**Date:**
**Name of first reviewer:**
**Name of second reviewer:**

| **Study details** | |
|---|---|
| Study title | |
| First author | |
| Co-authors | |
| Source of publication Journal yy;vol(issue):pp | |
| Language | |
| Publication type | |
| **Baseline characteristics** | |
| Population | |
| Intervention(s) | |
| Comparator(s) | |
| Outcome(s) | |
| Study design | |
| **Methods** | |
| Target population and subgroups | |
| Setting and location | |
| Study perspective | |
| Comparators | |
| Time horizon | |
| Discount rate | |
| Outcomes | |
| Measurement of effectiveness | |
| Measurement and valuation of preference based outcomes | |
| Resource use and costs | |
| Currency, price date and conversion | |
| Model type | |
| Assumptions | |
| Analytical methods | |
| **Results** | |
| Study parameters | |
| Incremental costs and outcomes | |
| Characterising uncertainty | |
| **Discussion** | |
| Study findings | |

| | |
|---|---|
| Limitations | |
| Generalizability | |
| **Other** | |
| Source of funding | |
| Conflicts of interest | |
| Comments | |
| **Authors conclusion** | |
| | |
| **Reviewer's conclusion** | |
| | |

**Date:** 18th August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of interferon-gamma release assay for tuberculosis screening of rheumatoid arthritis patients prior to initiation of tumour necrosis factor-α antagonist therapy |
| First author | Kowada |
| Co-authors | None |
| Source of publication<br>Journal yy;vol(issue):pp | Molecular diagnosis and therapy<br>2010;14(16):367-373 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Immunocompromised (Rheumatoid arthritis patients prior to tumour necrosis factor-α (TNF- α) therapy |
| Intervention(s) | QuantiFERON gold-in-tube (QFT-GIT) |
| Comparator(s) | Tuberculin skin test (TST) |
| Outcome(s) | Cost per quality-adjusted life-year (cost per QALY) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Not reported |
| Study perspective | Societal perspective |
| Time horizon | Lifetime horizon with one-year time cycle lengths |
| Discount rate | 3% per annum |
| Measurement of effectiveness | Quality-adjusted life-years |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Screening test for QFT-GIT and TST, costs for treatment of LTBI/TB and adverse events |
| Currency, price date and conversion | US dollars, costs were adjusted to 2009 Japanese Yen and converted to US dollars in 2009, 1 US$ = 93 Japanese Yen |
| Model type | Decision tree model with Markov nodes (No LTBI, LTBI, TB and death) |
| Assumptions | 1) The sensitivities for QFT-GIT and TST in people with rheumatoid arthritis are assumed to be lower than the sensitivities for an immunocompetent population. |
| Analytical methods | The author conducted one-way and two-way sensitivity analyses by changing key model input parameters to determine the impact on the deterministic results. Additionally, probabilistic sensitivity analysis (PSA) was undertaken to determine the uncertainty in the key model input parameters |
| **Results** | |
| Study parameters | Sensitivity and specificity for QFT and TST. Other parameters included probability of successful treatment, probability of recurrence of active TB |

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| | after TB adherence to rate of treatment |
| Incremental costs and outcomes | In the base-case analysis, QFT was less costly and more effective than TST, US$1040 vs. US$1820 and 23.0350 vs. 22.9815 QALYs, respectively |
| Characterising uncertainty | The results from the PSA showed that at society's willingness-to-pay per QALY, the probability of QFT testing strategy has a 100% probability of being cost-effective compared to the TST strategy |
| **Discussion** | |
| Study findings | The results showed/demonstrated that QFT was less costly and more effective than TST strategy |
| Limitations | 1) The sensitivities for QFT-GIT and TST in people with rheumatoid arthritis are assumed to be lower than the sensitivities for an immunocompetent population<br>2) There was a lack of information to populate the model on the natural history of TB regarding QFT-GIT conversion and reversion rate<br>3) A paucity of information exists on the incidence of LTBI and active TB in people with rheumatoid arthritis treated with TNF-α antagonists and this may have an impact on the results |
| Generalizability | The model presented here may be useful to determine the cost-effectiveness of QFT-GIT compared with TST for the diagnosis of LTBI in patients with rheumatoid arthritis prior to TNF-α treatment. The results presented here suggested that QFT is the dominant strategy compared to TST alone, but some of the key inputs are questionable, for example the utility value of 0.9 for nonfatal TB in people with rheumatoid arthritis. This utility value appears to be high for people who have rheumatoid arthritis. The model may be useful, but these results should be interpreted with caution |
| **Other** | |
| Source of funding | No source of funding |
| Conflicts of interest | No conflicts of interest |
| Comments | In table 1, Kowada presented the utility value of non-fatal TB, but have not presented other utility values for other health states<br><br>Additionally, the starting age of the hypothetical cohort is 40 years, but the author included information on the mortality due to people ages 20-29 years and 30-39 years<br><br>The author conducted probabilistic sensitivity analysis (PSA) on the outcome measure of cost per QALY. However, the distributions placed around the key model inputs have not been reported |
| **Authors conclusion** | |
| The author concluded that the QFT testing strategy is more effective and less costly than TST testing strategy for diagnosing LTBI in people with rheumatoid arthritis prior to treatment with TNF-α antagonists for both BCG vaccinated and unvaccinated groups | |
| **Reviewer's conclusion** | |
| The author used an appropriate modelling technique to demonstrate the cost-effectiveness of QFT compared to TST in people with rheumatoid arthritis. Various key health states which relate to LTBI/TB have been included in the model structure, but there is some uncertainty in key model input parameters. The authors have attempted to address this uncertainty by using sensitivity analysis and PSA, but have not presented information on the distribution used around these model parameters. Hence, we believe that these results should be interpreted with caution | |

