Introduction to Tuberculosis Modelling
48th World Union World Conference on Lung Health, Liverpool
11th October 2017

Practical 2: Modelling the impact and cost effectiveness of improved diagnostics

Overview and Objectives

This practical consists of a computer exercise using a mathematical model, which extends the model used in the first practical and explores the impact and cost-effectiveness of improved diagnostics.

By the end of this practical, you should:

- Know how you might estimate the impact of improved diagnostics.
- Describe and interpret different measures of cost-effectiveness

Introduction to the model

1. Start up Berkeley Madonna and open the file **TB_improved_diag.mmd** by clicking on the File option in the main menu, selecting the Open option and selecting the file from the appropriate location. This file was in the zip file that you downloaded before the course.

The model is identical to the version used in practical 1, except for the following:

a) The section on case-detection and cure-related parameters in the equations panel has been extended to include the details of the diagnostic pathway. When cases visit the health services their sputum is examined by smear microscopy. If they are smear-negative, a proportion (30%) receive a chest X-ray and a proportion of these (depending on the sensitivity of X-ray, which is assumed to equal 80%) are referred for treatment. A proportion (0.15) of those referred for treatment default from treatment, which is assumed to be identical for both smear-positive and smear-negative cases. Of those who start TB treatment, only 75% complete treatment.

b) There is an additional section in the equations panel called “Intervention-related parameters” which includes the parameters allowing the new diagnostic to be in place from 2014. In contrast with the situation before its introduction, the new diagnostic is used on all smear-negative cases and has a sensitivity of 70%. The new diagnostic is assumed to have no effect on detection of smear-positive cases. The model includes an indicator, called “intervention_on” which equals 1 if the new diagnostic is in place and 0 otherwise. Further details of how the model includes improved diagnostics are provided in Appendix A and B – you can explore this section later if you wish.

c) There is a new section called "Summary statistics for evaluating the impact of the intervention" which includes variables which count the number of infections, cases, deaths and diagnosed cases since the start of the intervention.

d) There is a new section called "Statistics for evaluating the cost of the intervention", which includes the costs of various components, the number of individuals (both TB and individuals who are suspected to have TB) whose sputum samples are examined using smear microscopy, the number of chest X-rays which are carried out and the number of tests with the new diagnostics which are carried out.

Exploring the impact of improved diagnostics on the TB incidence and number of cases prevented

The improved diagnostic was introduced on the 1st January 2014.

Q1. Would you expect the introduction of the improved diagnostic to have a large or a small impact on the disease incidence in:

i) The short term (1 year)

ii) The long term (10 years)

Give reasons for your answers.

1. Check your hypotheses by running the model by clicking on the run button for the current value for the effective contact (15/year) and completing the following table by reading off the corresponding values for the disease incidence, tuberculosis mortality rate and annual risk of infection by the end of 2014 and the end of 2023 from Graph 1. If you would like the model to run without the improved diagnostic, you just need to move the slider for intervention_on to 0. You may find it helpful to switch to the table view by clicking on the table button on the graph toolbar to read off the corresponding values.

	Without the intervention	**With the intervention**	
		End of 2014 (1 year)	**End of 2023 (10 years)**
TB incidence per 100,000 per year	197		
TB mortality rate per 100,000 per year	51		
Annual risk of infection (%/year)	2.4		

We will now explore how many cases are prevented in the short and long term.

2. Look at Graph 2, which shows the cumulative number of infections, cases or deaths since the start of 2014 and read off the number of cases which occurred in the population by the end of 2014 after running the model both with and without the improved diagnostic, and enter them into the following table.

	Without the improved diagnostic	With the improved diagnostic
Total number of cases in 2014		

3. Use these values to calculate the number of cases prevented in 2014 by introducing the improved intervention.

Q2. Based on these values, how many cases would you expect to prevent over a ten year period (i.e. 2014-2023) by introducing the improved diagnostic at the beginning of 2014?

4. Check your hypotheses by reading off the total number of cases which have occurred in the population by the end of 2023 both with and without the improved diagnostic and calculating the number of cases prevented within 10 years of the introduction of the diagnostic.

Q3. Is this finding what you expected? Why?

Q4. (optional) How do you think these values would change if you considered a setting in which the effective contact rate (and therefore the TB incidence) was very high, e.g. 20 per year? Test your hypotheses by running the model accordingly.

Calculating the cost and cost effectiveness of introducing the new diagnostic

We will now consider the cost and cost-effectiveness of introducing the new diagnostic. We will assume that, on presentation to the health services, the sputum samples of all individuals are examined by smear microscopy and those whose samples are smear-negative will be diagnosed using the new diagnostic. Previously, 30% of the latter individuals would have received a chest X-ray with a sensitivity of 80%.

The model contains unit costs for smear microscopy, X-rays and the new diagnostic test. These include both the costs of the tests themselves and the costs of the outpatient visits required to collect sputum and provide a result.

