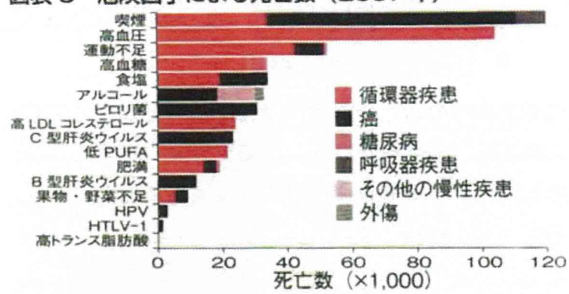
も我が国のイメージ向上が可能である。こうした方策は，現在のグローバルヘルスの潮流でもある。すなわち，資金やプロジェクトの供与のみではなく，バリュー感のある戦略とビジネスモデルの開発が重要となっている。資金は後からついてくるのである。

考えてみると，後藤新平が台湾で行ったことはまさに，日本型の医療，教育や農業のパッケージ輸出による地域おこし，国づくりであった。この日本型モデルに着目したのが，MDGsの土台を築いた著名なマクロ経済学者であるジェフリー・サックスである。彼は，アフリカの最貧地域がMDGsを達成するために，ミレニアム・ビレッジ・プロジェクト（MVP）を2006年に立ち上げ，保健医療，教育，農業，テクノロジーとイノベーション，水とエネルギー，ジェンダーと公平性，環境，ビジネスと起業家精神という8つのセクターごとに戦略を設定し，これに基づく施策をコミュニティ主導の包括的アプローチを用いて極度の貧困となる要因を削減しようとした。また，MVPは学界やビジネス，市民社会，政府の全員参加型アプローチを用いている。MVPは，日本政府やゲイツ財団の支援を受け，大きな成果を上げた[10]。

我が国の保健医療分野における過去50年間の最大の成果は，国民間での公平性を高めながら低コストで良好な健康アウトカムを実現したことである。健康アウトカムに関しては，日本は，食事等のおかげで虚血性心疾患および一部のがんの危険因子が元々低かったことから多大な恩恵を受けてきており，1950年代にはすでに他の先進国に比べて生活習慣病による死亡率は一般に低かった。ただし，脳卒中死亡率はきわめて高く，平均寿命の急激な伸びの一つの理由は，主に公衆衛生対策および血圧などの主要危険因子のプライマリ・ケアにおける管理によるものであり，やはり保健医療制度のインパクトは大きい[11]。また，我々の分析では，**少なくとも同じニーズをもつ人が同等の医療を受けられるか，医療費は公平に負担されているかという点，そして，家計の壊滅的な負担の予防の割合に関しては他国と比較しても比較的良好であり，現行の皆保険制度下での保健制度パフォーマンスは世界的にもこれまでは満足できるものであった**[12]。

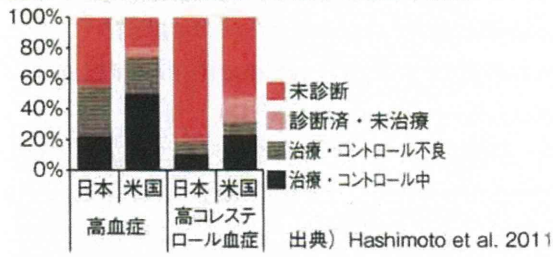
しかし，良好な健康アウトカムにも陰りが見え始めている。1990年代中頃以降は，他国に比べ成人男性死亡率の低下率が鈍化しており，成人女性も成人男性ほどではないが鈍化している。日本の男性の死亡率はスウェーデン，イタリア，オーストラリアの，また女性の死亡率はスウェーデンの後塵を拝している。近年の傾向が続けば，他の国の成人死亡率が日本を下回る可能性がある[13]。

図表3　危険因子による死亡数（2007年）



出典）Ikeda et al. 2011

図表4　日米の危険因子の診察率と管理の状況



出典）Hashimoto et al. 2011

ランセット日本特集号で池田らは，他の先進国に比べて喫煙や高血圧がまだ多いこと（**図表3**），肥満が少しずつ上昇していること，自殺率が高くまた上昇していることなど，実績悪化の原因を数多く提示している[1]。さらに，**日本には国民皆保険制度がありアクセスはよいが，提供されている医療の質が低い可能性も指摘されている。**例えば，我が国では高血圧や高コレステロール血症の患者が実際に治療される割合は他の先進国に比べてはるかに低い[12]。**図表4**に示すように，高血圧症および高コレステロール血症を抑える薬剤を現在処方されている患者のうち，目標数値を達成したのは半数にすぎなかった。さらに，未診察・未治療患者の割合は，アメリカの推計数よりも多かった。医療の質が不十分なことを考慮すれば，日本の健康アウトカムをさらに改善させるには保健医療制度を刷新する必要がある。

これまでの途上国型モデルは国外の医療展開にはきわめて有用であるが，国内ではそれでは対応できない。日本は基本政策として，診療報酬点数表により支払条件を供給側で厳格に管理する一方，サービスの提供方法については自由放任主義的アプローチを取ってきたために，深刻な受給ミスマッチが生じている[12]。

ワシントン大学のマレーは，経済停滞，政治の混乱，高齢化，十分ではないタバコ対策という状況のなかで，

日本は保健医療の新たな課題に効果的に対応しておらず，これらの課題に取り組むには，安価で多くの患者を診る，従来どおりのアクセスを全国民に保証する制度だけでは不十分であると指摘している。我が国は一致協力して取り組まなければ，アメリカと同様，世界での平均寿命ランキングが下がっていく可能性があるとさえ指摘する[13]。しかし，少子高齢化の進む今もなお，高度経済成長時代の制度が惰性的に継続されているのが現状である。また，橋本らの試算では，無保険者もすでに百万人以上おり，皆保険は実質破綻していると考える[12]。

また，医療費を賄うために税を投入しているが，社会保険のリスクシェアリングという原則，あるいは税の応能負担による所得再分配機能という二つの目的がきわめて曖昧にされながら，多くの保険制度改革議論は財源論に終始している。財源論はもちろん重要である。さらに，給付抑制，無駄なサービスのカットや成果に基づく支払い，混合診療，医療の規制緩和などは，やるかやらないかではなく，いつどのようにやるかというイシューであろう。だが，それらは必ずしも今後の医療の価値やあり方の本質ではない。我が国の医療のあり方を論ずることなく，**既存制度の財源をとりあえず確保し，延命するという現在の医療行政の継続はきわめて困難な時期にきている。**

7 国民皆保険制度が抱える今後の課題は世界から注目されている

日本は，**少子高齢化の進展，経済的不確実性の増大，そしてグローバル化という今日的文脈のもとで，「健康」の意味を考え直す必要に直面している。**特に，国民が健康に対して抱いている価値観に寄りそって，国内外ともに整合性のある健康ビジョンを策定する必要がある[4]。これが，ランセット日本特集号の最大のメッセージである。

日本は，伝統的な国家安全保障に加えて「**人間の安全保障**」，つまり，すべての人々を脅威から守り，生存・暮らし・尊厳のための糧を与えることを外交政策の礎にした。緒方貞子氏とアマルティア・セン教授を委員長として国連に「人間の安全保障委員会」を作り，その意義を広めた。それは日本が政治・経済・社会の発展の相互依存性を理解していたからであるといえよう。これまで機能してきた我が国の保健医療制度は破綻し始めており，最近の震災でも明らかなように，現在では国内の人間の安全保障をも脅かし始めている。**人間の安全保障がこれまで以上に重要であり，このコンセプトをもっと積極的に国内政策に応用することが必要である**と筆者は考える。アマルティア・センの弟子である経済学者アナンドは，**人間の安全保障のコンセプトの主要な課題の一つは人々の健康を守ることであり，そのために包括的な国民皆保険制度は必須である**，と述べている[14]。

