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Knowledge and practice of health workers about control and prevention of multidrug-resistant tuberculosis in referral hospitals, Ethiopia

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Abstract

Objective: The emergence of multidrug-resistance tuberculosis (MDR-TB) has become a major public health problem in a number of countries and an obstacle to the global and national TB control efforts. Health workers have key roles in the prevention and control of MDR-TB. The aim of this study was to assess the knowledge and practice of health workers towards MDR-TB in Amhara region referral hospitals, Ethiopia.

Design: A cross-sectional study.

Settings: Two large referral hospitals in Amhara region, Ethiopia.

Participants: Randomly selected health workers.

Outcomes: Participants' knowledge and practice on MDR-TB prevention and control were assessed using self-administered and structured questionnaire.

Results: A total of 377 health workers (with a response rate of 93.7%) were participated; majority of them were nurses 198 (52.5%) and medical doctors 59(15.6%). Overall, 149 (39.5%) of health workers rated their knowledge of MDR-TB as inadequate. Holding postgraduate degree (AOR=5.78; 95% CI: 2.33, 14.33), getting training on infection prevention (AOR= 1.79; 95% CI: 1.00, 3.17) and had past history of TB infection (AOR= 1.85; 95% CI: 1.12, 3.03) were significantly associated with health workers' knowledge on MDR-TB. Only, one fifth (19.6%) of health workers have good practice towards the prevention and control of MDR-TB. Working in Internal Medicine (AOR= 4.64; 95% CI: 1.99, 10.81) and Pediatrics (AOR=3.85; 95% CI: 1.11, 13.34) words, being in the age groups of 26-30 years (AOR= 2.70; 95% CI: 1.27, 5.76), and 30 years and above (AOR=4.42; 95% CI: 1.77, 11.00) were significantly associated with good practices of health workers.

Conclusions: Health workers in Amhara region referral hospitals lack adequate knowledge and good practice towards the prevention and control of MDR-TB. Making available MDR-TB guidelines to all health workers and providing training especially for diploma holder is needed to enhance health workers' knowledge and practice.

Strengths and limitations of this study

- The study was conducted in two large referral hospitals
- Data were collected among different health workers such as medical doctor, nurses, health officer, pharmacy, medical laboratory and midwifery.
- A potential limitation of this study is that the proportion of practice may be overestimated, due to social desirability bias, as we did not observe study participants for their practice.

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is defined as TB that is resistant to at least isoniazid and rifampin, the two most effective first-line, anti-TB drugs [1]. The emergence of MDR-TB is a major public health problem and is an obstacle for national and global TB control programs [2]. Globally, nearly half a million people are estimated to have MDR-TB annually, and only one fourth of them get adequate treatment[3-5]. In 2016, there were an estimated 490 000 new cases of MDR-TB, and approximately 240 000 deaths from MDR-TB [6 7]. Treatment for MDR-TB has substantially longer duration, higher costs and more toxicity than the treatment for drug-susceptible TB [8].

MDR-TB occurs in patients either due to the development of drug resistance during a course of first-line TB treatment (i.e. acquired MDR-TB)[9], or due to the transmission of a drug resistant strain from an infectious patient to a susceptible host (i.e. primary MDR-TB)[10]. Acquired MDR-TB occurs as a result of sub-optimal first line TB treatment related to health care providers or patient factors [11 12]. There is increasing evidence that primary MDR-TB is common and that many patients with MDR-TB had it from the start of treatment[13-15]. Inadequate knowledge and poor practice of health professional towards the prevention and control of MDR-TB may exacerbate the transmission of MDR-TB in health care settings [16]. Health workers have potential to contact with MDR-TB patients, and are very important stakeholders in health care settings to combat MDR-TB; however their knowledge and practices towards the prevention and control of MDR-TB has not been well studied, especially in high TB burden countries.

In Ethiopia - a high burden TB and MDR-TB country - the incidence of TB has decreased over time following the implementation of a range of interventions, including the delivery of TB care by health workers and directly observed therapy (DOT) [17 18] However, the number of MDR-TB cases has increased over time and has become a challenge for the national TB control and prevention program [18 19]. Assessing the knowledge and practice of health workers on MDR-TB, and identifying factors associated with inadequate knowledge and low practice are important for the prevention and control of MDR-TB. Therefore, the aim of this study was to assess the knowledge and practice of health works related to MDR-TB, and to identify factors associated with inadequate knowledge and low practice of health workers toward the prevention and control of MDR-TB in Amhara region referral hospitals, Ethiopia.

Methods

Study design and setting: A cross-sectional study was conducted in Amhara regional referral hospitals from January to May, 2014. Amhara region has 19 Governmental hospitals, 801 governmental health centers, 3302 health post, 861 private clinic, 8 private hospitals, 40 charity clinics and 65 diagnostic laboratory facilities. Five of the hospitals are referral from which Gondar University Hospital has MDR-TB center; its MDR-TB service was initiated in 2010 and currently it has around 80 MDR-TB patients. During the study period, Amhara Region Referral Hospitals have 304 Medical Doctors, 3790 nurses, 434 Public Health Officers and 287 Midwifery. The TB detection rate in the region is 34%.

Study population: The study population was consisted of a sample of health workers who were working in the two large Amhara regional referral hospitals, Gondar University Referral Hospital and Felege Hiwot Refereal Hospital. Those health workers who were temporarily employed in these hospitals were excluded from the study.

Sampling procedures: Sample size was calculated using single population proposition formula $[n = [(z\alpha/2)^2 * P(1-P)]/d^2]$ by assuming 95% confidence level of $Z\ \alpha/_2 = 1.96$, margin of error 5%, 50% proportion to have maximum sample size, and by adding 5% non-response rate a total of 402 health workers were considered. The sample size was proportionally allocated to the two referral hospitals based on their number of health professional. Medical doctor, Nurses, Health Officer, Pharmacy, Medical Laboratory and Midwifery were included in the study.

