefang, Jinxi Ding, Yingfang Liu, and Penghui Li. 2017. "The New Drug Conditional Approval Process in China: Challenges and Opportunities." *Clinical Therapeutics* 39 (5): 1040–51. https://doi.org/10.1016/J.CLINTHERA.2017.03.016.

Yi, Hongmei, Grant Miller, Linxiu Zhang, Shaoping Li, and Scott Rozelle. 2015. "Intended and Unintended Consequences of China's Zero Markup Drug Policy." *Health Affairs (Project Hope)* 34 (8): 1391–98. https://doi.org/10.1377/hlthaff.2014.1114.

Yi, XIn, Yi Liu, Cheng Han, Dawei Zhu, Zhigang Guo, Wensheng Li, Xiaodong Guan, and Luwen Shi. 2018. "Quxiao Yaopin Jiacheng Zhengce Dui Zhongguo 58 Jia Xianji Gongli Yiyuan Shouru Jiegou Yingxiang Fenxi 取消药品加成政策对中国 58 家县级公立医院收入结构影响分析 [An Analysis of the Impact of the Zero Markup Policy on the Income Structure of 58 County-Level Public Hospitals in China]." *Yaopin Pingjia 药品评价 [Pharmaceutical Review]* 15 (6): 18–21.

Yip, Winnie, and William C. Hsiao. 2015. "What Drove the Cycles of Chinese Health System Reforms?" *Health Systems & Reform* 1 (1): 52–61. https://doi.org/10.4161/23288604.2014.995005.

Yu, Wei, and Yan Xu. 2015. "Gaige de Xitongxing Jueding Chengbai: Yaopin Jiacheng Zhengce Dui Gongli Yiyuan de Yingxiang 改革的系统性决定成败—药品加成政策对公立医院的影响 [Systematic Reform Is the Key to Success: The Impact of Zero Markup Policy on Public Hospitals]." *Caizheng Yanjiu 财政研究 [Public Finance Research]*, no. 4: 40–44.

Yuan, Xun. 2018. "China's Vaccine Production Scare." *The Lancet* 392 (10145): 371. https://doi.org/10.1016/S0140-6736(18)31725-2.

Zeng, Jiazhi, Leiyu Shi, Xia Zou, Wen Chen, and Li Ling. 2015. "Rural-to-Urban Migrants' Experiences with Primary Care under Different Types of Medical Institutions in Guangzhou, China." *PLOS ONE* 10 (10): e0140922. https://doi.org/10.1371/journal.pone.0140922.

Zeng, W., L. L. Gustafsson, M. Bennie, A. E. Finlayson, and B. Godman. 2015. "Review of Ongoing Initiatives to Improve Prescribing Efficiency in China; Angiotensin Receptor Blockers as a Case History." *Expert Rev Pharmacoecon Outcomes Res* 15 (1): 157–69. https://doi.org/10.1586/14737167.2015.963557.

Zeng, Wenjie, Alexander E Finlayson, Sushma Shankar, Winnie de Bruyn, and Brian Godman. 2015. "Prescribing Efficiency of Proton Pump Inhibitors in China: Influence and Future Directions." *BMC Health Services Research* 15 (January). https://doi.org/10.1186/s12913-014-0638-6.

Zhang, Kang. 2017. "Woguo Xianjieduan Yaopin Guanli Cunzai de Wenti Yu Duice 我国现阶段药品管理存在的问题及对策 [Current Issues in Pharmaceutical Management in China and Solutions]." *Nongcun Jingji Yu Keji 农村经济与科技 [Rural Economy and Technology]* 28 (4): 115–16.

Zhang, S., W. Zhang, H. Zhou, H. Xu, Z. Qu, M. Guo, F. Wang, et al. 2015. "How China's New Health Reform Influences Village Doctors' Income Structure: Evidence from a Qualitative Study in Six Counties in China." *Hum Resour Health* 13 (May): 26. https://doi.org/10.1186/S12960-015-0019-1.

Zhang, Tingting, Hilary Mavis Graham, and Piran Crawfurd Limond White. 2018. "Healthcare Providers' Accounts of Influences of Antibiotic-Related Reforms on Their Behavior with Respect to the Use of Antibiotics for Children: A Qualitative Study in China." *Public Health Open Access* 2 (1). https://doi.org/10.23880/PHOA-16000122.

Zhang, W. Y., Y. R. Li, Y. J. Li, X. Q. Li, W. G. Zhao, and R. Z. Lu. 2015. "A Cross-Sectional Analysis of Prescription and Stakeholder Surveys Following Essential Medicine Reform in Guangdong Province, China." *BMC Health Serv Res* 15 (March): 98. https://doi.org/10.1186/s12913-015-0778-3.