国民皆保険制度が達成した成果は大きい。しかし，過去の成功が現状に合わなくなっているのも事実である。国民皆保険制度は目的ではなく，あくまでも保健医療の目標を達成するための一つの手段である。日本の国民皆保険制度が抱えている課題の一つは，財源もそうだが，保健医療のあり方やそれに対する人々の価値観が変わってきていることをまず認識すべきことである。今までのように，**安くて皆が同じような医療を受けられればそれでよいという時代ではなく，個人のニーズ，価値観を重視した高付加価値の保健医療へと質的に転換しなければならない。**そして，困っている人々には手厚い保護を行う。その際に核となる考えが「**人間の安全保障**」であり，それを達成する際に必要となる発想が「**保健医療は投資**」であるということである。

実状に合わせて我が国の保健医療制度をよりよいものにするには，官僚や学者，政治家任せにするのではなく，国民が自分たちの切実な問題として考え，従来の保健セクターを越えて連携し，行動しなくてはいけない。外交安全保障と同様に，保健医療は存在するのが当たり前ではなく，自分たちで守らなくてはいけない。日本のような急速に高齢化が進む国はほとんどなく，日本がこうした問題をどのように解決していくかは，今後のモデルとして世界中が注目している。

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Health-Related Financial Catastrophe, Inequality and Chronic Illness in Bangladesh

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Abstract

Background: Bangladesh has a high proportion of households incurring catastrophic health expenditure, and very limited risk sharing mechanisms. Identifying determinants of out-of-pocket (OOP) payments and catastrophic health expenditure may reveal opportunities to reduce costs and protect households from financial risk.

Objective: This study investigates the determinants of high healthcare expenditure and healthcare- related financial catastrophe.

Methods: A cross-sectional household survey was conducted in Rajshahi city, Bangladesh, in 2011. Catastrophic health expenditure was estimated separately based on capacity to pay and proportion of non-food expenditure. Determinants of OOP payments and financial catastrophe were estimated using double hurdle and Poisson regression models respectively.

Results: On average households spent 11% of their total budgets on health, half the residents spent 7% of the monthly per capita consumption expenditure for one illness, and nearly 9% of households faced financial catastrophe. The poorest households spent less on health but had a four times higher risk of catastrophe than the richest households. The risk of financial catastrophe and the level of OOP payments were higher for users of inpatient, outpatient public and private facilities respectively compared to using self-medication or traditional healers. Other determinants of OOP payments and catastrophic expenses were economic status, presence of chronic illness in the household, and illness among children and adults.

Conclusion: Households that received inpatient or outpatient private care experienced the highest burden of health expenditure. The poorest members of the community also face large, often catastrophic expenses. Chronic illness management is crucial to reducing the total burden of disease in a household and its associated increased risk of level of OOP payments and catastrophic expenses. Households can only be protected from these situations by reducing the health system's dependency on OOP payments and providing more financial risk protection.

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Introduction

The fundamental role of a healthcare system is not only to improve population health but also to protect households from financial catastrophe associated with illness [1]. Out-of-pocket (OOP) payments for healthcare can cause households to incur catastrophic expenditures, pushing them into poverty [2,3]. Globally, approximately 44 million households face catastrophic health expenditure annually, and about 25 million households are pushed into poverty by their health expenses [4,5]. In countries where risk pooling mechanisms are available people are protected from catastrophic spending [4] but many low- and middle-income countries experience high OOP payments and lack risk-sharing mechanisms, forcing households into hardship, asset depletion, debt, reduction of essential consumption, and sometimes financial catastrophe [4–11].

Like many developing countries, Bangladesh is also facing the double burden of disease [12,13], OOP payments remain the most important source of funding for healthcare, and health insurance is almost nonexistent except for small pockets of NGO-financed schemes [14]. Despite the possibly high incidence of catastrophic expenses and high OOP expenditure in Bangladesh [15,16], we are not aware of any study detailing determinants of OOP payments and catastrophic expenditures. To date, the only two studies reporting overall incidence of catastrophic expenses in Bangladesh are multi-country studies that present contradictory findings because of data limitations and methodological differences [16,17]: one of them found a very low (1.2%) incidence of catastrophic expenditure [17], while the other found a very high

incidence (15%) [16]. They also did not explore variations in OOP payments and catastrophic spending by healthcare facility, or by household or individual characteristics such as the presence of chronic illness. Several studies suggested that illness among a child or adult, presence of chronic illness [18–21], lack of health insurance [9,10,17,22], and use of inpatient or outpatient care [8,10,19,21–25] are key factors in high OOP payments and catastrophic health expenditure, but very few studies have considered these factors simultaneously. An interesting study in India examined determinants of OOP payments but did not extend the analysis to the associated problem of catastrophic expenditure [21]. Our study expands on this methodology to include assessment of the incidence of catastrophic expenditure, which is a key measure of the extent of financial risk protection as it judges whether the existing health financing system is able to protect its residents from the consequences of OOP payments [26].

Thus, previous estimates may have provided an incomplete picture of the impact of medical expenses on populations with a high prevalence of chronic illness and limited risk-pooling mechanisms. In designing healthcare financing systems, policy makers need to understand determinants not just of OOP payments, but also the related problem of catastrophic health expenditure associated with high OOP payments [17]. To address these questions, the study aims to investigate two closely linked phenomena: the determinants of OOP payments and catastrophic expenditure in Bangladesh. These analyses are conducted using double hurdle and Poisson regression models in combination with a probability survey.

Data and Methods

Study area

The study was conducted in Rajshahi city, Bangladesh, which is the third largest city in the country and broadly representative of many urban areas in Bangladesh [27]. Rajshahi has a population of 4.59 million, with an average household size of about five. The literacy rate is 71% and 62% for males and females respectively [27]. In rural areas of Bangladesh, there are some supplementary health financing programs such as demand-side financing (DSF), which reduce financial barriers to maternal healthcare among poor women. However, these programs do not exist in urban areas [28], where households suffer more illness, particularly non-communicable diseases (NCDs), and use more health facilities compared to rural households. Therefore, this study focused on urban areas of Rajshahi, in order to examine how urban households deal with OOP health expenditure in the absence of risk protection mechanisms like DSF or health insurance.

Study design

A cross-sectional three-stage cluster sampled household survey was performed during August to November 2011. The primary sampling unit (PSU) was the *Mahallah*, the lowest administrative region of a Bangladeshi city. In the first stage, 40 clusters were randomly selected from 159 eligible PSUs with probability proportional to size. In the second stage, a fixed number (40) of buildings was selected by systematic random sampling from each chosen cluster based on a household listing operation to provide the necessary frame for selecting buildings. During the final stage, one household was randomly selected from each building, with a target sample of 1600 households. Of these households, only seven refused interview or were not available to be interviewed, and the final effective sample size was 1593 households, resulting in a response rate of 99.6%.

Data collection

Respondents were administered a structured questionnaire developed based on the Bangladesh Household Income and Expenditure Survey (HIES) [29], and the Living Standards Measurement Survey (LSMS) [30]. The questionnaire was translated from English to Bengali and a pilot study was performed in order to detect implementation difficulties. Field activities were supervised by the study coordinator with the help of the University of Rajshahi, Bangladesh. Twenty-seven interviewers (social science, demography and statistics graduates with experience in survey methods) and five supervisors were recruited to administer this survey. All of them received 10 days' training and two days of practical sessions on the content of the questionnaire, techniques to elicit more information and strategies for obtaining complete and reliable data. For clarification of the research purpose, an interviewer and supervisor operational manual was provided two days before their training started, to ensure they understood their duties and responsibilities.