The number of tests carried out is multiplied by the number of people receiving each test to estimate the cost per person diagnosed with TB.

Q5. What do you think should happen to the number of new diagnoses as a result of the introduction of the new diagnostic? Test your hypotheses by running the model and looking at graph 3, which shows the number of new diagnoses occurring each week (left-hand y-axis), and the cumulative number of diagnoses since the start of the intervention (right-hand y-axis).

1. If you have time and would like to examine the breakdown of these changes in further detail, look at graph 4, where you can see the following:

a) The number of smear-positive and smear-negative TB cases whose sputum is examined using smear microscopy per week (indicated by the lines labelled Num_smear_exams_in_smpos and Num_smear_exams_in_smneg respectively)
b) The number of X-ray examinations which are conducted among smear-negative cases per week (indicated by the line labelled Num_Xray_exams_in_smneg)
c) The number of tests using the new diagnostic which are conducted among smear-negative cases per week (indicated by the line labelled Num_new_test_in_smneg).

Q6. Based on your answer to Q5 and the costs for conducting a sputum examination using smear microscopy ($5), the cost of X-ray ($10) and of the new diagnostic ($20), do you think that the cost resulting from introducing the intervention over a ten year period will be greater or less than that of not introducing the intervention?

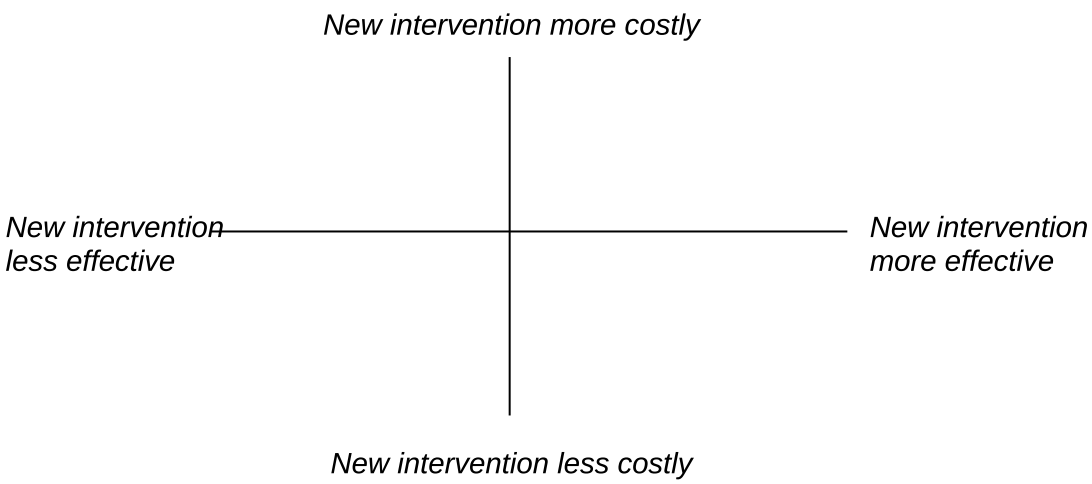
2. Test your hypotheses by running the model both with and without the intervention and looking at graph 5. This graph shows:
a) Total_cum_cost, which shows the total cost incurred as a result of smear microscopy, use of X-ray and the new diagnostic test since 2014.
b) Total_cum_cost_smear, which shows the total cost incurred as a result of smear microscopy since 2014.
c) Total_cum_cost_X_ray, which shows the total cost incurred as a result of the use of X-ray since 2014.
d) Total_cum_cost_new_test, which shows the total cost incurred as a result of the use of the new diagnostic test since 2014.

You can click on the buttons at the bottom of the graph to see the cost incurred through smear examination, X-ray examinations and using the new diagnostic.

Graph 6 shows the average cost per TB case diagnosed.

Q7.a) Which intervention has the lowest average cost-effectiveness ratio?

b) Which intervention is more cost-effective? To help answer this question, you should think about where the new diagnostic falls on the cost-effectiveness plane below compared to the current intervention.



c) What (if any) additional information is required in order to assess which intervention is the most cost-effective?

Q8. (optional) If the model population was larger than it as present, would you expect the cost per diagnosis to be the same?

Q9. (optional) The model includes no discounting of impact. How would the results be influenced if discounting was included?

Appendix A

Method for introducing the improved diagnostic

To introduce the improved diagnostic, the model has been changed as follows:

1. The equation for the rate of change in the number of smear-negative cases (see the equation d/dt(Smneg) in the section called "Differential equations – disease-related categories" section has been changed to use a parameter called used_rate_detect_and_recover_smneg, which is defined in the section on "Intervention-related parameters".