**Date:** 15 August 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of interferon-gamma release assay for school-based tuberculosis screening |
| First author | Kowada |
| Co-authors | None |
| Source of publication<br>Journal yy;vol(issue):pp | Molecular diagnosis and therapy<br>2012;16(3):181-190 |
| Language | English Language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Children/adolescents: Immunocompetent children/adolescents aged 16-19 years old; Students divided into BCG-vaccinated individuals and non BCG-vaccinated individuals |
| Intervention(s) | QFT-GIT, chest x-ray |
| Comparator(s) | TST |
| Outcome(s) | Cost per quality-adjusted life-years |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Not reported |
| Study perspective | Societal perspective |
| Time horizon | Life time horizon (up to 80 years old), one-year cycle length |
| Discount rate | 3% discount rate per annum |
| Measurement of effectiveness | Quality-adjusted life-years (QALYs) |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Cost of TST and QFT screening and cost of treatment and adverse events |
| Currency, price date and conversion | 2009 Japanese yen, converted to US$, using the OECD purchasing power parity rate in 2009 |
| Model type | Markov model (Healthy, LTBI, TB and dead) |
| Assumptions | The author assumed a high prevalence of LTBI in the Japanese population |
| Analytical methods | One-way and two-way sensitivity analyses were performed on key model input parameters<br>Probabilistic sensitivity analyses was undertaken to address the uncertainty around key model input parameters and was based on the outcome measure of cost per quality-adjusted life-year |
| **Results** | |
| Study parameters | Sensitivity and specificity for QFT, TST and chest x-ray. Other parameters included probability of successful treatment, probability of recurrence of active TB after TB adherence to rate of treatment |
| Incremental costs and outcomes | In the 16-year old sub-group QFT was less costly and more effective than |

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| | TST, US$628 vs. US$944 and 29.6984 vs. 29.6977 QALYs, respectively |
| Characterising uncertainty | Results from the sensitivity analyses showed that the results were robust to changes made to model input parameters. From the PSA, the author suggested that there was a 100% probability that QFT was cost-effective compared to TFT at all society's willingness-to-pay levels |
| **Discussion** | |
| Study findings | Base-case results showed that in the 16-year old sub-group the QFT test was cheaper and produced a moderate benefit in terms of QALYs |
| Limitations | 1) The author assumed that the prevalence of LTBI was high in this Japanese population, this estimate was based on the TST positivity rates<br>2) The Markov model did not include health states for people who received treatment for LTBI<br>3) The distress for LTBI testing was not measured in this study. |
| Generalizability | The author suggested that the results may be applicable to other countries where school-based TB testing is being conducted |
| **Other** | |
| Source of funding | No sources of funding |
| Conflicts of interest | No conflicts of interest |
| Comments | The author mentioned that in 2008 over 95% of the population had received BCG vaccination at least once. Specificity of TST were stratified by BCG-vaccinated and non-BCG vaccinated people, however, this was not done for QFT or chest x-ray |
| **Authors conclusion** | |
| The author demonstrated that the use of QFT provided greater benefits than screening with TST or chest x-ray in terms of lower costs and identifying more cases of LTBI in this population | |
| **Reviewer's conclusion** | |
| The author used an appropriate modelling technique to demonstrate the cost-effectiveness of QFT compared to TST. There were some limitations in the model which the author alluded to, for example, not including health states where people have received treatment for LTBI/TB. The author did not state the study setting within which the analysis would be undertaken, hence compromising the generalizability of these results. Additionally, we assumed the perspective of the study was the societal perspective because the author suggested that indirect costs relating to loss of productivity would be included, these costs were not reported in this paper. We did not think it would have been necessary to include indirect costs due to loss of productivity because these children/adolescents are assumed to be full-time students | |

**Date:** 18th August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of interferon-ɣ release assay for tuberculosis screening of hemodialysis patients |
| First author | Kowada |
| Co-authors | None |
| Source of publication<br>Journal yy;vol(issue):pp | Nephrology Dialysis Transplantation<br>2013;28:682-688 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Immunocompromised (haemodialysis patients 40 years of age); sub-groups for people who were BCG-vaccinated |
| Intervention(s) | QFT-GIT, |
| Comparator(s) | Tuberculin skin test (TST), chest x-ray (CXR) |
| Outcome(s) | Cost per quality-adjusted life-year (Cost per QALY) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Not reported |
| Study perspective | Societal perspective |
| Time horizon | Lifetime horizon |
| Discount rate | 3% per annum for costs and benefits |
| Measurement of effectiveness | QALY |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Direct (inpatient/outpatient) and indirect (loss of productivity) costs, screening costs for QFT, TST and CXR. Other costs included treatment for active TB, costs of smear and culture examinations of sputum and treatment of adverse events |
| Currency, price date and conversion | US$, 2012, costs adjusted to 2012 Japanese Yen, then converted to US dollars, using the OECD purchasing power parity rate in 2009 |
| Model type | Markov model (maintenance dialysis with no disorder, maintenance dialysis with LTBI, maintenance dialysis with TB and death) |
| Assumptions | 1) Kowada assumed that the risk of TB-related mortality in ESRD patients will increase with age<br>2) Key model input parameters (probability of developing TB from LTBI, adherence rate of standard treatment, the probability of treatment-induced hepatitis, the efficacy if the standard treatment, and the recurrence of active TB after treatment) were assumed/derived<br>3) Further assumptions were on the sensitivity and specificity of QFT, TST and CXR |
| Analytical methods | The author conducted one-way and two-way sensitivity analyses by changing key model input parameters to determine the impact on the |