The respondents in this study were the women in the household, the household head, or the most knowledgeable person in the household, where necessary. Informed consent was obtained prior to conducting the interviews. The survey questionnaire contained two main sections: the household questionnaire and the individual illness questionnaire. The household questionnaire covered survey and household identification and household consumption expenditure, including food consumption, non-food expenditure, housing and durable goods; the individual questionnaire contained demographic information such as age, sex, marital status, education and occupation of individuals in the household, and health problems in the past 30 days. The food consumption section covered purchased, home-produced and in-kind consumption in the past 30 days or past 12 months prior to interview. Following the same recall process as food consumption, the non-food expenditure section also covered purchased and in-kind goods. Housing rent or equivalent rents were recorded in the past 30 days and the durable goods section recorded detailed information on number of items, duration, present and past value of the most recent items in the one year recall period. Cost of medical expenses including fees (consultation/investigation fees, blood tests, etc.), drugs and medical supplies, transport costs for patients and accompanying family members, and other costs were recorded for each episode of illness in the past 30 days prior to interview. All expenditure was recorded in the Bangladeshi currency, taka (TK). In addition, data on timing and cost of all episodes of illness, care-seeking behavior and inpatient or outpatient care were recorded for the past 30 days prior to interview.

Measures of the burden of OOP payments

Consistent with common definitions, OOP healthcare expenditure was defined as 'catastrophic' if it exceeded 40% of household non-food expenditure or capacity to pay in the past 30 days [5,17,31,32]. Total household consumption expenditure was calculated according to the living standard measurement survey guidelines [33] and household consumption quintile was determined using the approach of Xu and colleagues [17]. Household consumption expenditure is the sum of food consumption, non-food expenditure, housing, and durable goods. Catastrophic healthcare expenditure and consumption quintile were calculated using household total consumption expenditure, capacity to pay and equivalent household size. This equivalent scale is used, rather than actual household size, because in low-and middle-income countries household consumption expenditure increases with increases in household size but that increase is less

than proportionate to the increase in household size [17]. We also calculated the ratio of medical expenses intensity proposed by Dror and colleagues [21]. This medical expenses intensity ratio was estimated by dividing the average medical expenses per episode of illness by the average consumption expenditure per household member. We excluded from this analysis the households whose household members did not suffer any kind of illness in the recall period. This ratio was then calculated for each expenditure quintile, as a measure of the burden of OOP payments standardized for illness intensity and household size.

Statistical analysis

Descriptive statistics were calculated using the mean (confidence interval), median (inter-quartile range) or frequency and proportions as appropriate. Trend tests were performed using the Mantel-Haenszel chi-square test for categorical variables and linear regression analysis for continuous variables, with ordinal numbers (1–5) assigned to the quintile categories. Double hurdle and Poisson regression models were used to identify the determinants of OOP payments and catastrophic expenditure, respectively. A brief description and motivation of the models is given below.

The double hurdle regression model

Reporting of zero expenditure is quite common in household consumption expenditure surveys. For example, both medical and tobacco consumption expenditure are zero for many individuals or households over a survey recall period. In addition, participation in expenditure and the magnitude of expenditure may not be statistically independent [34,35], and the same stochastic process may not affect participation and consumption level decisions. We used a double hurdle model to overcome these problems [23,35,36]. This model requires a subject to pass a consumption decision hurdle before the level of consumption can be modeled. The first hurdle involves the decision about whether or not to participate in healthcare consumption (the participation decision, modeled in the double hurdle model with a probit function). It is reasonable to assume that participation in healthcare spending is influenced by social and demographic factors [35,37]. The second hurdle concerns the level of health expenditure (the consumption decision, handled with a Tobit function). Thus the model uses information on both the probability and magnitude of expenditure simultaneously in assessing predictors of consumption.

The double hurdle model was used to assess the relationship between demographic and household variables and the size of OOP expenses. The dependent variable for the probit model is a dichotomous variable that indicates whether OOP expenses were incurred (the participation decision). The Tobit regression model analyses the natural logarithm of OOP payments as a function of the covariates (the consumption decision). This model can be presented symbolically through two related equations for participation and consumption.

Observed consumption:

$$y = d.y^{**} \tag{1}$$

Participation equation:

$$w = \alpha' z + u,\ u\tilde{N}(0,1)$$
$$d = \begin{cases} 1\ if\ w > 0 \\ 0\ otherwise \end{cases} \tag{2}$$

Consumption equation:

$$y^{*} = \beta' x + v,\ v\tilde{N}(0,\sigma')$$
$$y^{**} = \begin{cases} y^{*}\ if\ y^{*} > 0 \\ 0\ otherwise \end{cases} \tag{3}$$

Where d is a latent variable describing the household's decision to participate in the OOP healthcare expenditure, y^{*} is another latent variable describing household level of healthcare expenditure, y is the observed dependent variable (household expenditure on healthcare expenditure), z is a vector of variables explaining the participation decision, and x is a vector of variables explaining the expenditure decision. According to Jones, the likelihood function can be written as [34]:

$$L = \Pi_0[1 - \Phi(\alpha' z, \beta' x, \rho)]\ \times \Pi_+ \Phi$$
$$[(\alpha' z + \frac{\rho}{\sigma}(y - \beta' x))/\sqrt{1-\rho^2}]\frac{1}{\sigma}\phi[\frac{y-\beta' x}{\sigma}] \tag{4}$$

Where zero consumption is denoted as 0 and positive consumption is indicated with a +. In this likelihood function, p then denotes probability of expenditure, Φ and ϕ denote distributions and density functions, respectively, and $f(.) = \vartheta(.)/\Phi(.)$. The coefficients for the model are then obtained by maximizing the likelihood (equation (4)).

Poisson regression model

In the case of rare events, Poisson regression can provide more accurate estimates than logistic regression [38,39]. Because catastrophic health expenditure can be a rare event, in our study a multiple Poisson regression model was used to identify the determinants of catastrophic expenditure, with model selection based on backward stepwise model-building. This model is well-established for the analysis of counts of rare events [38,39].

All analyses at both the univariate and multiple regression stages were adjusted for the probability sample design. Statistical analysis was performed using Stata/SE Version 12.0.

Covariates

The study modeled households' OOP health payments and risk of catastrophic expenditure as a function of household characteristics and economic status and presence of illness and care-seeking behavior, using average illness per child and adult as a measure of illness [20]. Past studies suggested that average number of illnesses per child and adult is less likely to incur bias due to household age structure and more accurately reflects disease occurrence within a household than absolute number of illnesses [20]. In Bangladesh, households often use local, privately-run traditional healers or pharmacists as their prime point of care, and health-seeking behavior in this study was thus classified in three forms: traditional healers/self-medication/no care, outpatient, or inpatient services. Outpatient and inpatient services could be public or private facilities, but traditional healers, pharmacists and other forms of unregulated care provider are always privately run. The small number of respondents receiving inpatient care in this sample precluded separate presentation of this variable by private and public type, but outpatient facilities were divided into public and private facilities. We also could not consider the role of NGO providers separately, because very few households (13 households) in the study sample used NGO-based health services. As a result, these services were combined with private outpatient services

during analysis. In our study, care-seeking behavior was then grouped into five categories: inpatient care included those staying overnight in either a hospital or clinic; outpatient public facilities included district/sadar hospitals, maternal and child welfare centers (MCWC), urban health centers, family welfare centers (FWC), government satellite clinics, diabetic centers, other government facilities; outpatient private facilities included private hospitals or clinics, NGO clinics or satellite clinics, and qualified allopathic practitioners (MBBS doctors); both outpatient public and private included those who used outpatient public and private services simultaneously in the past 30 days, self-medication including drugs obtained at a pharmacy or drugstore, kabiraj or spiritual healers, homeopathic practitioners, shops, other traditional healers, or no service of any kind.