2. The section on "Time-keeping parameters" includes the year in which the intervention starts, ("year_start_intervention"), the number of years over which the impact is being evaluated (num_yrs_impact_evaluated) and the final year for which the impact is being evaluated (fin_year_impact_evaln, set equal to year_start_intervention+ num_yrs_impact_evaluated).

3. The section on "Intervention-related parameters" includes the following:

    a) An indicator variable, called "intervention_on", which takes the value 1 if the improved diagnostic has been introduced and 0 otherwise.
    b) The new parameter which has been set up to describe the rate at which smear-negative cases are detected and recover ("used_rate_detect_and_recover_smneg") is set to equal the pre-intervention value (held in preinterv_rate_detect_and_recover_smneg) if the year is before the year in which the intervention starts, and equals the post intervention value (interv_rate_detect_and_recover_smneg) if the year is after the year in which the intervention is introduced.
    c) The value for preinterv_rate_detect_and_recover_smneg is calculated using the sensitivity of the new diagnostic instead of the proportion of cases who are offered a chest X-ray and the sensitivity of X-rays for detecting smear-negative TB.

4. The section on "Statistics for evaluating the cost of the intervention" includes the following:
    a) Calculations of the numbers of sputum smear examinations ("cum_smear_since_start_intervention"), X-rays ("cum_X_ray_since_start_intervention") and tests using the new diagnostic ("cum_new_test_since_start_intervention") carried out with and without the intervention. These calculations account for the fact that individuals without TB disease will attend the health services at some reduced rate compared to those with tuberculosis.
    b) The total cost of the diagnostic tests carried out during the course of the intervention which is stored in "total_cum_cost".
    c) Calculation of the cost per diagnosed case.

Appendix B

Calculating the rate at which smear-positive or smear-negative cases are detected:

Smear-positive cases

The rate at which smear-positive cases are detected and put onto treatment is calculated using the following formula:

Rate at which cases come to the health centre and start treatment (=1/(average time until they visit a health centre and start treatment))
×
Proportion of cases who do not default from treatment (=0.85)
×
Proportion of cases for whom treatment is successful (=0.75)

The values for the last two terms in this formula is taken as the mid-point of values provided in Table S2.

The average time until cases visit a health centre and start treatment depends on several factors, namely the average time until they visit a health centre, the time delay until a sputum sample is take for examination by smear, the time until the smear result is smear is take .

Lin et al do not provide values for the average time until smear-positive or smear-negative cases visit a health centre; instead they provide the range of values for HIV-negative and HIV-positive individuals (1-25 and 1-7 months respectively). For consistency with Lin et al, we assume that the time for smear-negative and smear-positive cases is identical and equals 12 months or 52 weeks respectively. The average time until a sputum sample is provided after the initial health centre visit is said to be 30 days, with a further 3 days until the result returns and a further 5 days until treatment is initiated.

The average time until cases come to the health centre and treatment is initiated is approximately 52+30/7 +3/7 + 5/7 weeks $\approx$ 57 weeks

The rate at which smear-positive cases are detected is therefore given by:

$$\frac{1}{57} \times 0.85 \times 0.75 \approx 0.011 \text{ per week}$$

Smear-negative cases

The rate at which smear-negative cases are detected and put onto treatment is calculated in a similar way to that for smear-positive cases, except for the fact that it needs to account for the assumed proportion of smear-negative cases who are provided with a chest X-ray (0.3) and the sensitivity of the chest X-ray (80%), as given by the following formula:

Rate at which cases come to the health centre and start treatment if X-rayed (=1/(average time until they visit a health centre and start treatment if X-rayed))
×
Proportion of smear-negatives who have access to a chest X-ray (=0.3)
×
Sensitivity of chest X-ray for identifying smear-negative TB (=0.8)
×
Proportion of cases who do not default from treatment (=0.85)
×
Proportion of cases for whom treatment is successful (=0.75)

The rate at which smear-negative cases are detected is therefore given by:

$$\frac{1}{57} \times 0.3 \times 0.8 \times 0.85 \times 0.75 \approx 0.0026 \text{ per week}$$

Introducing the new diagnostic test

When the new diagnostic test is introduced, 100% of smear-negative cases receive the new diagnostic test instead of X-ray. The new test is assumed to have a sensitivity of 70%.

The rate at which smear-negative cases are detected after the introduction of the new test is given by the following formula:

Rate at which cases come to the health centre and start treatment if smear-negative (=1/(average time until they visit a health centre and start treatment if smear-negative))
×
Proportion of smear-negatives who have access to the new diagnostic test (=1)
×
Sensitivity of new test for identifying smear-negative TB (=0.7)
×
Proportion of cases who do not default from treatment (=0.85)
×
Proportion of cases for whom treatment is successful (=0.75)

The rate at which smear-negative cases are detected is therefore given by:

$$\frac{1}{57} \times 1 \times 0.7 \times 0.85 \times 0.75 \approx 0.0078 \text{ per week}$$