Data collection: Data were collected by pre-tested, structured, self-administered questionnaire. The questionnaire was available to participants with the help of data collectors. The completed questionnaires were turned back after checking its completeness. The questionnaire used for the data collection was developed by a team of health workers. The questions that used to assess the knowledge and practice of health workers were developed based on the national and WHO MDR-TB management guidelines [8 20].

Level of knowledge was assessed out of 10 questions. The questions were about MDR-TB definition, etiology, diagnosis, symptoms, treatment and prevention. The knowledge level was

categorized as good knowledge for those who score mean and above the mean; and poor knowledge for those who score less than the mean. Practice of health workers about MDR-TB prevention and control were assessed by using the following questions: do you have access to MDR-TB guideline?, how frequently are you referring the MDR-TB guideline?, does cross ventilation implemented in your working room?, have you ever participating in educating patient about MDR-TB?, does the hospital provided you Masks N95?, and frequency of using Masks N95 while attending the patients.

Data processing and analysis: The returned questionnaires were checked for completeness, cleaned manually and analyzed using SPSS windows version 20.0. Frequencies and cross tabulations were used to summarize descriptive statistics, tables and graphs were used for data presentation. Both bivariate and multivariable logistic regression models were used to identify variables which have an association with the dependent variables (i.e. knowledge and practice). Variables found to have p-value up to 0.2 in the bivariate analysis, entered in to multivariate logistic regressions for controlling the possible effect of confounders and finally the variables which have significant association were identified on the basis of OR, with 95%CI.

Results

Socio-demographic characteristics

A total of 377 health workers (with a response rate of 93.7%) were participated in the study. About two-thirds of them were males 60.7% and BSc degree 62.6% holders, and about half of them were nurses 52.5 %. The mean age of the study participants was 27.6 (±4.7 SD) years.

More than one third 37.1% were working at outpatient department (OPD) and ever diagnosed for TB 36.6%. Almost 90% and 80% of the health workers were not trained for TB/MDR-TB and infection prevention control, respectively. The mean number of years of working experience of the health workers was 6.5 years (Table 1).

Knowledge of health workers on MDR-TB

Only two-fifth (39.5%) (95% CI: 35.0%, 44.3%) of the study participants were knowledgeable on MDR-TB. Main knowledge gaps observed in the health workers are defining MDR-TB (30%), identifying MDR-TB symptoms (41.4%) and selecting the nationally recommended MDR-TB

treatment (44.6%). Other gaps were noted that 44.6% and 55.6% were unable to identify the correct duration of MDR-TB treatment and the nationally recommended MDR-TB treatment regimens, respectively [Table 1].

The multivariable analysis showed that educational level had an effect on knowledge of health professional on MDR-TB in which postgraduate degree holders [AOR 5.78 (95% CI: 2.33, 14.33)] had good knowledge towards MDR-TB as compared to diploma holders. Those health workers who had got training on infection prevention have also good knowledge on MDR-TB [AOR 1.79(95% CI: 1.00, 3.17)] as comparted to those health workers who had not got training on infection prevention. Similarly, those health workers who had been diagnosed for TB (AOR 1.85 (95% CI: 1.12, 3.03)) had good knowledge on MDR-TB as compared to their counterpart [Table 2].

Practice of health workers towards the prevention and control of MDR-TB

Less than one fourth of 19.6% (95% CI: 16.2, 23.8%) health workers had good practice towards the prevention and control of MDR-TB. One third (32.6%) of participates reported that they had access to MDR-TB guideline; and about 110 (29.17%) stated that they referred to these guidelines. About 163 (43.2%) of participants reported that they implemented cross-ventilation in their working room. About 103 (27.3%) of the participants stated that they received protective masks from the hospital while attending to patients.

The practices of health workers for the prevention and control of MDR-TB were significantly and independently associated with ages of the respondents, working site in the hospital, and types of health professions. Those health workers who were working in internal medicine [AOR=4.64 (95% CI: 1.99, 10.81) and pediatrics [AOR=3.85 (95% CI: 1.11, 13.34)] words were more likely to practice the prevention of MDR-TB than those health workers who were working at OPD, respectively.

A relatively elder health workers who were in the age group of 26-30 years [AOR= 2.70 (95%CI: 1.27, 5.76)] and >30 years [AOR=4.42 (95% CI: 1.77, 11.08)] were more likely to practice MDR-TB prevention than younger age groups (<25 years). Similarly, nurses were more likely to practice the prevention of MDR-TB as compared to medical doctors [AOR= 4.49 (95% CI: 1.03, 19.47)] [Table 3].

Discussion

Health workers have a key role in the prevention and control of MDR-TB, especially in resource-limited settings such as Ethiopia. However, in our study, only 39.5% of health workers had good knowledge about MDR-TB. Knowledge gaps were identified with regard to the definition of MDR-TB, the combination of nationally recommend drug and the duration of its treatment. Similar findings were reported from previous studies [21 22]. Health workers' knowledge about MDR-TB were associated with an increased level of education and taking of infection prevention training. Those health workers who have postgraduate and above had better knowledge about MDR-TB than diploma holders. This disparity was even more pronounced in those health professional who had been diagnosed for TB as they were more knowledgeable about MDR-TB. It clearly showed that there is further training need about MDR-TB for all diploma holder health workers.

It is found that only one forth (19.6%) of health works had good practice towards MDR-TB control and prevention. This low MDR-TB prevention and control practice among health workers is particularly risky in high TB burden countries such as Ethiopia because outbreaks of MDR-TB may occur in the hospitals. High rate of hospital transmission of MDR-TB has been reported in previous studies[23 24].

With regard to the practice of referring to the treatment guidelines, it is only one third (32.6%) of participants had access to MDR-TB guideline in the hospitals; and less than on third (29.17%) of the participants referred to these guidelines while treating the patients. Although this finding is consistent with a report by other studies that a high number of healthcare practitioners fail to comply with clinical practice guidelines, this is noteworthy finding [25 26]. It is important that regional health bureau and hospital administration address this issue by making the MDR-TB guidelines available to all Health workers in the healthcare settings.