Ethical considerations

This study received ethical approval from the Ethics Committee of The University of Tokyo and the Bangladesh National Research Ethics Committee, with reference number BMRC/NREC/2010-2013/1161. About one third of the population in Rajshahi city are still illiterate and even written consent is not common practice among them. Therefore, a consent form to obtain and document verbal or written consent from respondents was proposed and approved by the Ethics Committee together with the study protocol. Prior to the interview, our enumerator carefully read the consent form to the subject and then very briefly explained the aims and importance of the study. This consent form contained information on the objectives of the study, risks, benefits and freedom of participation, and confidentiality.

Results

Background characteristics and OOP payments

The incidence of catastrophic healthcare expenditure by illness, care-seeking behavior and household level characteristics is presented in Table 1. Table 1 also shows household characteristics. Of the 1593 households sampled, average total monthly household consumption expenditure was TK 15749.0 (US $ 209.5) (95% CI 10064.3–23720.0), 91.2% (95% CI 88.5–93.2) had incurred positive health expenditure and the share of OOP payments was about 10.6% (95% CI 8.6–12.5) of total expenditure. On average, residents spent TK 138.0 (US$ 1.8) (95% CI 42.5–366.6) per month on health-related goods and services. During the past 30 days recall period, 1501 households (about 94%) had at least one illness episode. Of these, 1148 (71%) households had at least one chronic illness and the average number of illnesses was 2.8 per household (95% CI 2.6–2.9). Overall, nearly 9% of the households incurred catastrophic healthcare expenditure at a capacity to pay threshold of 40%. At a non-food expenditure threshold of 25% and 40%, the incidence of catastrophic expenditure was 9.8% and 17.6% respectively. Figure 1 shows the association between household consumption quintile and per capita OOP payments and proportion of households facing catastrophic health expenditure. There was a statistically significant trend towards higher OOP expenditure in wealthier households ($p<0.01$) but lower risk of catastrophic expenditure ($p<0.01$). The average total cost of illness per household, per capita monthly expenditure and the medical expenses intensity ratio (the ratio of these two variables) are presented in Table 2. The overall median cost of one illness episode and per capita monthly consumption expenditure was TK 242 and TK 3517 respectively and these costs differed significantly by consumption quintile (p-value for trend $p<0.01$). About 50% of residents spent an amount equivalent to at least 7% of monthly per capita consumption expenditure on one episode of illness.

Determinants of OOP healthcare expenditure

Results of the double hurdle model are presented in Table 3. Because all subjects who received inpatient care incurred OOP payments, care-seeking behavior could not be included as a determinant of decision to spend, but was included in the second-stage equation. The participation and consumption decisions were not independent ($\chi^2_{(1)} = 8.88$; $p<0.01$), indicating a double hurdle model is appropriate for this data. Presence of chronic illness, household size, average illness per child and adult, care-seeking behavior, education level of the household head and household consumption quintile significantly affected the level of household OOP healthcare spending.

Determinants of catastrophic healthcare expenditure

Table 4 shows the results of the Poisson regression model of risk of catastrophic expenditure, defined as an expense in excess of 40% of the household capacity to pay (40% threshold) in the past 30 days. The average number of illnesses, both per child and per adult, significantly increased the relative risk of incurring catastrophic payments, by 1.12 times and 1.47 times for a single additional average illness in children and adults, respectively. The relative risk of catastrophic expenditure relative to households who used traditional healers or pharmacies only was higher for private than public outpatient facilities, and higher still for households who used both public and private outpatient facilities. Hospitalization was the biggest risk factor for catastrophic expenses. Households in the poorest quintile had more than four times the risk of catastrophic expenditure than the richest quintile and as the household head's education level declined the relative risk of catastrophic health expenditure increased.

Discussion

This paper, based on a representative household survey in Rajshahi city, Bangladesh, is the first to consider illness, care-seeking behavior, demographics of the household head, and household economic characteristics as household-level predictors of OOP payments and catastrophic expenditure. It is also among the few examples of studies that have reported the incidence of catastrophic healthcare expenditure in Bangladesh [16,17], and the first to estimate this incidence from a representative, probability-sampled survey.

This study found that sampled households, none of whom have any form of risk-pooling insurance, spend about 11% of their total household budget on healthcare, and nearly 9% of households experience financial catastrophe. At a 25% non-food expenditure threshold, the incidence of financial catastrophe was similar to another published study, at 18% [16]. The study demonstrated that the medical spending associated with an illnesses episode increased as household consumption expenditure increased, which is similar to another study in India [21]; however, we showed that despite this increase in spending, the risk of catastrophic expenditure decreased with household consumption expenditure. In addition to the common finding that household consumption quintile and receiving inpatient care are associated with financial catastrophe, this study showed the importance of the average number of illness episodes among children and adults, and the presence of chronic illness in a household as key determinants of high OOP payments and financial catastrophe. Higher levels of education in the household head were also protective against OOP

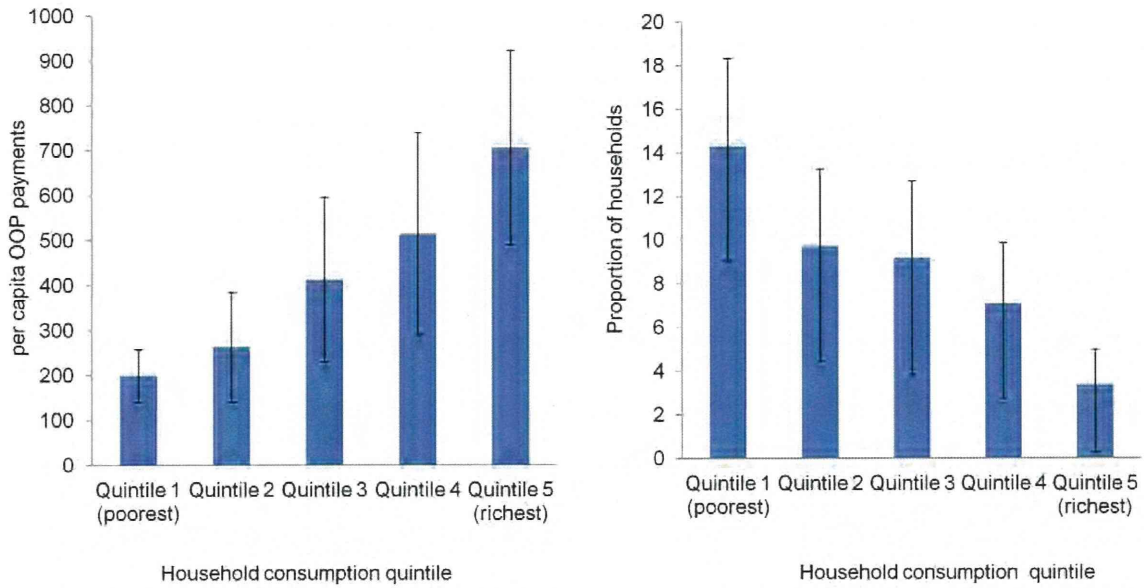

Figure 1. Association between household consumption quintile and per capita OOP payments and catastrophic expenditure.
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spending and catastrophic expenditure, similar to other developing countries [8,25].

