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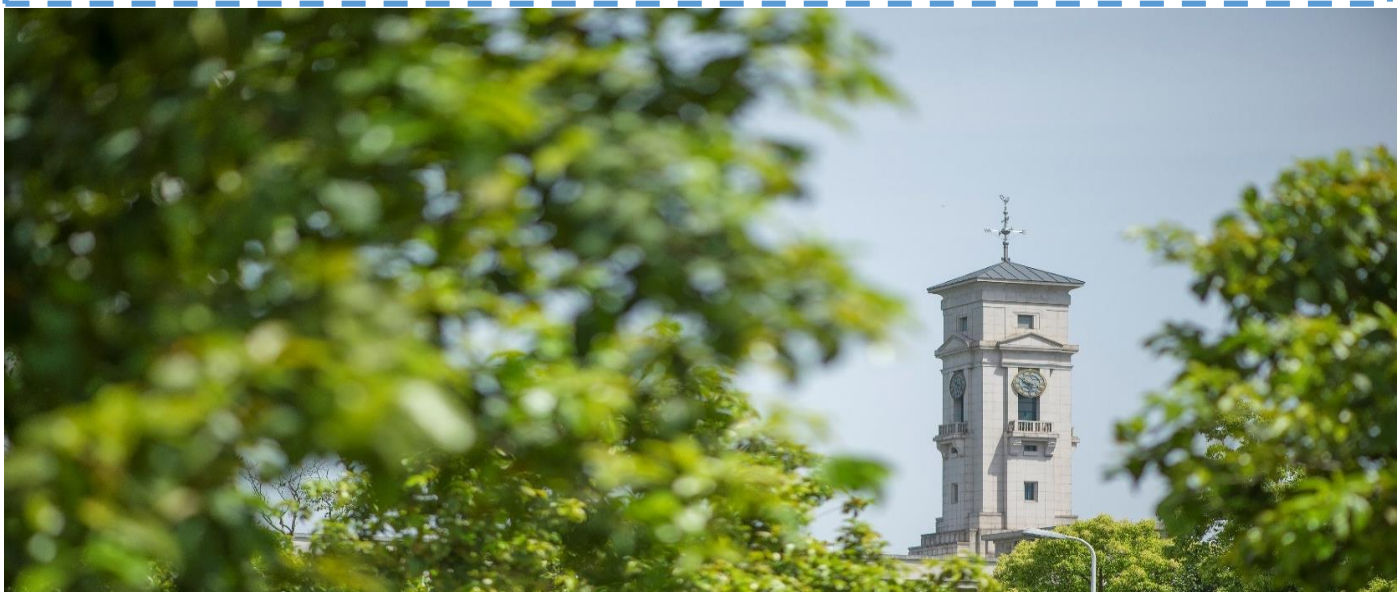

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Pharmacoeconomics of obesity in China: A scoping review

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ABSTRACT (maximum 200 words)

Background: With the growing rate of obesity and associated chronic conditions in China, there is a need to assess the health and economic burden of obesity and examine the effectiveness of pharmaceutical, medical, and comprehensive weight-loss interventions.

Areas covered: This article reviewed publications retrieved from PubMed and Google Scholar during 2010-2020 on pharmacoeconomic studies related to overweight and obesity in China. We identified five cost-of-illness studies and four cost-effectiveness analyses of weight-loss interventions, including bariatric surgeries and a comprehensive intervention program.

Expert opinion: There is a lack of pharmacoeconomic analyses of obesity in China. Existing studies have often taken the health system perspective without accounting for productivity loss. Cohort studies and studies based on electronic health records or claims data are needed to provide the epidemiologic parameters required for homegrown economic evaluations of the health and economic burden of obesity in China, as well as the cost-effectiveness of interventions to reduce obesity and its sequela.