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| | deterministic results. Additionally, probabilistic sensitivity analysis (PSA) was undertaken to determine the uncertainty in the key model input parameters |
| **Results** | |
| Study parameters | Sensitivity and specificity for QFT, TST and chest x-ray. Other parameters included probability of successful treatment, probability of recurrence of active TB after TB adherence to rate of treatment |
| Incremental costs and outcomes | In the base-case analysis, QFT was less costly and more effective than TST, US$7690 vs. US$9340 and 4.1926 vs. 4.1854 QALYs, respectively |
| Characterising uncertainty | <u>One-way sensitivity analysis</u><br>The cost effectiveness of the QFT compared with the TST was sensitive to the BCG vaccination rate. TST strategy was more cost-effective than QFT strategy at the willingness-to-pay level of US$50,000 per QALY gained when the BCG vaccination rate was o.18 or lower<br><br><u>Probabilistic sensitivity analysis</u><br>The cost-effectiveness acceptability curve of 40-year-old patients by Monte Carlo simulations for 10,000 trials demonstrated that the QFT was the most cost-effective, with a value of 100% at all willingness-to-pay level compared with TST and CXR strategies |
| **Discussion** | |
| Study findings | Base-case results showed that the QFT test was cheaper and produced a moderate benefit in terms of QALYs. The QFT testing strategy was dominant compared to TST testing strategy |
| Limitations | 1) No gold standard to diagnose LTBI in the end stage renal disease (ESRD) population<br>2) Paucity of information on the sensitivity and specificity of QFT-GIT and TST in people with ESRD<br>3) The parameters included in the model may be changeable in more precise investigations of TB dynamics |
| Generalizability | The model presented here may be useful to determine the cost-effectiveness of QFT-GIT compared with TST/CXR for the diagnosis of LTBI, but given the limitations highlighted on the key model input parameters, results should be interpreted here with caution |
| **Other** | |
| Source of funding | Not reported |
| Conflicts of interest | None declared |
| Comments | Author has not provided an illustrative structure of the Markov nodes used in the model. The author mentioned that in the TST testing strategy, BCG – vaccinated people with an induration of ≥5mm and unvaccinated people would have undergone a CXR. However, this has not been illustrated in the model. The author conducted PSA around the outcome measure cost per QALY. However, the distributions used around key model input parameters were not stated in this paper. Additionally, the cost-effectiveness acceptability curve was not provided in this paper |
| **Authors conclusion** | |
| The results demonstrated that that QFT screening strategy produced greater benefits in terms of QALYs and lower costs compared to TST/CXR for people who have ESRD | |
| **Reviewer's conclusion** | |
| The author used an appropriate modelling technique to demonstrate the cost-effectiveness of QFT compared to TST/CXR in people with ESRD. The author did not state the study setting within which the analysis would be undertaken, hence compromising the generalizability of these results. Additionally, we assumed the perspective | |

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| of the study was the societal perspective because the author suggested that indirect costs relating to loss of productivity would be included, these costs were not reported in this paper |

**Date:** 21st August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of interferon-gamma release assay for TB screening of HIVE positive pregnant women in low TB incidence countries |
| First author | Kowada |
| Co-authors | None |
| Source of publication Journal yy;vol(issue):pp | Journal of infection 2014;68:32-42 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Immunosuppression (HIV positive pregnant women). Immunosuppressed (20-year old HIV positive pregnant women) four sub-groups were analysed: non-BCG vaccinated cohort during pregnancy, BCG-vaccinated cohort during pregnancy, non-BCG vaccinated cohort postpartum period and BCG vaccinated cohort in postpartum period |
| Intervention(s) | Five strategies<br>1) TST alone, 2) QFT alone, 3) T-SPOT.TB, 4) TST followed by QFT and 5) TST followed by T-SPOT.TB |
| Comparator(s) | See above five compared strategies |
| Outcome(s) | Cost per QALY |
| Study design | Cost-effectiveness analysis |
| Setting and location | Hypothetical cohort followed until age 50 years in three most common screening situations; close contacts, immigrants from high burden countries and occasional screening in low TB incidence countries |
| **Methods** | |
| Study perspective | Health service perspective |
| Comparators | TST alone |
| Time horizon | 30-year time horizon with yearly cycles |
| Discount rate | 3% per annum for costs and benefits |
| Measurement of effectiveness | QALY |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Screening test for TST, QFT, T-SPOT.TB, chest x-ray, costs for treatment of LTBI/TB and adverse events (Hepatitis). |
| Currency, price date and conversion | US$, 2012, 1US$ = ¥ 103.9 (OECD purchasing power parity rate in 2012) |
| Model type | Markov model (Non-LTBI and non-TB, LTBI, non MDR-TB, MDR-TB and Dead) |
| Assumptions | Not clearly stated |
| Analytical methods | The author conducted one-way sensitivity analyses by changing key model input parameters to determine the impact on the deterministic results. Additionally, probabilistic sensitivity analysis (PSA) was undertaken to |