Zhen, Xuemei, Xueshan Sun, and Hengjin Dong. 2018. "Health Technology Assessment and Its Use in Drug Policies in China." *Value in Health Regional Issues* 15 (May): 138–48. https://doi.org/10.1016/J.VHRI.2018.01.010.

Zheng, Gelin, Lei Zheng, An Yang, Yongsheng Yang, and Luojia Chen. 2015. "Quxiao Yaopin Jiacheng Zhengce Qiyuan Fenxi 取消药品加成政策起源分析 [Origins of the Zero Markup Policy]." *Zhongguo Weisheng Jingji 中国卫生经济 [China Health Economy]* 34 (2): 37–40.

Zhou, Qing, Xiao-Yuan Chen, Zhi-Min Yang, and Yi-Long Wu. 2017. "The Changing Landscape of Clinical Trial and Approval Processes in China." *Nature Reviews Clinical Oncology* 14 (9): 577–83. https://doi.org/10.1038/nrclinonc.2017.10.

Zou, Wujie, Xiaodong Guan, Chunxia Man, Zhigang Guo, Lili Ma, Yi Liu, and Luwen Shi. 2016. "Woguo Gesheng Yaopin Jizhong Caigou Zhengce Luoshi Bijiao Fenxi 我国各省药品集中采购政策落实比较分析 [A Comparative Analysis of the Implementation of Pharmaceutical Centralised Tendering Policy across Provinces in China]." *Zhongguo Weisheng Zhengce Yanjiu 中国卫生政策研究 [Chinese Journal of Health Policy]* 9 (9): 35–40.

Appendix 1: Interview Questionnaires

Drug approval stakeholder

1. What impact has the fast-track approval launched in 2009 has on drug approvals? To what extent has approval been accelerated for these products?
2. The CFDA recently promised to create a system for rapid evaluation of innovative drugs for HIV/AIDS, cancer, major chronic diseases, orphan diseases, and drugs with high potential budget impact. How would this compare to the existing fast-track approval? What changes have been made?
3. What is the mechanism for fast-tracking priority medicines? Do these products jump the queue for review, face a shorter review time, or do they receive conditional authorisation on the basis of premature clinical evidence?
4. How has verification review been used in the context of drug approvals in China? Which overseas agencies are referenced in this process? By how much is drug approval accelerated through verification review?
5. The 2015 reforms in bioequivalence aimed to clear the backlog by the end of 2016 and to have approvals follow set timelines by 2018. Has this goal been achieved? What barriers and challenges remain for this target to be achieved?
6. What regulations are in place governing the use of medicines that have yet to be authorised by the CDA? Evidence suggests patients are illegally importing generic versions of innovative products that are pending approval in China. How has this problem been perceived within China? Has the problem worsened/remained the same, or improved in recent years? What steps have been taken to address this issue?
7. The NRDL is only updated every 3 years. How is drug approval integrated with pricing and reimbursement in China?
8. What changes do you anticipate in the next 5 years in drug approval within China?

Pricing and reimbursement stakeholder

1. Have the goals of the national essential medicines programme been achieved? Is the zero mark-up policy applied universally or do some health care facilities still mark-up medicines? Reports suggest the zero mark-up policy was being extended beyond essential medicines to other products on the NRDL. To what extent has the ZMU been applied throughout various levels of health care?
2. Have there been any unintended consequences of the zero mark-up policy? Are there any issues present in terms health facilities closing or downsizing staff due to loss of revenue? Reports suggest that some health care providers have shifted costs to other fee-for-service health services. How has the zero mark-up policy been integrated with general health policy to address these issues?
3. How much does drug pricing vary from province to province? Are some provinces able to achieve significantly lower prices than others? In 2015, the state council issued a notice that aimed to create a more transparent and unified tendering process. Has this been achieved or are there still significant differences across provinces in the tendering process?
4. Prior to 2015, the tendering process was criticised for prioritising price over quality. Have any quality assurance mechanisms been implemented in order to ensure that companies are not incentivised to lower quality in order to undercut prices?

5. Another criticism of the tendering process related to the issuance of separate tenders for off-patent originators and generic versions of a product. Does this still occur in practice? If so, is this a priority area for reform?
6. The recent negotiations pilot successfully achieved agreements for 36 of 44 products, which entered into the NRDL. Will the negotiation process be legislated and formalised for in-patent products? Will all in-products proceed through negotiation to determine price, or will only a subset of products be eligible? If only a subset of products are eligible, what are the eligibility criteria?
7. Tendering is the primary pricing mechanism for NRDL off-patent drugs and negotiations are the primary mechanism for in-patent products. What proportion of products are priced through tendering? How are other products priced? Does this occur centrally, provincially, locally?
8. Health technology assessment is integrated within the negotiations pilot. Are there plans to formalise the use of HTA to help inform pricing and reimbursement decisions? What are the key barriers towards achieving this? Without a formal HTA system, how are drugs currently selected for inclusion on the NRDL? How do provinces inform their decisions to modify the NRDL? How do local hospitals inform their decisions on which products within the NRDL to procure? If plans are in place, can you provide information regarding evidence requirements, assessment timeline, and assessment criteria?
9. In 2015, the NDRC issued guidance for the implementation of external reference pricing? Has this been operationalized? Can you provide any details on this process?
10. What changes do you anticipate within the next 5 years for the pricing and reimbursement of medicines within China?