Keywords: Bariatric surgery, China, cost-effectiveness, cost-of-illness, economic evaluation, obesity, overweight

Article highlights:

- There is a lack of pharmacoeconomic analyses of obesity treatments in China.
- Estimates of the total direct medical cost of overweight and obesity in China range between $8.4 - $23.9 billion, and indirect medical cost is estimated at $62.6 billion.
- The few pharmacoeconomic analyses of obesity treatment in China have assessed the cost-effectiveness of bariatric surgeries and comprehensive medical intervention (blood glucose management).
- Variations in methods used and study quality exist among the existing pharmacoeconomic analyses of obesity treatments in China.
- Guidelines and capacity building would benefit the field of pharmacoeconomic analysis of obesity in China.

Pharmacoeconomics of Obesity in China: A Scoping Review

1. Introduction

Obesity is a complex and multifactorial disease leading to heightened risks of morbidity and mortality [1]. The increased prevalence of obesity worldwide is associated with growing health and economic burdens [1-3]. Such a trend is seen among both high-income countries and transition economies [4-7]. In the Asia Pacific region, the economic development of many low- and middle-income countries has brought along dramatic increases in the prevalence of overweight and obesity. For example, although the prevalence of overweight and obesity in China is a third of that in Australia, the increase in China's prevalence over the last 20 years was 400% compared with 20% in Australia [8]. The burdens of overweight and obesity on health and economy are likely to grow in many developing countries in the years to come [8]. Evaluating options for obesity treatment and prevention is in urgent need in low- and middle-income countries, including China [2].

With the growing health and economic burden of chronic diseases associated with the increasing rates of overweight and obesity in China, examining the pharmacoeconomics of obesity provides a timely assessment of the methods and applications used in evaluating the alternative medical interventions that address obesity or its sequela. The objective of this paper is to provide a scoping review of the health and economic burden of obesity in China, the development of pharmacoeconomic evaluation of obesity treatments, technical issues related to pharmacoeconomic evaluation, and related policy implications to China.

2. Overweight and obesity in China

2.1 Prevalence rates

The prevalence of overweight and obesity has been increasing in China [9, 10]. However, substantial differences in the incidence of overweight and obesity across gender, ethnic group, and socioeconomic status exist in China [11]. Examining data from the National Free Preconception Health Examination Project in rural China from 2010 to 2014, researchers found that the prevalence of combined overweight and obesity (Body Mass Index (BMI) $\geq$ 24.0 kg/m^2) among men was 33.8% while the corresponding rate of obesity (BMI $\geq$ 28.0 kg/m^2) was 6.3% [12]. A study comparing two representative surveys of Hunan province conducted in 2013 and 2018 found that the adult prevalence rate of overweight increased 6.2 percentage points and the prevalence of obesity increased 3.1 points over the five years, with varying prevalence changes across demographic groups [13]. In the study sample, urban residents had a higher prevalence of overweight and obesity than rural residents, men had a higher prevalence of overweight and obesity than men regardless of residential status, and age had a nonlinear correlation with the rates of overweight and obesity peaked for mid-age groups [13]. Data from the China National Stroke Screening and Prevention Project Study from October 2014 – November 2015 showed significant differences in the prevalence rates across ethnic groups in China, with Uyghurs having the highest rates of overweight and obesity and Hui Muslims the lowest rates [7]. Although the direction of the socioeconomic gradient may differ from that in high-income countries, socioeconomic status is related to the incidence of obesity in China. For example, pocket money for children is associated with an increased incidence of childhood obesity in Chinese megacities [11, 14]. Environmental factors, such as neighborhood restaurant density also correlate with adult obesity in China [15].

2.2 Health Consequences of Obesity

Obesity is known to be associated with increased mortality and morbidity [16, 17]. Using data on a large prospective cohort study of 224,064 men during 1990-2006, Chen and colleagues showed a U-shaped association between BMI and all-cause mortality in the Chinese population [18]. They suggested that the earlier evidence may have overestimated the excess mortality at low BMI but underestimated that at high BMI, and stroke is one of the major conditions through which obesity is associated with excess mortality [18]. A prospective cohort study in a nationally representative sample of 169,871 Chinese men and women aged 40 years or older found that both underweight and obesity were associated with increased mortality [19].