Although this study did not assess whether Health workers used protective mask appropriately through observation, slightly more than a quarter (27.3%) of the participants stated that they received protective masks from the hospital while attending to patients. This is also very low percentage, as all health workers should use protective masks when dealing with TB patients. This is especially important for medical doctors, health officers and nurses who have regular contact with the patients. However, in this study medical laboratory and other health workers had good practice than medical

doctors. This may indicate that medical doctors, their family members, their patients and all other persons they interact with will be at higher risk of infection with MDR-TB [27 28].

The limitation of this study is that the proportion of practice in this study may be overestimated, due to social desirability bias, as we did not observe study participants for their practice.

Conclusions

Health workers' level of knowledge about MDR-TB was not adequate in Amhara region, Ethiopia, and significantly associated with educational level, provision of training, history of TB diagnosis. The practice of health workers towards MDR-TB is also very low. Intensive training, enhance educational level, and making available the national MDR-TB guideline and protective mask in all health hospitals are strongly recommended.

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Contributors: KAA and AA: study design; KA and AAA: data collection; KAA: analysis and drafting of the manuscript; SY, AAA, BDB, AA and DNK study design and revision of the manuscript. All authors revised and approved the final version of the manuscript.

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Competing interests: The authors declared that they have no competing interests.

Patient consent: Not required.

Ethics Approval: Ethics approval was obtained from the Ethical Review Board of University of Gondar and permission letter was also obtained from the Hospital Administration Offices. Data were collected using self-administered questionnaire by providing information about the purpose of the study, and the rights of the study participant not to return the questionnaire, if they are not interesting about the questions, on the cover page of the questionnaire. Hence, the return of the questionnaire was considered as getting informed written consent from each study participant. In order to keep confidentiality of any information provided by study subjects, personal identifiers such as name and address were not collected.

Data sharing statement: The data that support the findings of this study are available from the corresponding author on reasonable request.

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Table 1: Number and percent (%) of correct response among health profession towards all knowledge questions

Characteristics	Number	Percent
What is MDR-TB?	264	70.0
MDR-TB is contagious?	345	91.5
What is the cause of MDR-TB?	357	94.7
All people with MDR-TB infection have symptoms	148	39.3
What is the most common symptom of MDR-TB?	221	58.6
How MDR-TB is diagnosed?	368	97.6
The definitive way of assessing MDR-TB treatment outcome	241	63.9
The duration of treatment for MDR-TB is	209	55.4
MDR-TB can be treated with one the following drug combination	168	44.6
Putting on N95 can reduce the risk of transmission of MDR-TB	314	83.3

Table2: Socio-demographic characteristics and factors associated with health workers' knowledge on MDR-TB at Gondar University Hospital and Felege Hiwot Hospitals, Northwest Ethiopia

Variables	Number	Percent	MDR-TB Knowledge		95% CI	
			Good	Poor	COR	AOR
Working site						
Internal medicine	79	21.0	37	40	1:00	
Surgery	46	12.2	17	29	0.60 (0.28,1.26)	
Gynecology and Obstetrics	43	11.4	17	26	0.67 (0.31, 1.42)	
Pediatrics	52	13.8	24	28	0.87 (0.43, 1.77)	
OPD and Others	157	41.6	52	105	0.50 (0.29, 0.88)	
Age (year)						
<25	130	34.5	50	80	1:00	
26-30	189	50.1	80	109	1.17 (0.74, 1.85)	
>30	58	15.4	19	39	0.77 (0.40, 1.49)	
Sex						
Male	229	60.7	103	126	1.81 (1.17, 2.80)	
Female	148	39.3	46	102	1:00	
Marital status						
Married	155	41.9	57	98	0.82 (0.53, 1.25)	
Note married	222	49.1	92	130	1:00	
Profession						
MD	59	15.6	42	17	1:00	
Nurse	198	52.5	70	128	0.22 (0.11,0.41)	
Medical laboratory	44	11.7	13	31	0.17 (0.07,0.40)	
Other health professional*	76	20.1	24	52	0.18 (0.08,0.39)	
Educational level						
Diploma	75	19.9	16	59	1:00	1:00
BSc	236	62.6	99	157	2.32 (1.26, 4.26)	1.58 (0.81, 3.05)
Postgraduate above	66	17.5	34	12	10.44 (4.42,24.67)	5.78 (2.33, 14.33)
Staff categories						
Teaching staff	56	14.9	35	21	3.00 (1.68, 5.44)	
Hospital staff	321	85.1	114	207	1:00	
Working experience (years)						
<3	139	36.9	59	80	1.17 (0.73, 1.88)	
3-6	90	23.9	33	57	0.92 (0.53, 1.58)	
>6	148	39.3	57	91	1:00	
Ever diagnosed for TB						

Yes	138	36.6	35	103	2.68 (1.69, 4.25)	1.85 (1.12 ,3.03)
No	239	63.4	114	125	1:00	1:00
Trained for infection prevention						
Yes	79	21.0	23	55	1.78 (1.04, 3.05)	1.79(1.00, 3.17)
No	298	79.0	126	172	1:00	1:00

Table 3: Factors associated with practice of health workers with regard to the prevention and control of MDR-TB at Gondar University Hospital and Felege Hiwot Hospital Northwest Ethiopia.