This study revealed that the per capita monthly OOP health expenditure made by households was TK 138.0 (US$ 1.8), which is similar to national-level findings in Bangladesh [15]. The estimated proportion of catastrophic expenditure in our study is consistent with van Doorslaer et al [16] but contradicts the findings (1.2%) of Xu and colleagues [17], though our study supports their findings that poor households were less able to cope with any level of health payment than rich households [19,40,41]. The disagreement in proportions of catastrophic expenditure between our study and Xu et al is likely to be due to differences in data and measurement methods. Their study used the Bangladesh HIES, which mainly emphasized poverty assessment and was not designed to account for details of household illness and their treatment responses or costs. According to Xu and colleagues, the estimated proportion of households facing catastrophic expenditure in Bangladesh may be underestimated in the 1995 HIES survey due to missing information such as the absence of durable goods from the consumption calculation, and the very limited information collected on episode-of-illness level healthcare expenditure data, and care-seeking behavior. In their study, van Doorslaer and colleagues estimated the incidence of catastrophic expenditure based on total household consumption and non-food expenditure but they did not assess the incidence of catastrophic expenditure using household capacity to pay. In contrast, our study considered all household members who suffered any illness and their treatment response in the past 30 days, and then collapsed information into household level for analysis purposes. Therefore, our study offers more accurate information than the previous two studies conducted in Bangladesh, and also used a more detailed and accurate methodology for estimating the burden of OOP payments, with adjustments for household size and capacity to pay [42].

Consistent with other studies [19,20,22,43–46], although the richest households reported more illness, spent more on health and utilized more private facilities compared to the poorest quintile, risk of financial catastrophe was higher in the poorest households, indicating that the burden of financial catastrophe falls disproportionately on the poor. The three key preconditions for catastrophic health expenditure are the presence of health services requiring payments, low capacity to pay, and lack of prepayment or health insurance options [17]. These conditions are all present in the poorest households in Bangladesh, and the high proportion of catastrophic expenses in the lowest quintiles points to the urgent need to remove one or all of these preconditions. For example, the OOP share dropped markedly following the introduction of health insurance in China [47], Vietnam [48], and India [49], and the introduction of even basic prepayment or health insurance systems in Bangladesh may have a similar effect on the poorest households.

Our analyses demonstrate a negative impact of average illness per child and adult, and presence of chronic illness in the household, on the household economy. These results are similar to the determinants of catastrophic expenditure in Burkina Faso and India [18,20], such as lack of formal education, tuberculosis, diabetes, dementia, modern medical care, number of illness episodes among adults and chronic illness. In concordance with results from India [21], the level of OOP payments is higher among those who used inpatient care services and suffer from chronic illness. Moreover, the study also revealed the importance of the average number of illness episodes among children and adults, and larger household size as key factors responsible for high OOP payments. Chronic care for NCDs puts an enormous and continuous financial strain on household budgets. The costs of care of chronic NCDs often contribute to increased OOP payments, pushing households into impoverishment or below the poverty line [3,50]. In such critical situations, only a strong risk pooling mechanism can prevent the poorest households from risk of financial catastrophe. Health insurance can have the dual function of protecting families against health shocks that increase healthcare needs, and against economic shocks that reduce their capacity to finance healthcare [51].

Type of health service used was also another important determinant of OOP payments and financial catastrophe, with intensity of OOP payments at public outpatient facilities lower than private outpatient facilities. These findings are similar to

Table 1. Incidence of catastrophic health expenditure by illness and household characteristics.

Variable	Frequency (n = 1593)	Frequency of catastrophic expenditure	Proportion (95% CI)	P-value
Illness and care-seeking behavior				
Care-seeking behavior				
Inpatient	65	44	68.5 (56.6–78.4)	<0.01
Outpatient public	253	23	9.0 (5.6–14.2)	
Outpatient private	385	35	9.3 (6.5–13.1)	
Outpatient public and private	105	14	16.9 (10.2–26.8)	
Self-medication/traditional healer	785	21	2.8 (1.6–4.8)	
Member with chronic disease				
Yes	1148	115	10.5 (8.3–13.3)	0.01
No	445	22	5.2 (3.1–8.5)	
Household characteristics				
Household member over 65 years				
Yes	136	16	11.0 (6.4–18.3)	0.4
No	1457	121	8.8 (7.0–11.1)	
Gender of household head				
Male	1447	124	8.9 (7.2–11.0)	0.9
Female	146	13	9.5 (4.2–19.9)	
Educational status of household head				
No education	258	36	15.2 (11.1–20.5)	<0.01
Primary	310	38	11.4 (7.8–16.6)	
Secondary	420	33	7.2 (5.0–10.2)	
Higher	605	30	5.9 (4.1–8.4)	
Household consumption quintile				
Quintile 1 (poorest)	319	47	14.3 (10.3–19.6)	<0.01
Quintile 2	319	30	9.7 (6.2–15.0)	
Quintile 3	318	30	9.2 (5.7–14.5)	
Quintile 4	319	20	7.1 (4.3–11.4)	
Quintile 5 (richest)	318	10	3.4 (1.7–6.4)	

All percentages and confidence intervals incorporate the effect of the probability sampling structure.
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several studies from developing countries [8,52] but at variance with a Nepalese study [25,44]. Although public health facilities in Bangladesh are heavily subsidized by the Government [53,54], the risk of incurring OOP expenditure as well as catastrophic spending remains high for users of these facilities. This suggests that subsidized programs may not be working properly among disadvantaged groups. One reason could be that unofficial fees in public facilities can significantly exceed the amounts expected in

Table 2. Ratio between cost of illness per household and monthly expenditure per household member.

Characteristics	Median cost (TK) per illness episode	Median expenditure (TK) per household member	Median ratio of cost/income ratio
Consumption quintile			
Quintile 1 (poorest)	150	1785	0.08
Quintile 2	188	2623	0.07
Quintile 3	242	3481	0.07
Quintile 4	285	4997	0.06
Quintile 5 (richest)	467	7944	0.05
Total	242	3517	0.07
P-value for trend	P<0.01	P<0.01	P<0.01

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Table 3. Double–hurdle regression model of expenditure (total sample household data).

Variable	1st Stage			2nd stage		
	Participation (probit) equation			Expenditure (Tobit) equation		
	Coefficient	Standard error	p-value	Coefficient	Standard error	p-value
Constant	−0.7	0.34	0.04	4.81	0.16	<0.01
Illness and care-seeking behavior						
Average illness per child	0.17	0.07	0.02	0.1	0.02	<0.01
Average illness per adult	1.27	0.53	0.02	0.24	0.04	<0.01
Member with chronic disease						
Yes	0.49	0.13	<0.01	0.46	0.08	<0.01
No	0	NA		0	NA	
Care-seeking behavior						
Inpatient				3.17	0.13	<0.01
Outpatient public				0.78	0.07	<0.01
Outpatient private				1.21	0.08	<0.01
Outpatient both public and private				1.46	0.1	<0.01
Self-medication/traditional healer				0	NA	
Household characteristics						
Educational status of household head						
No education	−0.04	0.2	0.9	0.02	0.11	0.8
Primary	0.39	0.21	0.06	0.14	0.11	0.2
Secondary	0.2	0.13	0.1	0.19	0.09	0.03
Higher	0	NA		0	NA	
Age of household head (years)	0	0.01	0.7	0.01	0	<0.01
Household size	0.16	0.06	0.01			
Household consumption quintile						
Quintile 1 (poorest)				−0.62	0.12	<0.01
Quintile 2				−0.52	0.11	<0.01
Quintile 3				−0.29	0.1	0.01
Quintile 4				−0.24	0.11	0.03
Quintile 5 (richest)				0	NA	

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official payments, and fee exemptions are not always possible [53], suggesting that public facilities are not providing their expected financial protection in practice. Another possible reason is the need to purchase drugs and ancillary health services such as medicines or tests on the private market. This suggests the need for state-subsidized public clinics to provide more holistic and inclusive services. Finally, similarly to other studies [19,43], those receiving inpatient care were at high risk of OOP expenditure and catastrophic spending. In the absence of a risk-pooling mechanism, all households face high risk of financial catastrophe from OOP payments for inpatient care.