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| | determine the uncertainty in the key model input parameters |
| **Results** | |
| Study parameters | Probability of having LTBI among HIV positive pregnant women, incidence of TB among HIV positive pregnant, increased mortality among HIV positive pregnant women, probability of successful treatment, adherence rate of treatment, sensitivity and specificity for TST, QFT, T-SPOT.TB and chest x-ray |
| Incremental costs and outcomes | The results from the base-case analysis showed that T-SPOT.TB was least costly and more effective with an incremental cost of US$ 596 and incremental QALYs of 0.00705 compared with TST in HIV positive pregnant women (non-BCG vaccinated) in close contacts |
| Characterising uncertainty | Results from the one-way sensitivity analysis showed that the cost-effectiveness was sensitive to the sensitivity of T-SPOT.TB, the sensitivity of QFT, specificity of T-SPOT.TB and the specificity of QFT in close contacts during pregnancy and other changes in key model input parameters<br><br>The results from the PSA showed that at society's willingness-to-pay per QALY, there was a 100% probability that TST followed by QFT strategy is likely to be cost-effective compared to other testing strategies |
| **Discussion** | |
| Study findings | The results showed that the T-SPOT.TB is less costly and was more effective compared to other strategies |
| Limitations | There were some assumptions which the author acknowledged:-<br><br>1) The probability estimates used in the model were obtained from different countries<br>2) Estimates on sensitivity and specificity of IGRAs and TST were values based on meta-analysis of published literature and assumptions made. The author further suggested that there is little evidence to suggest the impact of pregnancy on the sensitivity/specificity of IGRAs and TST to diagnose LTBI.<br>3) The cost of the side effect by MDR-TB therapy was not calculated in the model<br>4) The use of chemoprophylaxis for pregnant women is still a controversial issue<br>5) A paucity of information on the incidence of TB in pregnant women and the prevalence of LTBI in HIV positive pregnant women |
| Generalizability | Given the assumptions and the limitations, the model presented may be generalizable in a population with women who are pregnant and have HIV |
| **Other** | |
| Source of funding | Author reported no source of funding |
| Conflicts of interest | Author reported no conflict of interest |
| Comments | None |
| **Authors conclusion** | |
| Kowada concluded that the use of IGRA to screen for TB in HIV positive pregnant women is cost-effective in countries with low incidence of TB | |
| **Reviewer's conclusion** | |
| The model presented here is very useful to inform on the cost-effectiveness of IGRAs compared with TST for the diagnosis of TB in this patient group. The author has used an appropriate modelling structure to show LTBI progression | |

**Date:** 18th August 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of latent tuberculosis screening before steroid therapy for idiopathic nephrotic syndrome in children |
| First author | Laskin |
| Co-authors | J Goebel, JR Starke, DP Schauer |
| Source of publication<br>Journal yy;vol(issue):pp | American journal of kidney diseases<br>2013;61(1):22-32 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Immunosuppressed (Idiopathic nephrotic syndrome in children): children up to five years old with idiopathic syndrome |
| Intervention(s) | Interferon-gamma release assays (second model) |
| Comparator(s) | Tuberculin skin test |
| Outcome(s) | Marginal cost per quality-adjusted life-years (cost per QALY) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Not reported |
| Study perspective | Societal perspective |
| Time horizon | Life-time horizon with a three-month cycle length |
| Discount rate | 3% per annum on costs and benefits |
| Measurement of effectiveness | Quality- adjusted life-years |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Screening tests, nephrotic onset, nephrotic relapse and treatment of LTBI/TB |
| Currency, price date and conversion | US$, 2010 prices |
| Model type | Decision tree structure to model the short term events followed by a Markov modelling structure (Well, LTBI, TB, nephrotic relapse and dead) for the longer-term events |
| Assumptions | 1) Children in the model are assumed to be adherent to the medication<br>2) Initial risk of reactivation decreases by 10% per decade<br>3) Children can only develop active TB on one occasion throughout their lifetime<br>4) After presentation with LTBI, children were not allowed to be screened again for LTBI<br>5) In the model, children did not develop multidrug-resistant disease<br>6) Authors assumed that people surviving acute infection have decreased lung function, hence, lower utility values |
| Analytical methods | These authors conducted one-way and two-way sensitivity analyses by changing key model input parameters to determine the impact on the deterministic results. Additionally, probabilistic sensitivity analysis (PSA) was undertaken to determine the uncertainty in the key model input |

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| | parameters |
| **Results** | |
| Study parameters | Screening test characteristics, prevalence, nephrotic onset, nephrotic relapse, mortality and treatment of LTBI/TB |
| Incremental costs and outcomes | In the base-case analysis, universal IGRA was less costly and more effective than universal TST, US$2300 vs. US$2480 and 29.3355 vs. 29.3347 QALYs, respectively. However the 'no screening' strategy dominated the other strategies (universal IGRA, universal TST) being less costly and more effective |
| Characterising uncertainty | The base-case results were robust when indirect medical costs were excluded from the analysis<br><br>In the secondary model, targeted screening with a questionnaire followed by IGRA was cost-effective compared with no screening at a prevalence >4.9% |
| **Discussion** | |
| Study findings | These authors demonstrated that universal IGRA was less costly and produced moderately more QALYs compared to universal TST |
| Limitations | 1) Lack of gold standard for the diagnosis of LTBI in this patient population<br>2) The authors acknowledged that indeterminate results and the need for venepuncture. They suggested that indeterminate results which can lead to false-negative results in children may have an impact on the overall results |
| Generalizability | The model presented here may be useful to determine the cost-effectiveness of IGRAs compared with TST for the diagnosis of LTBI in children with idiopathic nephrotic syndrome. The results presented here suggested that the 'no screen' strategy was the dominant strategy compared to universal IGRA and universal TST alone. However, these results should be interpreted with caution because the discounted and undiscounted costs were similar in the base case results |
| **Other** | |
| Source of funding | No source of funding to conduct study has been stated |
| Conflicts of interest | No conflicts of interest declared |
| Comments | A discount rate of 3% per annum was applied both to the costs and benefits. These authors presented results both on the undiscounted and discounted costs and benefits. From these results presented, the undiscounted and discounted costs are identical.<br><br>These authors have not distinguished between the IGRAs being used in the model. They justified this by suggesting that the use of IGRAs in this population has not yet been approved |
| **Authors conclusion** | |
| Based on the results, these authors demonstrated that at a LTBI prevalence of 1.1%, both universal testing and targeted TST testing are not cost-effective prior to commencing treatment for five-year olds who are newly diagnosed with idiopathic nephrotic syndrome | |
| **Reviewer's conclusion** | |
| The model used here may be useful, and adds to the existing literature to demonstrate the various screening strategies for the diagnosis of LTBI in a population at risk of immunosuppression. The model includes key health states to show the disease progression of LTBI. Given the limitations outlined by the authors, these results showed that the no screening strategy dominated other strategies compared in the model. However, these results should be interpreted with caution because the undiscounted and discounted costs are similar | |