Variables	Practice		COR	AOR
	Yes	No		
Working site				
Internal medicine	29	50	3.21(1.71, 6.04)	4.64 (1.99,10.81)
Surgery	5	41	0.67 (0.24, 1.88)	1.11 (0.33, 3.74)
Gynecology and Obstetrics	11	32	1.90 (0.84, 4.28)	2.57 (0.95, 6.99)
Pediatrics	5	47	0.59 (0.21,1.63)	3.85 (1.11, 13.34)
OPD and Others	24	133	1.00	1.00
Age (years)				
<25	13	117	1.00	1.00
26-30	43	146	2.65 (1.36, 5.16)	2.70 (1.27,5.76)
>30	18	40	4.05 (1.82, 9.00)	4.42 (1.77,11.00)
Sex				
Male	34	195	1.00	
Female	40	108	0.47 (0.28, 0.78)	
Profession				
MD	8	51	1.00	1.00
Nurse	48	150	2.04 (0.90,4.60)	4.49 (1.03, 19.47)
Medical laboratory	7	37	1.20 (0.40, 3.62)	5.21 (0.86, 31.51)
Other health professional	11	67	1.07 (0.44, 2.88)	2.20 (0.25,10.73)
Educational level			1.00	
Diploma	27	48	0.32 (0.18, 0.58)	
BSc	40	219	0.31 (0.12, 0.81)	
Residence/masters and above	7	39		
Staff categories				
Teaching staff	13	43	1.28 (0.65, 2.54)	
Hospital staff	61	260	1.00	
Working experience (year)				
<3	21	118	0.76 (0.41, 1.41)	
3-6	25	65	1.64 (0.88, 3.05)	
>6	28	120	1.00	
Knowledge on MDR				
Good	20	129	2.00 (1.14, 3.50)	
Poor	54	174	1.00	

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Knowledge and practice of health workers about control and prevention of multidrug-resistant tuberculosis in referral hospitals, Ethiopia: A cross-sectional study

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Abstract

Objective: The aim of this study was to assess the knowledge and practice of health workers about MDR-TB prevention and control.

Study design and settings: A cross-sectional study was conducted at Gondar University Referral Hospital and Felege Hiwot Referral Hospital.

Participants: Randomly selected health workers (i.e. medical doctor, nurse, health officer, pharmacy, medical laboratory and midwifery) were the study participants.

Outcome measures: The main outcomes were knowledge and self-reported practice of health workers about MDR-TB.

Results: A total of 377 health workers (with a response rate of 93.7%) participated in the study. The majority of respondents were nurses (52.5%, n=198) and medical doctors (15.6%, n= 59). The mean knowledge score was seven out of 10; 149 (39.5%) of respondents scored seven or more which was considered as good knowledge. MDR-TB knowledge of health workers was significantly associated with having a postgraduate degree (AOR=5.78; 95% CI: 2.33, 14.33), taking infection prevention training (AOR= 1.79; 95% CI: 1.00, 3.17) and having a history of TB (AOR= 1.85; 95% CI: 1.12, 3.03). The mean self-reported practice score was four out of seven; one-fifth (19.6%) of respondents scored four or more which was considered as good practice. Self-reported practice of health workers was significantly associated with working at Internal Medicine (AOR= 4.64; 95% CI: 1.99, 10.81) and Pediatrics (AOR=3.85; 95% CI: 1.11, 13.34) wards, being in the age groups of 26-30 years (AOR= 2.70; 95% CI: 1.27, 5.76), and 30 years and above (AOR=4.42; 95% CI: 1.77, 11.00).

Conclusions: This study found low knowledge and self-reported practice score among health workers. MDR-TB knowledge of health workers was significantly associated with educational status, infection prevention training, and previous history of TB. This finding highlights the potential of providing MDR-TB training for health workers to increase their knowledge about MDR-TB.

Strengths and limitations of this study

- This study is the first to explore the knowledge and practice of health workers regarding MDR-TB in two large referral hospitals in Ethiopia.
- The participants were selected randomly among different health workers such as medical doctor, nurses, health officer, pharmacy, medical laboratory and midwifery.
- There is a possibility that health workers may not report their actual practices as the information was self-reported.
- The findings from this study may not be generalizable to health workers in other hospitals in the country.

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is defined as TB that is resistant to at least isoniazid and rifampin, the two most effective first-line TB drugs [1]. The emergence of MDR-TB is a major public health problem and is an obstacle for national and global TB control programs [2]. Globally, nearly half a million people are estimated to have MDR-TB annually, and only one-fourth of them get adequate treatment[3-5]. In 2016, there were an estimated 490 000 new cases of MDR-TB, and approximately 240 000 deaths from MDR-TB [6 7]. Treatment for MDR-TB has substantially longer duration, higher costs and more toxicity than the treatment for drug-susceptible TB [8].

MDR-TB occurs in patients either due to the development of drug resistance during a course of first-line TB treatment (i.e. acquired MDR-TB)[9] or due to the transmission of a drug-resistant strain from an infectious patient to a susceptible host (i.e. primary MDR-TB)[10]. Acquired MDR-TB occurs as a result of sub-optimal first-line TB treatment related to health care providers or patient factors [11 12]. There is increasing evidence that primary MDR-TB is common and that many patients with MDR-TB had it from the start of treatment[13-15]. Inadequate knowledge and poor practice of health professional towards the prevention and control of MDR-TB may exacerbate the transmission of MDR-TB in health care settings [16]. Health workers have the potential to contact with MDR-TB patients and are very important stakeholders in health care settings to combat MDR-TB. Previous studies have been conducted to assess the knowledge and practices of health workers towards the prevention and control of TB[17-21]. However, there is a limited study regarding the knowledge and practices of health workers about the prevention and control of MDR-TB in Ethiopia.

Ethiopia is one of 30 high TB and MDR-TB burden countries[22]. The incidence of TB has decreased over time in Ethiopia following the implementation of different interventions, including the delivery of TB care by health extension workers and the expansion of directly observed therapies, short course (DOTS) [23 24]. However, the number of MDR-TB cases has increased over time and has become a challenge for the national TB control and prevention program [24 25]. Assessing the knowledge and practice of health workers on MDR-TB, and identifying factors associated with inadequate knowledge and low practice are important for the prevention and control of MDR-TB. Therefore, the aim of this study was to assess the knowledge and self-reported practice of health works related to MDR-TB and to identify factors associated with inadequate knowledge and low

self-reported practice of health workers toward the prevention and control of MDR-TB in Amhara region referral hospitals, Ethiopia.