The research protocol and sampling process in our study was designed to avoid any biases in the results, but our study has several limitations. We examined only urban households in one metropolitan area of the country, so the results cannot necessarily be generalized to the whole country. However, the representative nature of the sample means that the results may be applicable to other cities, and thus the study may reflect the reality of health market participation for a large proportion of the Bangladeshi population. Inpatient service use is infrequent (4%) and a much larger sample is required to explore the role of chronic vs. acute illness in hospitalization and costs. Such an analysis might better describe the role of preventable hospital admissions in catastrophic spending. Consumption and expenditure were self-reported and prone to error, although estimates were confirmed by other household members or aged persons in the community. For example, female interviewees frequently over- or under-estimated the cost of bicycles, sewing machines and cars, but we minimized the bias by asking another household member or an older member of the household.

This study identifies determinants of high medical expenditure and financial catastrophe: illness either in children or in adults, chronic illness, receiving inpatient care, poorer economic status and lower education level of the household head. The chronic care of NCDs requires long-term routine clinic visits, testing, and medications, reducing households' flexibility to respond to the cost of unexpected hospitalization or other illness episodes. It is clear that immediate action is necessary to reduce levels of catastrophic health expenditure by reducing the burden of OOP payments in Bangladesh, which can be achieved by:

- Implementing compulsory health insurance for salaried workers in both public and private sectors, and voluntary memberships for dependents, farmers and self-employed

Table 4. Multiple Poisson regression model for catastrophic expenditure.

Variable	Relative risk	95% confidence interval	p-value
Illness and care-seeking behavior			
Average illness per child	1.12	(1.03–1.23)	0.01
Average illness per adult	1.47	(1.13–1.93)	0.01
Care-seeking behavior			
Inpatient	28.36	(16.49–48.77)	<0.01
Outpatient public	2.93	(1.66–5.16)	<0.01
Outpatient private	4.38	(2.31–8.30)	<0.01
Outpatient public and private	7.03	(3.37–14.66)	<0.01
Self-medication/traditional healer	1.00	NA	
Household characteristics			
Educational status of household head			
No education	2.35	(1.25–4.41)	<0.01
Primary	1.62	(0.88–3.00)	0.1
Secondary	1.30	(0.74–2.27)	0.4
Higher	1.00	NA	
Household consumption quintile			
Quintile 1 (poorest)	3.76	(1.46–9.68)	<0.01
Quintile 2	2.55	(1.02–6.38)	0.01
Quintile 3	2.61	(1.22–5.54)	0.01
Quintile 4	2.25	(1.09–4.65)	0.01
Quintile 5 (richest)	1.00	NA	

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persons, similarly to programs in Vietnam that have been shown to reduce OOP payments to lower levels than observed in this study [55]

- Improving routine management of NCDs, to reduce the cost of chronic disease management, and incorporating chronic disease management into public services and health financing initiatives, to ensure that this expenditure is included in risk-pooling and welfare initiatives and the high OOP payments associated with chronic illness that were identified in this study can be ameliorated by better and more equitable management, prevention and treatment
- Incorporating ancillary services into basic care packages in public facilities, so that users are not required to pay significant OOP expenses for essential pharmaceutical or other ancillary services which are supposed to be almost free, but which our study found were still associated with high OOP payments and catastrophic expenditure risk

If necessary reforms are implemented, especially those targeted at the poorest members of Bangladeshi society, significant reductions in the burden of OOP payments can be made, with consequent improvements in the health of the population.

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Author Contributions

Critical revision of the manuscript for important intellectual content: SG KS. Administrative, technical, or material support: PS. Study supervision: MMR PS. Conceived and designed the experiments: MMR ES KS. Performed the experiments: MMR PS. Analyzed the data: MMR SG. Contributed reagents/materials/analysis tools: MMR SG. Wrote the paper: MMR.

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Interventions during the antenatal period for preventing stillbirth: an overview of Cochrane systematic reviews (Protocol)

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[Overview of Reviews Protocol]

Interventions during the antenatal period for preventing stillbirth: an overview of Cochrane systematic reviews

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The objective of this overview is to summarise the evidence from Cochrane systematic reviews regarding the effects of antenatal interventions for preventing stillbirth during pregnancy.

BACKGROUND

Description of the condition

Global estimates indicate that at least 2.6 million (uncertainty range 2.08 million to 3.79 million) stillbirths occurred in the last trimester of pregnancy in 2008 (at least 1000 g birthweight or at least 28th week of gestation), with more than 55% in the antepartum period (Cousens 2011). Antepartum stillbirths (1.46 million) need improved care during pregnancy, targeting maternal infections, hypertension, and poor fetal growth (Lawn 2011). Yet, the total number of stillbirths including those earlier in gestation (22 weeks and before 28 completed weeks of gestation) is far greater, but are hardly ever counted in low-income countries (Froen 2009; Froen 2011; Lawn 2011). The vast majority (98%) of these stillbirths occurred in low- and middle-income countries. Worldwide, 67% of stillbirths occur in rural areas, 55% in rural sub-Saharan Africa and south Asia, where skilled birth attendance and caesarean sections are much lower than that for urban births (Lawn 2011). Third-trimester stillbirths are estimated to occur slightly lower than the three million early neonatal deaths every year (Lawn 2011).

Despite this large burden, stillbirths have been ignored in global statistics or in international health policy; stillbirths are not included in the Millennium Development Goals (MDGs) or in estimates of the global burden of disease. Furthermore, most countries generally under-report or do not include stillbirths in their vital statistics reporting systems (Bhutta 2011). It is largely known that MDG5 (to improve maternal health) has shown the least progress among all MDGs (UN 2010). Maternal mortality is correlated with stillbirth; in low- and middle-income countries, prolonged labour, infections and haemorrhage, asphyxia, and trauma are the leading causes of maternal death or stillbirth (McClure 2007; Weiner 2003). Major risk factors for stillbirths in high-income countries are maternal overweight and obesity (body-mass index 25 kg/m^2 or higher), maternal age over 35 years, primiparity, and smoking (Flenady 2011).

The International Classification of Diseases, 10th revision (ICD-10) defined fetal death as "birthweight of 500 g or more; if birthweight is unknown, by gestational age of 22 completed weeks or more; or, if both criteria are unknown, by crown-heel length of 25 cm or more" (WHO 1993). The World Health Organization, for international comparability, defines stillbirth as the reporting of late fetal deaths at 1000 g or more birthweight or 28 or more completed weeks of gestation, at least 35 cm body length. In this overview, we define the term "stillbirth" to include all fetal deaths at birthweight of at least 500 g or at 22 weeks of gestation or later. We define miscarriage before 22 weeks of gestation. We will focus on interventions during antenatal care to prevent stillbirth during pregnancy. We will exclude interventions for stillbirth during intrapartum period, as it would be covered in a separate overview review.

Description of the interventions

In high-income countries, fetal death during labour is rare, although congenital or karyotypic anomalies are often identified as causes of stillbirth (Yakoob 2010). However, in approximately half of all stillbirths, a specific cause cannot be identified, even in high-income countries where placental pathological examinations and autopsies are available (Silver 2007). In low- and middle-income countries, infections such as syphilis, gram-negative infections, gestational hypertensive disorders, especially poor management of pre-eclampsia and eclampsia, malaria in first pregnancy with malaria-endemic areas, and obstructed or prolonged labour with associated asphyxia, infection, and birth injury with low availability of caesarean section are the most common causes (McClure 2006; Smith 2007).