A range of chronic conditions may result from excessive bodyweight. Obesity was associated with type 2 diabetes among a sample of middle-aged and older adults in Jinan, China, with different impacts between men and women [20]. Obesity also affects mental health status. Obesity at midlife may contribute to dementia at a later age, accounting for a large portion of the projected 26.2 million dementia patients in China by 2050 [21]. Chinese may be at a high risk of diabetes with a moderate level of BMI, prompting some researchers and practitioners recommending a lower threshold of BMI at 24.0 kg/m^2 for obesity among the Chinese population [22].

Evidence also suggests an "obesity paradox" among the Chinese population. While moderate obesity ($30 \leq BMI < 35$) might offer protective effects in health-related quality of life (HRQoL), particularly among older adults, class II obesity ($35 \leq BMI < 40$) was associated with reduced physical functioning [23]. The finding is consistent with the extant literature. A systematic review suggested that obesity was associated with significantly higher all-cause mortality, although no association was found for class I obesity ($30 \leq BMI < 35$) [24]. Researchers examined the Chinese Longitudinal Healthy Longevity Study, a community-based prospective

cohort study conducted in 23 provinces of China, with multiple-year follow-up and recruitment of new participants. They found that higher BMI was associated with a lower risk of disability in activities of daily living (ADL) among Chinese adults age 80 years or older. The authors argued that underweight, rather than overweight or obesity, continues to be a priority for the prevention of disability in ADL after age 80 years [25]. However, such a pattern might depend on initial health status. Among a prospective cohort of Chinese people 65 years or older enrolled from 1998 to 2000 at Elderly Health Centers in Hong Kong, obesity was associated with better outcomes among those with poor health status, but with a worse outcome for those with initially good health [26].

3. Pharmacoeconomics of Obesity in China

3.1 Development and Use of Pharmacoeconomics in China

Pharmacoeconomics has a relatively short history of practice in China, dating back to the efforts introducing pharmacoeconomics into China in the early 1990s [27]. However, the academic community and policymakers have increasingly recognized the need for and importance of evidence-based decision-making after the 2009 Healthcare Reform [28]. Pharmacoeconomic research conducted in China has experienced a dramatic increase, but a systematic review has identified limitations of the pharmacoeconomic publications in English during 2003-2014 [29]. There is a lack of guidelines and local epidemiologic, economic, and quality-of-life data [30, 31]. China's institutionalization of Health Technology Assessment (HTA) is low, although this may be changing. China's newly-established major payer, the National Health Security Administration (NHSA), has encouraged the use of HTA in determining drug coverages [32].

3.2 Pharmacoeconomics of Obesity in China

While pharmacoeconomic research of obesity outside of China has covered a wide range of pharmaceutical and surgical treatments of obesity [33-35], such studies have been limited in China. A contributing factor may be because obesity is not a recognized disease condition in China. This is not surprising given that obesity was considered a disease in the US only since 2013 [36]. The US Centers for Medicare & Medicaid Services (CMS) does not cover weight-loss drugs yet, although its Medicare Part C (Medicare Advantage plans in partnership with private insurance) may provide extended coverage of weight-loss drugs. US Medicare does cover certain weight-loss surgeries under specific conditions if the patient is morbidly obese [37]. In China, while anecdotal evidence suggested that weight-loss drugs had been considered reimbursable in some localities, the NHSA has formally excluded weight-loss drugs from its coverage since September 2020 [38].

3.2.1 Scoping Review

A careful search on Google Scholar of articles on pharmacoeconomic analysis on obesity in China (search keywords: pharmacoeconomic AND obesity AND China) published during 2010-2020 yielded 4,250 hits, but only five studies were identified by two of the co-authors as relevant, with obesity as the primary condition studied and China as the study setting [6, 39-42]. By searching the articles cited in these studies, we identified two additional studies published before 2010 [5, 43]. A similar search on PubMed produced no additional hits. A search of the Chinese translation of the keywords on Google Scholar produced 3,130 hits of articles published in Chinese during 2010-2020, but only one study was deemed relevant [44]. Additional searches led to another cost-of-illness study published in 2013 in Chinese [45]. Table 1 provides a summary of the nine studies. The studies include five cost-of-illness analyses of overweight and

obesity and four cost-effectiveness analyses with obesity as an outcome or an important lifestyle factor.