Hospital management stakeholder

1. How are decisions made regarding which products from the NRDL to supply? Do you supply any products from outside of the NRDL?
2. Do you conduct negotiations directly with manufacturers for the procurement of drugs? If so is this for all products or a subset of products?
3. Does your facilities ever face issues with stocking essential drugs? Has the supply of drugs and funding been adequate?
4. What impact has the zero mark-up policy and essential medicines programme had at hospital level? Have revenues levels been adequately compensated through increases in government subsidies? If not, what were the consequences of decreased revenue?
5. To what extent does clinical guidance play a role in the prescribing of medicines? Is clinical guidance routinely disseminated from provincial or state level? Is it mandatory to follow clinical guidance? How do you monitor the extent to which clinical guidance is followed?
6. What is your view on the quality of generic products? Are they considered to be bio-equivalent and interchangeable with originator products? Do you have any policies in place to promote greater use of generic medicines?
7. In 2011, the Chinese government launched the National Action Plan for Antibiotic Stewardship. Has this initiative significantly impacted the way in which health care professionals prescribe antibiotics in your hospital? How frequently is your facility monitored to ensure they are complying with regulations on antibiotic use? Have doctors been able to manage patient expectations regarding antibiotics? Does your hospital have adequate equipment and facilities to follow guidelines?

8. What additional incentives have been provided to your hospital to reduce inappropriate prescribing? Are there any pay-for-performance incentives or penalties linked to prescribing?
9. To what extent do out-of-pocket payments prevent patients from using hospital services?
10. Has your hospital implemented any initiatives which aim to improve patient health literacy?
11. What changes do you expect within the next 5 years in terms of the regulation of hospital activities?

Primary care facility stakeholder

1. What impact has the zero mark-up policy and essential medicines programme had at primary care facility level? Have revenues levels been adequately compensated through increases in government subsidies? If not, what were the consequences of decreased revenue?
2. How has the role of primary care providers changed since the 2009 reforms? Has utilisation of primary care facilities improved substantially? Have the goals of the 2009 reform been achieved?
3. The Chinese government offers incentives for implementing public health activities? Have these incentives been successful? Has the focus on public health increased over the past decade?
4. Does your facilities ever face issues with stocking essential drugs? Has the supply of drugs and funding been adequate?
5. In 2011, the Chinese government launched the National Action Plan for Antibiotic Stewardship. Has this initiative significantly impacted the way in which health care professionals prescribe antibiotics in your facility? How frequently is your facility monitored to ensure they are complying with regulations on antibiotic use? Have doctors been able to manage patient expectations regarding antibiotics? Does your facility have adequate equipment and facilities to follow guidelines?
6. What is your view on the quality of generic products? Are they considered to be bio-equivalent and interchangeable with originator products? Do you have any policies in place to promote greater use of generic medicines?
7. What additional incentives have been provided to your facility to reduce inappropriate prescribing? Are there any pay-for-performance incentives or penalties linked to prescribing?
8. To what extent do out-of-pocket payments prevent patients from using primary care services?
9. Has your facility implemented any initiatives which aim to improve patient health literacy?
10. What changes do you expect within the next 5 years in terms of the regulation of primary health facility activities?

Health insurance fund stakeholder

1. The Chinese government recently announced plans to merge the URBMI, NCMS and UEBMI insurance plans in order to promote more unified coverage? Has this been operationalized? Has this had any impact on reducing the disparity in coverage between rural and urban residents? Are premiums be pooled at national level or at provincial level?
2. How do levels of coverage vary from province to province?
3. What safety nets are in place for significantly poor patients in China that will struggle to pay for co-payments?

4. What is the mechanism for setting reimbursement ceilings? In the new unified health insurance, are ceilings applied equally across all patients? How has the reimbursement ceiling evolved over time? Does this vary across provinces?
5. Are there future plans to expand insurance coverage and government funding? To what extent is the pharmaceutical prioritised for future expansions in coverage?
6. Currently, payment models for health services are predominantly based on a retrospective fee-for-service model. A number of prospective payment model pilots have been implemented in China with mixed results. Are there any plans in place to change the payment model for health services within China with the aim of delinking volume of health services provided from revenue? What are the current challenges and barriers in place which prevent implementation of this type of model?
7. What changes do you envision within the next 5 years in terms of provision of health insurance to patients in China?