Bhutta et al reviewed 35 potential interventions to prevent stillbirths, of which they strongly recommended 10 for implementation: periconceptional folic acid fortification, insecticide-treated bed nets or intermittent preventive treatment for malaria prevention, syphilis detection and treatment, detection and management of hypertensive disease of pregnancy, detection and management of diabetes in pregnancy, detection and management of fetal growth restriction routine induction to prevent post-term pregnancies, skilled care at birth, basic emergency obstetric care, and comprehensive emergency obstetric care (Bhutta 2011). They also mentioned that antenatal care is low cost and highly effective against stillbirths relating to infection and under nutrition, and can be provided through outreach workers and services.

In this overview review, we will focus on interventions during antenatal care to prevent stillbirth during pregnancy. These include the following interventions.

1. Dietary intervention: periconceptional folate supplementation, energy and protein intake in pregnancy, zinc supplementation, vitamin C supplementation, vitamin A supplementation, vitamin E supplementation, calcium supplementation, magnesium supplementation, iron or iron+folate supplementation, multiple micronutrient supplementation, marine oil and other prostaglandin precursor.
2. Prevention and management of infection: community-based intervention packages, tetanus vaccine, insecticide-treated nets for preventing malaria, drugs for preventing malaria.
3. Prevention, detection, and management of other morbidities: smoking cessation, support for women at increased risk of low birthweight, women carrying their own case notes, midwife care, traditional birth attendant training, alternative versus standard packages of antenatal care, diuretics for preventing pre-eclampsia, nitric oxide for preventing pre-eclampsia and its complications, progesterone for preventing pre-eclampsia and its complications, antioxidants for preventing pre-eclampsia, and altered dietary salt.
4. Screening and management of fetal growth and well-being: ultrasound for fetal assessment in early pregnancy, routine ultrasound in late pregnancy, fetal movement counting, fetal and

umbilical Doppler ultrasound, utero-placental Doppler ultrasound, fetal and umbilical Doppler ultrasound, antenatal cardiotocography for fetal assessment, and symphysial fundal height measurement (SFH) in pregnancy for detecting abnormal fetal growth.

How the intervention might work

1. Dietary interventions

The nutritional status of pregnant women is important for a healthy pregnancy outcome (WHO 1995). Inadequate dietary intake can lead to adverse perinatal outcome due to increasing requirement of macro and micronutrients during pregnancy (Abu-Saad 2010; De Onis 1998). Di Mario et al reviewed risk factors for stillbirth in low- and middle-income countries, and concluded that maternal nutritional status is one of the factors significantly associated with stillbirth (Di Mario 2007). Balanced energy protein intake improves fetal growth and reduces the risk of fetal and neonatal death under maternal undernutritional conditions (Imdad 2011). Folic acid supplementation before pregnancy and during the first two months of pregnancy reduces the risk of neural tube defects (NTDs), which account for a small proportion of NTDs related stillbirths (Blencowe 2010). Replacing iron-folic acid supplements with multiple micronutrient supplements in the package of health and nutrition interventions delivered to mothers during pregnancy will improve the impact of supplementation on fetal growth and development and on birthweight (Shrimpton 2009). While the immediate association between stillbirth and dietary interventions is limited in accurate and robust evidence, dietary interventions during pregnancy have closely related to perinatal and neonatal outcomes. For example, low maternal serum zinc levels during pregnancy are associated with an increased risk of low birthweight (Kirksey 1994). An increased dietary intake of vitamin C in early pregnancy has been associated with small increases in birthweight and placental weight (Mathews 1999). Vitamin E has a preventive effect on many maternal and perinatal complications such as pre-eclampsia, growth restriction, preterm premature rupture of membranes and serious neonatal morbidities (Rumbold 2006). Calcium supplementation is associated with a significant benefit in the prevention of pre-eclampsia (Hofmeyr 2011). Magnesium deficiency especially has been linked with pre-eclampsia and preterm delivery which have higher rates of perinatal and neonatal mortality relevant to stillbirth (Chein 1996).

2. Prevention and management of infection

Infections such as TORCH infections includingToxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), Herpes, malaria, and various others are a leading cause of stillbirth worldwide, and account for about 15% of stillbirths in high-income countries, and half of the stillbirths in low- and middle-income countries (Di Mario 2007; McClure 2009; Schmid 2007; Van Geertruyden 2004). Syphilis may cause congenital syphilis by being transmitted to the fetus transplacentally or by placental infection which results in the decrease of blood flow to the fetus and also causes fetal death (Goldenberg 2003). A review of nine hospital studies found that placental malaria was associated with twice the risk of stillbirth, which shows that placental damage is the likely cause for many of the fetal deaths with maternal malaria (Van Geertruyden 2004). A Cochrane review concluded that the prevention of malaria in pregnancy through chemoprophylaxis or IPT is associated with reductions in placental malaria, low birthweight, severe maternal anaemia, and perinatal mortality in the first two pregnancies (Garner 2002). Chloroquine has not been found to have any harmful effects on the fetus when used in the recommended doses for malaria prophylaxis or chemoprophylaxis; pregnancy is not a contraindication to malaria prophylaxis with chloroquine or hydroxychloroquine.

3. Prevention, detection and management of other morbidities

Globally, pre-eclampsia/eclampsia which occurs in about 6% of pregnancies, and decreases blood flow, causing poor fetal growth and hypoxia, often results in stillbirths (McClure 2009). A population-based study has shown that pregnancy-induced hypertension is associated with increased risk of stillbirth and neonatal mortality (Ananth 2010). Existing interventions for reducing the risk of pre-eclampsia include calcium and aspirin used for prevention; and use of anti-hypertensive drugs and magnesium sulphate for management of pre-eclampsia/eclampsia (Jabeen 2011). Yet, there are no treatments available to reduce the incidence of pre-eclampsia; the stillbirth rates could be substantially reduced with screening and medical management, including early delivery (Menzies 2007).
Tobacco smoking during pregnancy is potentially preventable cause of adverse pregnancy outcomes, including placental abruption, stillbirth, preterm birth (less than 37 weeks' gestation), and low birthweight (less than 2500 g) (Hammoud 2005; Salihu 2007; U.S. 2004). Nicotine and other harmful compounds in cigarettes restrict the supply of oxygen and other essential nutrients, retarding fetal growth (Crawford 2008).
Post-term pregnancy is associated with an increased rate of stillbirth (Norwitz 2007). The major cause of perinatal morbidity and mortality in post-term pregnancy is presumed to be the progressive uteroplacental insufficiency (Hussain 2011; Sanchez-Ramos 2003).

4.Screening and management of fetal growth and well-being

Screening and detection for detecting fetal compromise, especially impaired growth and distress, have been developed to identify

problems during pregnancy (Haws 2009). These interventions include detection of intrauterine growth restriction through clinical examination such as ultrasound screening or fundal height measurement. Symphisical fundal height measurement aim for the detection of fetuses that are poorly grown as delay in the diagnosis of this fetal condition may lead to stillbirth (Challis 2002). Fetal hypoxia or compromise can lead to reduction in fetal movements, which can be identified in pregnant women with formal assessment of fetal movement counting or fetal phonocardiography (Bhutta 2011). Also, some advanced technologies for assessing adverse perinatal risks have been developed to detect umbilical vascular flow patterns such as doppler velocimetry, which measures blood flow dynamics in uterine, umbilical, and fetal arteries (Alfirevic 2010; Haws 2009; Hoffman 2009).