**Date:** 19th August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Priorities for screening and treatment of latent tuberculosis infection in the United States |
| First author | Linas |
| Co-authors | AY Wong, KA Freedberg and CR Horsburgh |
| Source of publication<br>Journal yy;vol(issue):pp | American journal respiratory and critical care medicine<br>2011;184:590-601 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Various risk groups (immunocompromised and recently arrived immigrants) |
| Intervention(s) | Interferon-gamma release assays (IGRAs), Tuberculin skin test (TST) |
| Comparator(s) | No screening |
| Outcome(s) | Number needed to screen to prevent one case of active TB, life expectancy, quality-adjusted life expectancy |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Setting not reported |
| Study perspective | Health service |
| Time horizon | Lifetime horizon |
| Discount rate | 3% per annum for costs and benefits |
| Measurement of effectiveness | Health-related quality of life |
| Measurement and valuation of preference based outcomes | Euroqol five dimensions (EQ-5D) and Medical Outcomes Study (SF-36) |
| Resource use and costs | Costs for screening LTBI with TST, IGRA, costs of treatment of LTBI and active TB, costs of treatment of adverse events |
| Currency, price date and conversion | US$, 2011 |
| Model type | Markov model (health states included, LTBI with Isoniazid (INH), LTBI no INH, INH related hepatitis, < 6 months INH, 6-8 months INH, 9 months INH, Active TB, post active TB and death) |
| Assumptions | 1) People who did not return for TST reading were not eligible for INH therapy<br>2) Approximately 10% of TST-positive persons lose their skin test reactivity over a decade of follow-up. People here are believed to have self-cured. These authors assumed that a 10% reduction in the rate of reactivation each year<br>3) The health-related quality of life for people cured for active TB was assumed to be the same for healthy people<br>4) High-risk groups for screening were already identified and managed by existing resources, and did not require programmatic costs associated with expanded screening interventions |
| Analytical methods | Authors conducted one- and two-way sensitivity analysis by varying all |

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| | model input parameters to explore the uncertainty in these parameter estimates |
| **Results** | |
| Study parameters | Estimates of the prevalence of true LTBI in each risk-group, sensitivity and specificity for IGRA and TST, probability of people with TST +ve who start INH treatment, probability of INH-related hepatitis and utility values for various health states |
| Incremental costs and outcomes | People who had end-stage renal disease (ESRD), the reported ICER for TST screen compared to no screen was $824, 500 and $1, 168, 300 for the IGRA strategy compared with no screen<br><br>In the base-case analysis, for people who are HIV-infected, TST screen was marginally more costly and more effective than the no screen option with an ICER of $12, 800. In this same sub-group, IGRA was marginally more costly and more effective than the no screen option with an ICER of $23, 800<br><br>For people who were on immunosuppressive medication, the reported ICER for TST screen compared to no screen was $129, 000 and $227, 900 for the IGRA screen compared with no screen<br><br>For people who were recent immigrant adults, TST screening strategy dominated the no screen strategy. Whilst IGRA was marginally more costly and more effective than the no screen strategy with an ICER of $35, 200 |
| Characterising uncertainty | Various sensitivity analyses were conducted. Results from the sensitivity analysis showed that increasing the reactivation TB rate in people who are immunosuppressive reduced the ICER to below $100, 000 per QALY. Additionally, increasing the proportion of people with INH-induced hepatitis did not have an impact on the results. The base-case results were sensitive to changes in the health-related quality of life of people treated for active TB. The authors applied a 10% decrement on utility instead of assuming people returned to full health. The results demonstrated that screening with IGRA or TST the ICER was less than $100, 000 per QALY |
| **Discussion** | |
| Study findings | Based on the results reported by these authors, people who are taking immunosuppressive medications, TST screen was not likely to be cost-effectives to the no screening strategy. Similar results were reported for people with ESRD |
| Limitations | There were some limitations to which the authors acknowledged<br><br>1) There are no prospective observational data in the united stated to inform on the rate of reactivation TB. The availability of INH prophylaxis for patients with identified LTBI renders natural history cohorts unethical<br>2) There is no gold standard available to confirm the diagnosis of LTBI<br>3) The model included direct medical costs, but not indirect costs, such as loss of productivity time and transportation costs |
| Generalizability | Authors may have used information relevant to setting and location that the study was conducted. However, they have not reported the setting the analysis was undertaken. Hence, compromising the generalizability of the results |
| **Other** | |
| Source of funding | Supported by the National Institute of Allergy and Infectious Diseases (K01AI073193, K24AI062476, R37AI42006) |
| Conflicts of interest | No conflicts of interest declared |

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| Comments | The model presented here adds to the existing literature on the cost-effectiveness of IGRA compared to TST for the diagnosis of LTBI in various high-risk populations. The model incorporates key health states for the treatment pathway for people being screened and treated for LTBI. Table 3 presents the base-case results, these authors have presented information on the number needed to screen to prevent a case of active TB, discounted lifetime costs per person, undiscounted per person life expectancy, discounted per person quality-adjusted life expectancy (in months) and cost per QALY. From this table of results, we question the authors' values to estimate the ICER given the values presented in this table |
| **Authors conclusion** | |
| These authors concluded that the use of IGRA in screening people who are close contacts, infected with HIV, and foreign-born is likely to be cost-effective when compared to TST | |
| **Reviewer's conclusion** | |
| The model seems useful and adds to the existing literature on the diagnosis of LTBI. However, these authors have not suggested which IGRA is being used in the model. In terms of diagnosing LTBI, the sensitivity and/or specificity may differ between these populations | |