Methods

Study design and setting

This was a cross-sectional study conducted from March to May 2014 among health workers in Amhara regional referral hospitals. Amhara region is the second largest region in Ethiopia. The region has five referral hospitals, and the study was conducted in two (randomly selected) of these five referral hospitals: Gondar University Referral Hospital and Felege Hiwot Referral Hospital. During the study period, Amhara region referral hospitals have 304 medical doctors, 3790 nurses, 434 public health officer and 287 midwiferies. TB is the leading cause of death among an infectious disease in the region[26]. TB detection rate (all forms), which is defined as the number of new and relapse TB cases notified in a given year, divided by the estimated number of incident TB cases for the same year, was 34% in Amhara region[26].

Gondar University Hospital is the oldest hospital in the country which is located in Gondar, 750 km northwest of Addis Ababa (the capital city of Ethiopia). It provides health care services for a catchment population of approximately five million people in North Gondar and the adjacent zones. The hospital established the MDR-TB treatment centre in 2010 and it had around 80 MDR-TB patients during the data collection period.

Felege Hiwot Referral Hospital is located in Bahirdar (the capital city of Amhara National Regional State), 562 km northwest of Addis Ababa and 180 km southeast of Gondar. The hospital serves a catchment population of more than five million, and about 500 clients visit the hospital daily. The hospital has 273 beds and offers different specialized services in four major departments: Pediatric, Surgery, Gynecology and Obstetrics and Internal Medicine.

Sample size and sampling procedures

The sample size for this study was determined using single population proportion formula, by taking the following assumptions: margin of error (5%), expected response rate (5%), and confidence interval (95%). There was no study in Ethiopia that showed the prevalence of good knowledge or practice of health workers about MDR-TB. Therefore, to allow for maximum variation, we took a

prevalence of 50%. Based on these assumptions, the final sample size was 402. To select the study participant random sampling technique was used. First, two of the five referral hospitals in Amhara region were selected randomly (i.e. Gondar University Referral Hospital, and Felege Hiwot Referal Hospital). Then the sample size was proportionally allocated to these hospitals based on their number of health workers. The list of health workers (i.e. sampling frame) was obtained from the office of human resource of each hospital. Finally, the sample was selected from each hospital by simple random sampling technique. The sample includes a medical doctor, nurse, health officer, pharmacy, medical laboratory and midwifery. Those health workers who were temporarily employed in the hospitals were excluded from the study.

Data collection instrument

The questionnaire for this study was developed by the research team based on the Ethiopia Programmatic Management of Drug-resistant Tuberculosis Guideline 2013[27], the 2014 World Health Organization (WHO) Guidelines for the Programmatic Management of Drug-resistant Tuberculosis[28], and previous studies[29-33]. The details of the questionnaire are available as an additional file in the appendix. The questionnaire contains the following section: socio-demographic profile of the participants (such as age, sex, marital status, level of education, years of experience, type of occupation); and questions about knowledge and practice of health workers about MDR-TB. Knowledge of health workers was assessed based on the number of correct answers provided to 10 closed-ended questions (i.e. multiple choice, yes/no and true/false) on the definition, cause, diagnosis, treatment and prevention of MDR-TB. Each attracts a score of one (for a correct answer) or zero (for a wrong answer). The knowledge score was calculated for each study participants by summing up the points of all questions, and the score ranging from 0 to 10. Then knowledge score was categorized into good and poor score if it is equal to or above the mean and below the mean, respectively. Similarly, the self-reported practice of health workers about MDR-TB prevention and control was assessed by seven questions. The practice questions were about access to the MDR-TB guideline, implementation of cross ventilation in the hospital, provision of health education to the patients about MDR-TB, and access and use of Masks N95. If there was a self-reported practice earned a score of one otherwise zero. Participants who scored equal to or above the mean were considered as having a good practice and below the mean considered as a poor practice.

To improve the adequacy, accuracy and appropriateness of the questionnaire content and face validation was performed. Prior to the main survey, the questioner was pre-tested among 20 health workers (i.e. 5% of the sample) in other hospitals. The questionnaire was administered to study participants with the help of data collectors. The questionnaires were then collected after one or two days. The questionnaire front page contains information, describing the survey and asking for their voluntary participation. By reading and responding, they gave their consent.

Data analysis

The data were entered and analyzed using the Statistical Package for Social Science (SPSS) version 20.0. The data were cleaned and checked for accuracy. Percentages and numbers were used to summarize categorical data. Mean and standard deviation (SD) were used to describe normally distributed continuous variables. A bivariate logistic regression model was first fitted, and the variables which had a p-value <0.2 in the bivariate analysis were fitted in the final multivariable logistic regression model. Variables with a p-value <0.05 in the final multivariable logistic regression model were considered significantly associated with the dependent variables (i.e. knowledge and practice). Crude and adjusted odds ratios (OR) with 95% CI were calculated to measure the strength of association between the dependent and independent variables.

Ethics Approval

This study was approved by the University of Gondar Ethics Review Board (reference number RPC/59/2014) on 26 March 2014 before initiation of the study. Permission was granted to access health workers from each hospital administrations. Information about the purpose of the study, and the rights of the study participant not to complete the questionnaire, if they are not interested about the questions, was provided on the cover page of the questionnaire. Hence, the return of the questionnaire was considered as getting written consent from each study participant. In order to keep confidentiality of any information provided by study participants, personal identifiers such as name and address were not collected.

Patient and public involvement

No patients or public were involved in this research.

Results

Socio-demographic characteristics

A total of 377 health workers participated in the study, with a response rate of 93.7%. Table 1 shows the demographic profile of the respondents. The majority of respondents were nurses (52.5%, n=198) and medical doctors (15.6%, n= 59). The mean age of the participants was 27.6 (±4.7 SD) years. Most of the respondents were males (60.7%, n=229) and BSc degree holders (62.6%, n=236).