Heterogeneities in the use of pharmacoeconomics in the nine studies exist. Most studies have used the healthcare system perspective or societal perspective, although only one of the studies specifically provided the study perspective. Many studies used modeling because of the lack of epidemiologic parameters, which calls for a systematic approach to collect epidemiologic information from large-scale surveys or electronic health records. A minor difference in the definition of obesity exists, with the earliest cost-of-illness study conducted by researchers outside of China using higher thresholds of BMI to define overweight and obesity [43]. The other studies have used a definition of overweight and obesity for East Asian populations [15]. More details of the studies are provided in the following sections.

3.2.2 Cost of Overweight and Obesity

Substantial economic burdens result from overweight and obesity. A systematic review concluded that obese individuals had medical costs that were approximately 30% greater than their normal-weight peers [46]. However, there is a dearth of systematic analysis on the economic burden of overweight and obesity in China. Only five studies reviewed in the paper have ventured into this area and shed light on the cost of overweight and obesity in China but with different choices of time, population, and geographic locations.

The first study reviewed the full economic costs of poor diet, lack of physical activity, and obesity in China as a case study [43]. The authors used data from the China Health and Nutrition Survey 2000 wave and the 1998 National Survey of Health Services for China to calculate the total costs of overweight and obesity at US$49.4 billion in 2000, including $5.9 billion direct

costs and $43.5 billion indirect costs. The latter included lost productivity due to premature death, decreased years of disability-free life, and reduced time to work.

In another study that examined national data, researchers from the Chinese Center for Disease Control and Prevention (China CDC) used population attributable risk (PAR) from a cohort study on coronary heart disease (CHD) and other risk factors during 1985-2000, coupled with estimates from the 2002 China National Nutrition and Health Survey and the Third National Health Service Survey 2003 wave [5]. They estimated the total annual medical cost attributable to overweight and obesity at 21.11 billion Yuan (RMB) (approximately US$2.74 billion), accounting for 3.7% of national total medical costs in 2003 [5]. The authors warned that the cost of overweight and obesity could reach $4.8 billion if the ratio of overweight and obesity approaches 1.1:1. Of note on this study is that the authors had to borrow the percentages from the US estimates for the portions of direct costs of the four chronic diseases attributable to overweight and obesity. Zhang et al. used a similar strategy and updated the estimate for the direct economic cost associated with overweight and obesity at 90.8 billion Yuan (RMB) in the year of 2010 (approximated US$15.7 billion in 2019 price) [45].

Studies also examined the economic costs of obesity in particular regions or among specific population groups. Li et al. surveyed 2,474 men and 2,505 women aged 35 and older in the rural area of Yunnan province on their health and body weight status in 2015 [39]. A team of medical students measured blood pressure and glucose and took anthropometric measurements from the participants. Using published annual per-person costs of hypertension, diabetes, CHD, and stroke, the authors estimated the total economic burden of the four diseases associated with obesity and central obesity in rural Southwest China at $3.9 billion and $8.7 billion (2015US)

[39]. The study did not specify its perspective, but it appears to have taken a societal approach, with lost productivity being accounted for in the indirect costs. Its estimate ($3.9 billion in 2015US$ for rural southwest China) is much higher than the cost in Zhao et al. ($3.4 billion in 2015US$ for China), potentially due to the difference in the study time period and the inclusion of productivity loss.