**Date:** 28th August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Clinical diagnosis and management of tuberculosis, and measures for its prevention and control: cost-effectiveness analysis of interferon gamma release assay (IGRA) testing for latent tuberculosis |
| First author | CG117 |
| Co-authors | Not applicable |
| Source of publication Journal yy;vol(issue):pp | Clinical guideline |
| Language | English language |
| Publication type | Clinical guideline |
| **Baseline characteristics** | |
| Population | Recently arrived adults from high endemic countries with active TB |
| Intervention(s) | IGRA, tuberculin (TST) followed by IGRA for people with +ve TST results, no testing |
| Comparator(s) | TST |
| Outcome(s) | Cost per quality adjusted life-year (cost per QALY) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | UK |
| Study perspective | National Health Service (NHS) and Personal Social Service (PSS) perspective |
| Time horizon | 15-year time horizon |
| Discount rate | 3.5% per annum on costs and benefits |
| Measurement of effectiveness | QALY |
| Measurement and valuation of preference based outcomes | Not reported |
| Resource use and costs | Cost of assessment of active TB, cost of tests (IGRA and TST), cost of treatment (LTBI and active TB) |
| Currency, price date and conversion | UK £ sterling, 2008/2009 prices |
| Model type | Decision tree structure |
| Assumptions | 1) Authors used a decision tree model structure which does not take into account the dynamic transmission of tuberculosis. Assumed that each primary case of active TB is associated with a fixed number of secondary cases<br>2) People who did not have a TST test result were assumed to have the same prevalence of LTBI and of active disease as those who do<br>3) An average time delay of 0.5 years before people with LTBI who go on to develop active TB<br>4) For people without current LTBI or active TB who develop TB later in life, authors assumed this will occur after an average time delay of 0.5 years<br>5) The number of secondary cases is assumed to be reduced when the index case is detected through contact tracing |

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| | 6) Side-effects as a result of treatment were ignored<br>7) People who started treatment for LTBI/TB were assumed to have adhere to treatment |
| Analytical methods | One-way and two-way sensitivity analyses were performed on key model input parameters (costs of the IGRA, return rate of the TST results, secondary cases, test accuracies, varying the prevalence of LTBI and varying the transformation from LTBI to active TB) |
| **Results** | |
| Study parameters | Prevalence of LTBI in population, proportion of infected people with active TB. Proportion of TST results read, sensitivity and specificity (IGRA and TST), cost of assessment of active TB, cost of tests, cost of treatment |
| Incremental costs and outcomes | TST/IGRA compared with the no testing strategy was more costly and produced more QALYs, £316 vs. £403 and 9.08686 vs. 9.99015, respectively. IGRA compared with no testing strategy was more costly, and produced more QALYs. Both strategies were likely to be cost-effective with incremental cost-effectiveness ratios (ICERs) below the £30, 000 per QALY threshold |
| Characterising uncertainty | There was no impact on the results when the return rate for TST test results where changed. The increase in the number of secondary cases had a positive effect on the cost-effectiveness results. Results from varying the accuracy of the tests showed that at high levels of specificity of an IGRA test the results showed to be cost-effective at £20, 000 per QALY. For the TST test alone, when the specificity was increased to 80% or above, the results showed to be cost-effective. Conversely, the specificity of the combined strategy needed to be low to achieve £20, 000 per QALY |
| **Discussion** | |
| Study findings | The results showed that TST +ve followed by IGRA and IGRA testing strategies were associated with ICERs below £30, 000 per QALY compared with no testing strategy. The results from the sensitivity analyses showed that varying the cost of an IGRA (£50 to £60) changes the direction of the cost-effectiveness results |
| Limitations | The model used here is subject to limitations, but these were not acknowledged by the authors |
| Generalizability | The model structure used here may be helpful to show the cost-effectiveness between testing strategies for LTBI in this population. The authors have stated assumptions made in the model but have not fully accounted for uncertainty in the analyses, hence compromising the generalizability of the model |
| **Other** | |
| Source of funding | NICE |
| Conflicts of interest | Not reported |
| Comments | The model here adds to the existing literature on the use of IGRA and TST for the diagnosis of LTBI in the recently arrived immigrants from high prevalence of TB countries. The model structure used here, along with some of the assumptions are subject to limitations which were not highlighted by the authors |
| **Authors conclusion** | |
| These authors concluded that IGRA and the TST followed by IGRA testing strategies are likely to be cost-effective | |
| **Reviewer's conclusion** | |

Given the assumptions and the limitations of the model, these results demonstrated that TST +ve followed by IGRA and IGRA testing strategies are likely to be cost-effective in a population with people from high endemic TB countries. The decision tree structure may be subject to some limitations, for example, introducing too much static for people developing active TB