One-third (36.6%, n=138) of the respondents were previously diagnosed for TB, and 140 (37.1%) were working at outpatient departments (OPD). The majority (80%, n=298) of study participants were not trained for infection prevention within the last 12 months. One hundred and forty-eight (39.3%) of respondents had work experience of more than six years.

Knowledge of health workers about MDR-TB

The mean knowledge score was seven points out of a total possible score of 10 points. Two-fifth (39.5%) (95% CI: 35.0%, 44.3%) of respondents scored equal to or more than the mean score which was categorized as good knowledge. Table 2 shows the number and percentage of correct responses of health workers for knowledge questions. The majority of respondents knew that MDR-TB occurs when TB treatments are not properly administered (97.6%), culture with drug susceptibility testing (DST) is the best diagnostic methods for MDR-TB (94.7%), and MDR-TB is transmitted by droplet spread (91.5%). Knowledge was less accurate regarding the treatment and symptoms of MDR-TB. Less than half of the respondents answered questions correctly about the nationally recommended treatment regimen (44.6%) and the most common symptoms (39.3%) of MDR-TB. Knowledge gap was also observed among respondents regarding the duration of MDR-TB treatment (55.4%) [Table 2].

In the bivariate analysis, sex, working sit, profession, educational status, staff categories, previous history of TB, and taking infection prevention training were significantly associated with knowledge of respondents about MDR-TB. However, in the stepwise multivariate analysis, educational level, previous history of TB, and taking infection prevention training were remained significantly associated with knowledge of respondents about MDR-TB after controlling other factors (Table 3).

Accordingly, health workers who had a postgraduate degree were more likely to have good knowledge about MDR-TB than health workers who had a diploma [AOR 5.78 (95% CI: 2.33,

14.33)]. Those health workers who had been trained for infection prevention were more likely to have good knowledge about MDR-TB than those health workers who had not been trained for infection prevention [AOR 1.79(95% CI: 1.00, 3.17)]. Similarly, health workers who had a history of TB were more likely to have good knowledge about MDR-TB than health workers who had no a history of TB (AOR 1.85 (95% CI: 1.12, 3.03)).

Practices of health workers towards the prevention and control of MDR-TB

A total of 123 (32.6%) respondents reported having access to the MDR-TB guideline, and 110 (29.17%) mentioned that they referred to the guidelines when providing care to TB or MDR-TB suspected patients. One hundred and sixty-three (43.2%) respondents reported the implementation of cross-ventilation in their working room. More than a quarter 103 (27.3%, n=103) of participants reported that they always wore a protective mask (N95) when carrying out clinical procedures and attending patients. The mean self-reported practice score was four points out of a total possible score of seven points. Less than a quarter (19.6%; 95% CI: 16.2, 23.8%) of health workers were scored equal to or above the mean score which was categorized as good practice towards the prevention and control of MDR-TB.

To identify factors associated with the self-reported practice of MDR-TB, logistic regression models were fitted. In the bivariate analysis, working site, the age of respondents, sex, profession, educational level, and knowledge about MDR-TB were significantly associated with the self-reported practice. However, in the multivariate analysis, working site, the age of respondents, and profession were significantly associated with self-reported practice (Table 4). Health workers who were working at Internal Medicine [AOR=4.64 (95% CI: 1.99, 10.81) and Pediatric [AOR=3.85 (95% CI: 1.11, 13.34)] wards were more likely to have good self-reported practice than health workers who were working at OPD. Those health workers in the age group of 26-30 years [AOR= 2.70 (95%CI: 1.27, 5.76)] and >30 years [AOR=4.42 (95% CI: 1.77, 11.08)] were more likely to have good self-reported practice as compared to those health workers with the age group of <25 years. Nurses were more likely to have good self-reported practice than medical doctors [AOR= 4.49 (95% CI: 1.03, 19.47)].

Discussion

Health workers have a key role in the prevention and control of MDR-TB, especially in resource-limited settings such as Ethiopia. In our study, knowledge gaps were identified with regard to the definition of MDR-TB, the combination of nationally recommend drug and the duration of MDR-TB treatment. Similar findings were reported from previous studies [34 35]. Health workers' knowledge about MDR-TB were associated with an increased level of education and taking of infection prevention training. Health workers who had a postgraduate degree had better knowledge about MDR-TB than health workers who had a diploma. This disparity was even more pronounced in health professionals who had been trained for infection prevention in the last 12 months and who had been previously diagnosed for TB. This finding highlighted the importance of providing infection prevention training for health works to increase their knowledge about MDR-TB.

Our study also found that only one-fourth of health works had good self-reported practice towards the prevention and control of MDR-TB. This low MDR-TB prevention and control practice among health workers is particularly risky in high TB burden countries such as Ethiopia because outbreaks of MDR-TB may occur in the hospitals. A high rate of hospital transmission of MDR-TB has been reported in previous studies[36 37].

With regard to the practice of referring to the treatment guidelines, it is only one-third (32.6%) of participants had access to the MDR-TB guideline in the hospitals; and less than a third (29.17%) of participants referred to these guidelines while treating the patients. Although this finding is consistent with a report by other studies that a high number of healthcare practitioners fail to comply with clinical practice guidelines, this is noteworthy finding [38 39]. It is important that the regional health bureau and hospital administration address this issue by making the MDR-TB guidelines available to all health workers in the healthcare settings.

Although this study did not assess whether health workers used protective mask appropriately through observation, slightly more than a quarter (27.3%) of participants reported that they always wore a protective mask when carrying out clinical procedures and attending patients. This is also a very low percentage, as all health workers should use protective masks when dealing with TB patients. This may indicate that health workers, their family members, their patients and all other persons they interact with will be at higher risk of infection with MDR-TB [40 41]. This is especially important for medical doctors, health officers and nurses who have regular contact with the patients.

This study has several limitations. First, there is a possibility that health workers may not report their actual practices (due to social desirability bias) as the information was self-reported. Second, the findings of this study may not be generalizable to health workers in other hospitals of the country as the study was limited only to two referral hospitals in Amhara region. Third, there could be a possibility of selection bias as the number of health workers who had prior TB appeared to be exceptionally high (36.6%), suggesting they may have been more interested to participate in the study. Fourth, given that the study was based on a cross-sectional study design, it is important to acknowledge that a temporal relationship between the explanatory and outcome variable could not be established.