Shi et al. analyzed data from the China Health and Retirement Longitudinal Study 2011 wave. They estimated that overweight and obese groups were 15.0% and 35.9% more likely to incur total healthcare costs and had significantly higher total direct health care costs (RMB 2246.4, RMB 2050.7, respectively), as compared with the normal-weight group (RMB 1886.0), among middle-aged and older adults in China [6]. Their results translate to increased total direct healthcare costs of RMB 360 and RMB 165 per overweight or obese person, respectively, which leads to total direct healthcare costs of $22.3 billion (in 2015US$) in China, assuming the same prevalence of overweight and obesity in 2010.

Hence, a conservative estimate of the direct medical cost of overweight and obesity is $23.9 billion (converted to 2019 US$). In comparison, the economic burden of cardiovascular diseases in China is estimated at $35.5 billion (in 2019 US$), including both direct medical cost and direct non-medical cost [47]. When lost productivity is accounted for, the economic cost of obesity could be even larger. A modeling study suggests that in 2017 in China, diabetes, a disease strongly correlated with obesity, is associated with 4.1 million more premature deaths, the loss of an additional 22.7 million years of life (3.7%), and the loss of an additional 75.8 million productivity-adjusted life-years (15.1%) that equated to a total of Chinese RMB17.4

trillion (US$2.6 trillion) in lost GDP owing to reduced productivity, among which a large proportion are associated with obesity [48].

Table 2 provides a comparison of the economic burden associated with overweight and obesity with the economic cost of other conditions in China, including chronic diseases associated with air pollution [49], Alzheimer's disease [50], pneumoconiosis [51], and disease-associated malnutrition [52]. The comparison highlights the burden of overweight and obesity in China, although a systematic assessment is needed to determine the ranking of the disease or conditions in terms of economic burden.

3.2.3 Cost-effectiveness analyses of obesity treatment

As weight-loss drugs and treatments are not officially covered by China's primary insurer, NHSA, pharmacoeconomic evaluations of drugs and treatments for obesity were limited, often with weight-status as an intermediate outcome. Three studies have examined gastric bypass procedures for weight-loss among diabetes patients in China. One of the studies, Tu et al., examined the cost-effectiveness of Laparoscopic Roux-en-Y gastric bypass (RYGB) surgery using data of 106 obese Type 2 Diabetes patients who underwent RYGB from 2011-2013 and a control group of 106 diabetes patients who were enrolled in the conventional medical management in China. They found that RYGB is cost-effective for Chinese patients with Type 2 Diabetes and obesity four years after the operation with an incremental cost-effectiveness ratio of US$19,359 per quality-adjusted life years (QALY) gained [40].

Wan et al. also examined the cost-effectiveness of bariatric surgery but with a Markov analysis. They concluded that bariatric surgery, as compared with medication therapy strategy, led to significant cost savings (RMB26,869, about $4,299 in 2015 US$) to the health insurance

payer and increases in health benefits (2.51 QALY) in a 40-year time horizon, compared to medication therapy [41].

Yang et al. used retrospective analysis to examine the cost-effectiveness of laparoscopic bypass surgery among Type 2 Diabetes patients who were obese during June 2014 and May 2016. They concluded that pharmacotherapy treatment was more cost-effective than laparoscopic bypass surgery. However, a close examination found no randomization of the two study arms, and there is no attempt to adjust selection bias into the group that had undergone surgery, thus the evidence may not be conclusive.

Another Markov modeling study found that the comprehensive intervention program for blood glucose management of overweight and obese patients with diabetes is cost-effective for the middle-aged male group (ICER of RMB104,000, or $15,147 in 2018US$, per QALY gained) and elderly female group, respectively [42].

4. Conclusions

This scoping review aimed to assess obesity-related pharmacoeconomic studies in China. We have identified a limited number of cost-of-illness or cost-effectiveness studies on obesity and related chronic disease treatment in China. The studies have provided limited but consistent evidence of a growing economic burden of overweight and obesity in China – although preventing the complications associated with underweight and malnutrition may continue to be a priority among older adults in China. The cost-effectiveness analyses have shown the effectiveness of gastric bypass procedures in treating diabetes patients who are overweight or

obese. We did not find any pharmacoeconomic studies on the effectiveness of weight-loss drugs in China.