**Date:** 15th August 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Modelling the cost-effectiveness of strategies to prevent tuberculosis in child contacts in a high-burden setting |
| First author | A Mandalakas |
| Co-authors | A Hesseling, R Gie, H Schaaf, B Marais |
| Source of publication Journal yy;vol(issue):pp | Thorax 2012;68(3):247-255 |
| Language | English Language |
| Publication type | Journal article |
| **Inclusion criteria/study eligibility/PICOS** | |
| Population | Children |
| Intervention(s) | QFT and T-SPOT.TB |
| Comparator(s) | TST |
| Outcome(s) | Cost per life year saved (LYS) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | High-burden TB setting |
| Study perspective | Provider and societal perspectives |
| Comparators | TST alone, IGRA alone, +ve TST followed by IGRA and –ve TST followed by IGRA |
| Time horizon | 15 year time horizon |
| Discount rate | 3% discount rate per annum |
| Measurement of effectiveness | Life years saved |
| Measurement and valuation of preference based outcomes | Not applicable |
| Resource use and costs | Tests for infection, chest radiography, culture, HIV testing, in/outpatient visits, laboratory tests, treatment for LTBI and TB |
| Currency, price date and conversion | US dollars, 2009 prices, conversion not stated |
| Model type | Decision tree structure with Markov nodes (no infection, re-infection, LTBI, PTB, disseminated TB, death and death from other causes) |
| Assumptions | When used as a confirmatory test following an accurate tuberculin skin test (TST), the interferon γ release assay (IGRA) is 100% accurate (sensitive and specific)<br>Test properties do not vary by age<br>The duration of protection offered by a 6-month course of IPT is limited to the initial exposure and for the duration of treatment only<br>Following Mycobacterium tuberculosis infection and completion of IPT, children remain M tuberculosis infected<br>Following the initial exposure, children cannot progress from the M tuberculosis infection state to active disease states unless they are re-infected<br>Children with a history of household TB exposure have the same subsequent annual risk of infection as calculated by formal surveys in the setting |

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| | Children can only progress to the TB death state from the pulmonary or disseminated TB states. The disseminated disease state includes TB meningitis and other forms of non-pulmonary TB<br>Children have the same risk of disease progression following each subsequent TB exposure<br>Isoniazid-related adverse events are negligible/rare in children |
| **Results** | |
| Study parameters | Sensitivity and specificity for TST, IGRA, TST +ve followed by IGRA, TST –ve followed by IGRA. Transition probabilities between health states |
| Incremental costs and outcomes | In the 0-2 cohort, the no testing strategy dominated other strategies, it was least costly and most effective<br><br>In the 0-3 cohort, the TST –ve followed by IGRA was the most cost-effective with a reported ICER of approximately US$233 000 per LYS |
| Characterising uncertainty | <u>One-way sensitivity analysis</u><br>In the 0-2 cohort, TST –ve followed by IGRA strategy was the most effective strategy when reducing the sensitivity of TST<br>In the 3-5 cohort, the no testing strategy dominated the TST –ve followed by IGRA when increasing the estimates of sensitivity of TST<br>Increasing the rates of LTBI, the IGRA after negative TST became more effective that the no testing strategy in both age cohorts |
| **Discussion** | |
| Study findings | In the 0-2 cohort, the no testing strategy dominated other strategies. In the 3-5 cohort, the TST –ve strategy followed by IGRA was the most cost-effective |
| Limitations | Test performance estimates were derived from studies that examined the test accuracy for the identification of TB disease. These authors assumed that IPT usage was similar across strategies |
| Generalizability | Unclear |
| **Other** | |
| Source of funding | Thrasher Research Fund |
| Conflicts of interest | No conflicts of interest |
| Comments | Authors have not conducted probabilistic sensitivity analysis |
| **Authors conclusion** | |
| Screening for TB infection and provision of IPT in young children < 5 years is highly cost-effective | |
| **Reviewer's conclusion** | |
| These authors used an appropriate modelling technique to estimate the cost-effectiveness of various strategies for the prevention of TB. The model was subject to some limitations, for which the authors acknowledge and the impact these would have made to the results. Authors have conducted one-way sensitivity analysis, but have not undertaken probabilistic sensitivity analysis to show the joint parameter uncertainty and its impact on the base-case results | |

**Date:** 20th August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Community-based evaluation of immigrant tuberculosis screening using interferon-gamma release assays and tuberculin skin testing: observational study and economic analysis |
| First author | M Pareek 2013 |
| Co-authors | M Bond, J Shorey, S Seneviratne et al. |
| Source of publication Journal yy;vol(issue):pp | Thorax 201;68:230-239 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Recently arrived immigrants to the UK: Recently arrived immigrants to the UK (arrival within the last five years, aged ≥ 16 years (with symptoms of TB) or from a country with a TB incidence of ≥ 40/100 000 (asymptomatic) |
| Intervention(s) | T-SPOT.TB alone, QFT-GIT alone, TST plus confirmatory T-SPOT.TB (if TST positive), and TST plus confirmatory QFT-GIT (if TST positive) |
| Comparator(s) | No screen |
| Outcome(s) | Cost per case of active TB avoided |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Primary care setting and UK |
| Study perspective | National health service (NHS) perspective |
| Time horizon | 20-year time horizon |
| Discount rate | 3.5% per annum for costs and benefits |
| Measurement of effectiveness | Cases of active TB |
| Measurement and valuation of preference based outcomes | Not applicable |
| Resource use and costs | Costs for screening LTBI with TST, IGRA, costs of treatment of LTBI and active TB, costs of treatment of adverse events |
| Currency, price date and conversion | UK £ sterling, 2010 |
| Model type | Decision tree model |
| Assumptions | A number of assumptions were made for which the authors acknowledged:-<br>1) Immigrants are screened for LTBI once at the start of the time horizon<br>2) Tuberculin skin test positivity is classified as per UK guidelines (≥6mm in BCG unvaccinated and ≥15mm in BCG vaccinated<br>3) All IGRA results are determinate and no repeat testing is required<br>4) The proportion of immigrants with HIV is reflective of the HIV prevalence in their country of origin<br>5) A proportion of immigrants with LTBI are infected by a resistant strain of Mycobacterium tuberculosis<br>6) A proportion of active tuberculosis cases are drug-resistant<br>7) Amongst those individuals identified with LTBI and treated with |