Conclusions

This study has revealed poor knowledge and practice of health workers about MDR-TB prevention and control in Amhara region referral hospitals, Ethiopia. The study also found that higher educational level, provision of training, and previous history of TB were significantly associated with good knowledge of health workers. This finding highlighted the importance of providing infection prevention training for health works to increase their knowledge about MDR-TB.

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Table1: Socio-demographic characteristics of health workers at Gondar University Referral Hospital and Felege Hiwot Referral Hospital, Northwest Ethiopia

Variables	Number	Percent
Working site		
Internal medicine	79	21.0
Surgery	46	12.2
Gynaecology and Obstetrics	43	11.4
Paediatrics	52	13.8
OPD and Others	157	41.6
Age (year)		
<25	130	34.5
26-30	189	50.1
>30	58	15.4
Sex		
Male	229	60.7
Female	148	39.3
Marital status		
Married	155	41.9
Not married	222	49.1
Profession		
MD	59	15.6
Nurse	198	52.5
Medical laboratory	44	11.7
Other health professionals	76	20.1
Educational level		
Diploma	75	19.9
BSc degree	236	62.6
Postgraduate and above	66	17.5
Staff categories		
Teaching staff	56	14.9
Hospital staff	321	85.1
Working experience (years)		
<3	139	36.9
3-6	90	23.9
>6	148	39.3
Ever diagnosed for TB		
Yes	138	36.6
No	239	63.4
Trained for infection prevention		

Yes	79	21.0
No	298	79.0

Table 2: Number and percent (%) of correct response among health profession towards all knowledge questions

The correct response to knowledge questions	**Number**	**Percent**
MDR-TB is defined as TB that is resistant to isoniazid and rifampicin	264	70.0
MDR-TB is transmitted by droplet spread	345	91.5
MDR-TB occur when TB treatments are not properly administered	357	94.7
All people with MDR-TB infection may not have symptoms	148	39.3
A cough or chest pain is the most common symptom of pulmonary MDR-TB	221	58.6
Culture with drug susceptibility test (DST) is the best diagnostic methods for MDR-TB	368	97.6
Culture conversion is the major element to assess MDR-TB treatment cure	241	63.9
MDR-TB treatment takes 18 months and above	209	55.4
Nationally recommended MDR-TB treatment regimen	168	44.6
Putting on N95 can reduce the risk of MDR-TB transmission	314	83.3

Table 3: Factors associated with knowledge of health workers about MDR-TB at Gondar University Referral Hospital and Felege Hiwot Referral Hospitals, Northwest Ethiopia

Variables	MDR-TB Knowledge			
	Good	Poor	COR (95% CI)	AOR (95% CI)
Working site				
Internal medicine	37	40	1:00	
Surgery	17	29	0.60 (0.28,1.26)	
Gynaecology and Obstetrics	17	26	0.67 (0.31, 1.42)	
Paediatrics	24	28	0.87 (0.43, 1.77)	
OPD and Others	52	105	0.50 (0.29, 0.88)	
Age (year)				
<25	50	80	1:00	
26-30	80	109	1.17 (0.74, 1.85)	
>30	19	39	0.77 (0.40, 1.49)	
Sex				
Male	103	126	1.81 (1.17, 2.80)	
Female	46	102	1:00	
Marital status				
Married	57	98	0.82 (0.53, 1.25)	
Not married	92	130	1:00	
Profession				
MD	42	17	1:00	
Nurse	70	128	0.22 (0.11,0.41)	
Medical laboratory	13	31	0.17 (0.07,0.40)	
Other health professionals	24	52	0.18 (0.08,0.39)	
Educational level				
Diploma	16	59	1:00	1:00
BSc	99	157	2.32 (1.26, 4.26)	1.58 (0.81, 3.05)
Postgraduate above	34	12	10.44 (4.42,24.67)	5.78 (2.33, 14.33)
Staff categories				
Teaching staff	35	21	3.00 (1.68, 5.44)	
Hospital staff	114	207	1:00	
Working experience (years)				
<3	59	80	1.17 (0.73, 1.88)	
3-6	33	57	0.92 (0.53, 1.58)	
>6	57	91	1:00	
Ever diagnosed for TB				

Yes	35	103	2.68 (1.69, 4.25)	1.85 (1.12 ,3.03)
No	114	125	1:00	1:00
Trained for infection prevention				
Yes	23	55	1.78 (1.04, 3.05)	1.79 (1.00, 3.17)
No	126	172	1:00	1:00

Table 4: Factors associated with the self-reported practice of health workers regarding the prevention and control of MDR-TB at Gondar University Referral Hospital and Felege Hiwot Referral Hospital, Northwest Ethiopia.

Variables	Practice		COR (95% CI)	AOR (95% CI)
	Yes	No		
Working site				
Internal medicine	29	50	3.21 (1.71, 6.04)	4.64 (1.99,10.81)
Surgery	5	41	0.67 (0.24, 1.88)	1.11 (0.33, 3.74)
Gynaecology and Obstetrics	11	32	1.90 (0.84, 4.28)	2.57 (0.95, 6.99)
Paediatrics	5	47	0.59 (0.21,1.63)	3.85 (1.11, 13.34)
OPD and Others	24	133	1.00	1.00
Age (years)				
<25	13	117	1.00	1.00
26-30	43	146	2.65 (1.36, 5.16)	2.70 (1.27,5.76)
>30	18	40	4.05 (1.82, 9.00)	4.42 (1.77,11.00)
Sex				
Male	34	195	1.00	
Female	40	108	0.47 (0.28, 0.78)	
Profession				
MD	8	51	1.00	1.00
Nurse	48	150	2.04 (0.90,4.60)	4.49 (1.03, 19.47)
Medical laboratory	7	37	1.20 (0.40, 3.62)	5.21 (0.86, 31.51)
Other health professionals	11	67	1.07 (0.44, 2.88)	2.20 (0.25,10.73)
Educational level			1.00	
Diploma	27	48	0.32 (0.18, 0.58)	
BSc	40	219	0.31 (0.12, 0.81)	
Residence/masters and above	7	39		
Staff categories				
Teaching staff	13	43	1.28 (0.65, 2.54)	
Hospital staff	61	260	1.00	
Working experience (year)				
<3	21	118	0.76 (0.41, 1.41)	
3-6	25	65	1.64 (0.88, 3.05)	
>6	28	120	1.00	
Knowledge on MDR	20	129	0.50 (0.28, 0.88)	
Good	54	174	1.00	

Poor				

1

My name is ……., I am working for the University of Gondar. We are collecting data on health professionals.