5. Expert Opinions

Several factors underlie the lack of obesity-related pharmacoeconomic research in China. In the remainder of this review, we attempt to provide explanations, voice our "wishes and grumbles," and surmise the future of the field in five years.

5.1 Obesity prevention and control

The lack of pharmacoeconomic research on obesity in China may not be coincidental. In an interview with policymakers, Dr. Bin Wang, Deputy Director of the Disease Control Division, of then the National Health and Family Planning Commission of China, voiced reservations on reimbursing pharmacological treatments for obesity from public health insurance [53]. Instead, he has argued that primary prevention programs should be implemented to achieve the maximum impact. Such programs include the National Chronic Disease Prevention and Control Demonstration Areas, in the spirit of the Health-in-All-Policies initiatives [54]. For primary prevention programs aiming to reduce overweight and obesity, a slightly different approach of economic evaluation, prevention effectiveness, which focuses on community-based prevention strategies, health education and promotion strategies, rather than pharmacoeconomic evaluation, may be used [55].

5.2 Invest in epidemiologic and cost data

With the rapid growth in obesity and noncommunicable diseases (NCDs), the Chinese government has put in tremendous efforts in obesity prevention and control [9]. The government

has supported nationally representative surveys on population nutrition and NCDs, covering both adults and children [56, 57]. These surveys, however, have their limitations if we intend to use them for economic evaluations on obesity. First, many of the large studies are consecutive cross-sectional surveys rather than cohort data and thus of limited value for causal inference. Second, limited information was recorded on the impact of interventions and lifestyle modifications, if occurred, for overweight and obesity. Except for a few studies, such as Daqing and Shougang cohorts covering large regional population or employees [58, 59], there is no established large national cohort in China collecting information on the effectiveness and cost of interventions on obesity or bodyweight. Other sources indicating the effectiveness of interventions, such as claims data, are not accessible due to confidentiality or technical issues. The lack of evidence on nutrition and obesity calls for collecting observational data from established cohorts, claims data, and representative population-based survey data in China. As the popular saying "garbage in, garbage out" stated, biased or "borrowed" parameters from other countries may undermine the validity and credibility of economic evaluations on obesity-related interventions and treatment and thus may hamper allocative efficiency in healthcare.

5.3 Modeling health and non-health outcomes

An appropriate health economic model will be useful for extrapolating the long-term outcomes of obesity that are unavailable, unobservable, or for which clinical data are unethical to collect. Though economic models have been more popular in China to model various health conditions, few exist specifically for obesity in China. Applying models developed using data from other populations and settings is not without concern, as the clinical pathways and population characteristics are significantly different between countries. Researchers may develop models

appropriate for the Chinese population and calibrate the health and non-health outcomes associated with overweight and obesity.

The non-health outcomes refer to the outcomes surrounding obesity and associated interventions but not directly associated with the QALY outcomes, such as productivity loss [60]. The Second Panel on Cost-Effectiveness in Health and Medicine noted that decision-makers need a "quantification and valuation of all health and non-health effects of interventions"[61]. A gap in research related to productivity loss due to obesity in China exists [60]. Practitioners of pharmacoeconomic analysis in China may consider the valuation of non-health outcomes of obesity, particularly productivity loss, in future research.

It is important to note that the lack of transparency in many pharmacoeconomic analyses compromises the confidence of health policymakers and the public in those analyses. Researchers should improve model transparency and confidence in the validity of the modeling by providing full disclosure of the underlying assumptions and thorough validation analysis (e.g., face/internal/external validity) of the models [62].

5.4 Discount rate

Most pharmacoeconomic studies discounted the costs and health outcomes, usually at 3% [63], consistent with the recommendation for the US [64]. UK researchers have used 3.5% for both costs and health outcomes since 2004 [65], while Canada recommends the use of 5% [66]. The newly released Chinese pharmacoeconomics guidelines recommend the use of 5% in the base case and 0~8% for the sensitivity analyses [67]. The discount rate depends on the economic context and the economic context in low-and middle-income countries (LMICs) differs from that

in high-income countries. Subsequently, researchers may derive different discount rates for LMICs, by using the shadow price of capital, marginal productivity of capital, social opportunity costs of capital, or other economic approaches.