Why it is important to do this overview

In countries with a high burden of stillbirths, interventions can substantially reduce stillbirths and could also improve maternal and neonatal outcomes (Bhutta 2011). The implement improvements in pregnancy-related care can facilitate reductions in the large stillbirth burden in low-income and middle-income countries (Goldenberg 2011; Pattinson 2011) The impact of stillbirth loss can be devastating for women and their families who experience stillbirths (Froen 2011). Evidence-based interventions and strategies are needed to prevent stillbirths. There is no overview on Cochrane systematic reviews on interventions for preventing stillbirth during pregnancy.

OBJECTIVES

The objective of this overview is to summarise the evidence from Cochrane systematic reviews regarding the effects of antenatal interventions for preventing stillbirth during pregnancy.

METHODS

Criteria for considering reviews for inclusion

Types of studies

In this overview of reviews, we will include all published Cochrane systematic reviews of randomised controlled trials of antepartum interventions aiming to prevent stillbirth/perinatal mortality/fetal loss/fetal death as long as stillbirth is listed as a primary or secondary outcome. Cochrane reviews are regularly updated and employ methods to minimise bias (Moher 2007; Shea 2007). We will add to the relevant Cochrane reviews the recent primary clinical trials, which have not yet been included in the reviews and which include our primary and secondary outcomes.

Types of participants

We will consider reviews that include either 'low risk populations, or all pregnant women (i.e. unselected populations). We will exclude reviews which include only women in high-risk groups, e.g. women at risk of imminent very preterm birth or HIV positive pregnant women. Overview reviews of these high-risk populations exist in the title registration which covered stillbirth as an outcome as well, e.g. PMTCT overview review exist in the title registration in HIV group.

Types of interventions

We will consider all types of interventions used for preventing stillbirths for pregnant women. We will include the following interventions: nutritional interventions; behaviour interventions; social support; education; medical intervention; screening; vaccination; treatment; and so on.

Types of outcomes

Primary outcomes

1. Stillbirths/perinatal mortality/fetal loss/fetal death (defined by trialist)

In the absence of stillbirth data or if there are limited numbers of stillbirth data for an outcome, we will use perinatal mortality, fetal loss and fetal death as outcomes.

Secondary outcomes

1. Low birthweight (less than 2500 g)
2. Small-for-gestational age (defined by trialist)
3. Neonatal intensive care unit stay

Search methods for identification of reviews

We will work with the Trials Search Co-ordinator of the Cochrane Pregnancy and Childbirth Group in order to identify all relevant published Cochrane systematic reviews that assess the effects of interventions which aim to prevent stillbirth.

To capture the new trials that are not yet included in these reviews, we will search from the Cochrane Pregnancy and Childbirth Group's Trials Register (via the Trials Search Co-ordinator). The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We will not apply any language restrictions.

Data collection and analysis

The methodology for data collection and analysis is based on Chapter 22 of the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2011)

Selection of reviews

Two review authors will independently assess for inclusion all the potential Cochrane systematic reviews we identify with the Trials Search Co-ordinator of the Cochrane Pregnancy and Childbirth Group in order to identify all relevant published Cochrane systematic reviews that assess the effects of antenatal interventions which aim to prevent stillbirth during pregnancy, reviewing the objectives and methods, including outcomes and participants. We will resolve any disagreement through discussion or, if required, we will consult a third person.

Data extraction and management

Two authors will independently extract data from the reviews using a predefined data extraction form, and another author will verify the extracted data. We will resolve discrepancies through discussion or, if needed, through arbitration by a third person. If any information from the reviews is unclear or missing, we will access to the published papers of the individual trials. If the information cannot be obtained from the published papers, in that we will contact the individual review authors or authors of the original papers for further details.

Assessment of methodological quality of included reviews

Two authors will independently assess the quality of evidence in included reviews and the methodological quality of the systematic reviews. We will resolve discrepancies through discussion or, if needed, through arbitration by a third person.

Quality of evidence in included reviews

We will examine the methods used for evaluating the quality of the evidence using the GRADE approach in included reviews for outcome our primary outcomes (Guyatt 2008). The GRADE approach uses four levels of quality (very low, low, moderate and high) over several domains covering the limitations in the design and implementation of the studies, indirectness of evidence, unexplained heterogeneity or inconsistency in the results, imprecision of the results and high probability of publication bias.

Quality of included reviews

We will assess the methodological quality of each systematic review using the AMSTAR (A Measurement Tool to Assess Reviews) instrument (Shea 2007). AMSTAR evaluates the methods used in a review against 11 distinct criteria and assesses the degree to which review methods are unbiased.

Each item on AMSTAR is rated as yes (clearly done), no (clearly not done), cannot answer, or not applicable.

These criteria, and the way they will assess review quality, are as follows.

1.	Was an 'a priori' design provided? (Yes: the research question and inclusion criteria were established before conducting the review.)
2.	Was there duplicate study selection and data extraction? (Yes: at least two people working independently extracted the data and the method was reported for reaching consensus if disagreements arose.)
3.	Was a comprehensive literature search performed? (Yes: at least two electronic sources were searched; details of the databases, years searched and search strategy were provided; the search was supplemented by searching of reference lists of included studies, and specialised registers, and by contacting experts.)

(*Continued*)

4.	Was status of publication used as an exclusion criterion? (Yes: the authors stated that they excluded studies from the review based on publication status. No: authors searched for reports irrespective of publication type. They did not exclude reports based on publication from the systematic review.)
5.	Was a list of studies (included and excluded provided)? (Yes: a list was provided.)
6.	Were the characteristics of the included studies provided? (Yes: data on participants, interventions and outcomes were provided, and the range of relevant characteristics reported.)
7.	Was the scientific quality of the included studies assessed and reported? (Yes: predetermined methods of assessing quality were reported.)
8.	Was the scientific quality of the included studies used appropriately in formulating conclusions? (Yes: the quality, and limitations, of included studies were used in the analysis, conclusions and recommendations of the review.)
9.	Were the methods used to combine the findings of studies appropriate? (Yes: if results were pooled statistically, heterogeneity was assessed and used to inform the decision of the statistical model to be used. If heterogeneity was present, the appropriateness of combining studies was considered by review authors.)
10.	Was the likelihood of publication bias assessed? (Yes: publication bias was explicitly considered and assessed.)
11.	Was the conflict of interest stated? (Yes: sources of support were clearly acknowledged.)

For all items except item 4, a rating of 'yes' is considered adequate. For item 4, a rating of 'no' (that is, the review did not exclude unpublished or grey literature) is considered adequate. A review that adequately meets all of the 11 criteria is considered to be a review of the highest quality. For this overview, we will consider reviews that achieve scores of between 8 to 11 as high quality; scores of 4 to 7 as medium quality; and scores of 0 to 3 as low quality.

Two authors will independently assess the quality of the included reviews using AMSTAR, and another author will verify this assessment. We will resolve differences by discussion and consensus and, if needed, through arbitration by a third person.

We will identify and discuss differences in quality between reviews, and will use the review quality assessment to interpret the results of reviews when synthesised in this overview.

Data synthesis

We will provide individual review narrative summaries of the relevant results for the individual reviews and present these as tables and figures using 'Overview of reviews' table' including the characteristics of included reviews, the summary of quality of evidence within individual systematic reviews of our primary outcomes using GRADE, and for each systematic review using AMSTAR ratings. Where Cochrane reviews have not been updated with recent data available for the outcome 'stillbirth', we will, with the authors' permission, add our primary and secondary outcomes data to the relevant Cochrane reviews.

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tion, including any revisions or updates to the manuscript which WHO may make from time to time.

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