This self-administered questionnaire is designed to assess the knowledge and practices of health professionals about the prevention and control of multidrug-resistant tuberculosis (MDR-TB) in Amhara region referral hospitals. You are selected randomly to participate in this study and you would be asked some questions about MDR-TB. The answers will be used only for the purpose of this study. You will not request to write your name nor your addresses. Hence, readers will not be able to find out who gave certain answers.

I would be pleased if you participated, but your participation is voluntary. If you don't want to participate, please feel free to say NO, and not complete this self-administered questionnaire.

Would you agree to participate in this study? Yes ☐ No ☐

If yes, signature_____

I. Socio-demographic characteristics of the respondent		
000	Place of data collection	1. University of Gondar Referral Hospital 2. Felege Hiwot Referral Hospital
101	In which Ward/OPD do you currently work?	3. Internal medicine 4. Surgery 5. Gynaecology and Obstetrics 6. Paediatrics 7. Others (specify):- ----------
102	What is your age?	_____ in years
103	What is your gender?	1. Male 2. Female
104	What is your religion?	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others (specify)_____
105	What is your marital status?	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated
106	What is your profession?	1. Medical Doctor 2. Nurse 3. Health Officer 4. Pharmacy 5. Medical Laboratory 6. Midwife 7. Others_____
107	What is your highest level of educational attainment?	1. Diploma 2. Bachelor degree 3. Medical doctor 4. Masters 5. Specialized 6. Sub specialized
108	Staff category	1. Teaching staff 2. Hospital staff
109	How long have you worked as a health professional?	_____years
110	Have you ever been diagnosed for TB?	1. Yes 2. No
111	Have you been trained for TB or MDR-TB within the last 12 months	1. Yes 2. No
112	Have you been trained for infection prevention within the last 12 months	1. Yes 2. No

II. Questions about knowledge of MDR-TB		
201	What is multidrug-resistant tuberculosis or MDR-TB?	**1. TB that is resistant to isoniazid and rifampicin** 2. TB that is resistant to isoniazid and ethambutol 3. TB that is resistant to rifampicin, ethambutol and pyrazinamide 4. TB that is resistant to streptomycin and pyrazinamide
202	How does MDR-TB transmit?	1. Sexually **2. By droplet spread** 3. By direct contact 4. By sharing needles
203	How does MDR-TB occur?	1. When a person exposed to other TB patients 2. When a person co-infected with HIV **3. When TB treatments are not properly administered** 4. When a person had not been infected with TB previously
204	All people with MDR-TB infection show symptoms	1. True **2. False**
205	What is the most common symptom of pulmonary MDR-TB?	**1. A cough or chest pain** 2. Abdominal pain 3. Diarrhoea 4. Loss of appetite 5. High-grade fever
206	What is the best diagnostic methods for MDR-TB?	1. Culture examination 2. Sputum smear examination **3. Culture with drug susceptibility test (DST)** 4. Chest x-ray
207	What is the major element to assess MDR-TB treatment cure?	**1. Culture conversion** 2. Chet x-ray 3. Skin test 4. All of the above
208	How long MDR-TB treatment takes?	1. 4 months 2. 6 months 3. 9 months **4. 18 months and above** 5. Don't know
209	Which one of the following is the nationally recommended MDR-TB regimen regiment?	**1. Pyrazinamide, Kanamycin, Levofloxacin, Prothionamide, Cycloserine, Ethambutol** 2. Rifampicin, Kanamycin and Levofloxacin 3. Kanamycin, Prothionamide, Cycloserine, Rifampicin Pyrazinamide, Kanamycin, Levofloxacin, Prothionamide, Cycloserine, INH
210	Putting on N95 can reduce the risk of transmission of MDR-TB?	**1. True** 2. False

II. Questions about MDR-TB prevention and control practices		
401	Do you have an access to the MDR-TB guidelines	**1. Yes** 2. No
402	Do you refer to the MDR-TB guidelines when caring for TB or MDR-TB suspected patients?	**1. Yes** 2. No
403	Is cross ventilation implemented in the wards at this hospital?	**1. Yes** 2. No
404	Do you open the windows when caring for the patient?	**1. Yes** 2. No
405	Do you collect a sputum specimen for the patient in the ward?	1. Yes **2. No**
406	Have you ever participated in educating patients about MDR-TB prevention?	**1. Yes** 2. No
407	Does this hospital provide you with masks N95?	**1. Yes** 2. No
408	How often do you use them (N95)?	**1. Always when attending MDR-TB or TB suspected patients** 2. Frequently 3. Rarely 4. Never

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1&2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6*
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6 & 7
		(*e*) Describe any sensitivity analyses	NA

Continued on next page

Results			**Pages**
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7
		(b) Give reasons for non-participation at each stage	7
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	7
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*NA*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*NA*
		Cross-sectional study—Report numbers of outcome events or summary measures	*8 & 9*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	*8 & 9*
		(*b*) Report category boundaries when continuous variables were categorized	*8 & 9*
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	*8 & 9*
Discussion			
Key results	18	Summarise key results with reference to study objectives	9&10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9&10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.