Haacker et al. (2020) calculated a social discount rate of 8.7% for China, which separated China from other LMICs due to its fast and steady economic growth [63]. This is a useful supplement to the official guidelines with valid econometric analysis. Researchers may extrapolate the results and examine the provincial discount rates due to the vast difference across Chinese provinces in economic growth. Further research is needed because the discount rate is an essential component of pharmacoeconomic analyses.

5.5 Utility for health states

Utility-based measures are increasingly used in economic evaluations, among which QALY is one of the most popular metrics [68]. A Chinese guideline on pharmacoeconomics recommends the use of QALY, leading to increased adoption of QALY in practice among Chinese health economists[67]. There is currently no official confirmation by China's governmental agencies that QALY should be used as an outcome measure, and we expect recommendations to be made on this issue with explicit reasoning for the appropriateness of QALY—or other metrics—in the Chinese context. Additionally, we note that generic and specific instruments from other countries are widely applied in China, such as EQ-5D. However, the validity and reliability of these instruments were in question when adapted in China [69], and many health conditions, including obesity, have no accurate utility values for economic evaluation [70]. The lack of utility values might be a barrier for pharmacoeconomic applications related to obesity. Efforts are needed to facilitate health utility measurement for obesity, to develop appropriate generic or specific

instruments for the Chinese population with obesity, and to establish practice guidelines on measuring the health utility of the obese population.

5.6 Threshold of willingness-to-pay

While economic evaluation or HTA has increasingly been used in China to inform public-funded insurance for reimbursement decisions, clearly defined and measurable thresholds for willingness-to-pay (WTP) are lacking. In China, a recent study estimates that 63% of GDP per capita per disability-adjusted life-year (DALY) averted reflects health opportunity costs in the health care system by considering the elasticity of health outcomes with respect to changes in government health expenditure [71]. However, debates exist on whether the marginal productivity of health expenditure could be used as the threshold. A threshold of $50,000 per QALY had been widely used in the US and Canada, with no consensus on its origin or justification [72]. A higher range (US$100,000 - $150,000) was used later in the US [73]. Outside of the US, commonly used thresholds are one, two, and three times the GDP per capita per DALY. These thresholds were historically recommended by the World Health Organization (WHO) that an intervention costing less than one times GDP per capita was considered highly cost-effective while costing less than three times GDP per capita was cost-effective. The WHO, however, has stopped recommending the use of thresholds for HTA [74]. The use (or not to use) of the willingness-to-pay threshold and the choice of the threshold will continue to be a subject of debate in conducting pharmacoeconomic studies of obesity in China.

5.7 A five-year view

Despite existing barriers, we are cautiously optimistic about the field of pharmacoeconomic evaluation of overweight and obesity in China. Several high-quality, nationally representative

surveys have collected multiple rounds of data, enabling secondary data analyses to generate epidemiologic parameters [15, 75]. The widespread use of electronic medical records may facilitate the development of epidemiologic modeling related to chronic diseases and obesity over time. On a different front, with China's NHSA being pressed to improve the value of health investment and increase coverage, the use of economic evaluation, HTA, and pharmacoeconomics will garner more attention and, hopefully, investment. We also anticipate additional guidelines that may be suitable for Chinese practitioners and policymakers that facilitate the pharmacoeconomic evaluation of overweight and obesity in China.

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Table 1: Economic evaluations related to overweight and obesity in China

Study	Type of Analysis	Study design	Perspective	Population	Time frame	Overweight and obesity	Main conclusions (all $ are in 2019 US$)
Cost of Illness Studies							
Popkin et al.[43]	Direct costs and indirect costs	PAR	Societal	Adults	Annual (Yr. 2000)	Overweight: 25≤BMI <30 Obesity: BMI≥30 (kg/m^2)	Total costs (including both direct and indirect costs) of overweight and obesity at $71 billion ($8.4 bn direct costs, $62.6 bn indirect costs)
Zhao et al.[5]	Direct medical costs	PAR	Healthcare system	Adults	Annual (Yr. 2002- 2003)	Overweight: 24≤BMI <28 Obesity: BMI≥28	Total medical cost attributable to overweight and obesity was estimated at $3.67 billion
Shi et al.[6]	Direct medical costs	Secondary data analysis	Healthcare systems	Adults 45 years old and above	Annual (Yr 2011)	Overweight: 24≤BMI <28 Obesity: BMI≥28	Total direct medical costs of $23.9 bn associated with overweight and obesity
Zhang et al. [45]	Direct medical costs	PAR	Healthcare systems	Adults	Annual (Yr 2010)	Obesity: BMI≥30 (kg/m^2)	Total direct medical costs of $15.7 bn associated with overweight and obesity among patients with five chronic conditions
Q Li et al.[39]	Direct costs and indirect costs	Survey + economic modeling	Societal	Adults 35 years old and above	Annual (2015)	Overweight: 24≤BMI <28 Obesity: BMI≥28	Total economic burden of the four chronic diseases associated with obesity and central obesity in rural Southwest China at $4.2 billion and $9.3 billion
Cost Effectiveness Studies							
Yang et al. [44]	Cost-effectiveness analysis	Retrospective study	Healthcare systems	76 obese type 2 diabetes patients	June 2014-May 2016	Overweight: 24≤BMI <28 Obesity: BMI≥28	Pharmacotherapy is more cost-effective than laparoscopic bypass surgery in controlling HbA1C
Tu et al.[40]	Cost utility analysis	Patient cohort study with control	Healthcare systems	106 obese type 2 diabetes patients	February 2011-November 2013	Not Applicable	RYGB is cost-effective 4 years after operation with an ICER of US$21,371 *per* (QALY) gained

Wan et al.[41]	Cost effectiveness analysis	Patient cohort & Markov analysis	Health insurance perspective	215 type 2 diabetes patients	Hypothetical 40 year time horizon	BMI≥28 (kg/m^2)	bariatric surgery leads to cost savings ($4,614) and increases in health benefits (2.51 QALY)
Wang et al.[42]	Cost effectiveness analysis	Patient cohort & Markov analysis	Societal	Men/women age 18-70 T2DM patient	April 2018-April 2019	Overweight: 24≤BMI <28 Obesity: BMI≥28	blood glucose management is cost-effective for the middle-aged male group (ICER: $15,417 per QALY gained)

Notes: QALY: Quality-adjusted life years: BMI: Body mass index; PAR: population attributable risks; T2DM: Type 2 Diabetes

Table 2: Economic Burden of Diseases or Conditions in China

Study	Disease/Condition	Study Period	Main conclusions (all $ are in 2019 US$)
Popkin et al.[43] Zhao et al.[5] Shi et al.[6] Zhang et al. [45]	Overweight and obesity	2000 - 2011	Total costs: US$71 billion Indirect Costs: $62.6 billion Direct medical costs: $3.67 – 23.9 billion,
Chen and Bloom[49]	Cardiovascular disease associated with air pollution Chronic respiratory disease associated with air pollution Cancer associated with air pollution Diabetes associated with air pollution	Projected 1990-2030	$10.4 billion average annual economic impact $4.5 billion average annual economic impact $2.7 billion average annual economic impact $3 billion average annual economic impact
Clay et al. [50]	Alzheimer's disease	2010 2050	Direct medical costs: $15.6 billion in 2010 Direct medical costs: $56.9 billion in 2050 (projected)
Liang et al. [51]	Pneumoconiosis	1992	Direct medical costs: $1.5 billion
Linthicum et al. [52]	Disease-Associated Malnutrition	2009	$78 billion (lost Disability-adjusted life years)