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| | chemoprophylaxis, a three month course of rifampicin and isoniazid is considered to have equivalent efficacy to six months of isoniazid<br>8) Individuals who commence chemoprophylaxis and subsequently develop drug-induced liver injury which does not resolve are assumed to only complete 4 weeks of therapy which affords no reduction in the risk of progressing from LTBI to active TB<br>9) No individuals who develop drug induced liver injury die due to this adverse effect<br>10) Equal proportions of HIV negative and positive immigrants develop drug-induced liver injury from chemoprophylaxis<br>11) Chemoprophylaxis will have no efficacy in those immigrants who have a resistant strain causing their LTBI<br>12) An individual with LTBI who has completed successful chemoprophylaxis is assumed to have cleared the infection with Mycobacterium tuberculosis and will not experience any further outcomes during the time course of the model (such as reinfection)<br>13) An individual who does not have LTBI on arrival in the UK does not become infected during the time-period considered by the model<br>14) Drug sensitive and drug resistant strains are assumed to be equally transmissible (in other words drug resistance does not result in any fitness cost)<br>15) There is no HIV acquisition within the cohort during the time horizon of the model<br>16) Data on the test performance of the IGRA was based on the most recent meta-analysis obtained from meta-analyses where sensitivity was calculated using culture-confirmed active TB as the reference standard whilst specificity was calculated from BCG-vaccinated individuals at low risk of infection<br>17) Point estimates for test sensitivity were assumed to be different for HIV positive individuals<br>18) All individuals diagnosed with drug-sensitive active tuberculosis are assumed to accept treatment for active TB and to complete the 6 month course of drugs<br>19) All individuals diagnosed with drug-resistant active tuberculosis are assumed to accept treatment for active TB and to complete the course of drugs |
| Analytical methods | Authors conducted one-way sensitivity analyses on key model input parameters to explore the impact on the results of the cost-effectiveness |
| **Results** | |
| Study parameters | HIV prevalence, drug-resistant tuberculosis, sensitivity and specificity of various screening tests, prevalence of LTBI and progression rate from LTBI to active tuberculosis disease |
| Incremental costs and outcomes | Base-case results of the cost-effectiveness showed that the screening strategy no port-of-entry chest x-ray and screening with one-step QFT-GIT was cost-effective with an ICER of 21,570 per case of TB avoided and the no port-of-entry chest x-ray and screening with one-step QFT-GIT was cost-effective, with an ICER of £31,870 per case of active TB avoided. These strategies were cost-effective in immigrants whose country of origin had an incidence of TB of 250/100,000 and 150/100,000, respectively |
| Characterising uncertainty | Results from the sensitivity analyses showed that varying some key model input parameters affected the ICER for each of the strategies, but the order of the cost-effectiveness results remained the same. The authors found that varying the diagnostic specificity of the different screening tests. Reducing the specificity of the screening strategies resulted in high ICERs. Additionally, changing the proportion of immigrants who commenced, and |

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| | adhered ti treated also had an impact of the results, making them less cost-effective. Furthermore, the estimates for ICERs were sensitive to changes in the costs of screening tests |
| **Discussion** | |
| Study findings | Using the decision analytical model, these authors demonstrated that screening of recently arrived immigrants from countries of origin with moderate (not defined) TB incidence is likely to be cost-effective by the use of one-step IGRA testing for LTBI |
| Limitations | There were some limitations to which the authors have acknowledged while undertaking this study. They highlighted that the sample size was relatively small and not all of the immigrants received the three tests. Additionally, other areas in the UK may have a greater number of immigrants compared to the areas that have been included in the study. Finally, in line with the UK guidelines, the HIV status of immigrants was not tested |
| Generalizability | The model structure used here may be helpful to show the cost-effectiveness between testing strategies for LTBI in this population. The authors have stated assumptions made in the model, and have used information relevant to the setting in which the analyses were undertaken |
| **Other** | |
| Source of funding | This study was conducted at St. Mary's Hospital, Imperial College Healthcare NHS Trust which is supported by the NIHR Biomedical Research Centre funding scheme. Westminster Primary Care Trust provided funding for this project |
| Conflicts of interest | AL is inventor for patents underpinning T-cell-based diagnosis. The ESAT-6/CFP-10 ELISpot was commercialised by an Oxford University spin-out company (Oxford Immunotec, Abingdon, UK) in which Oxford University and Professor Lalvani have a minority share of equity. All other authors have no conflict of interest |
| Comments | Drug induced liver injury as a result of treatment for active TB/LTBI. The authors suggested that this may be a rare occurrence in this population. However, they have not included other adverse events such as hepatitis C<br><br>Authors have not conducted any probabilistic sensitivity analysis<br><br>The illustrative modelling structure was presented in a supplementary web-appendix, but unfortunately, these figures were illegible |
| **Authors conclusion** | |
| The authors concluded that immigrant screening may be cost-effective in the UK by removing the mandatory chest x-ray on arrival of immigrants and to screen for LTBI with an IGRA. They suggested that this screening should be undertaken in recently arrived people from countries where the incidence is greater than 250, 150 or 40 cases per 100,000 of active TB | |
| **Reviewer's conclusion** | |
| These authors evaluated, with the aid of a decision analytical model, the cost-effectiveness of various screening strategies for LTBI. They have collected data to inform on the performance (sensitivity and specificity) of these test based on immigrants from three areas in the UK. The methods used to undertake these analyses seem to be robust, but due to the illegibility of the modelling structure, it was difficult to appraise the model | |

**Date:** 22nd August, 2014
**Name of first reviewer:** Peter Auguste
**Name of second reviewer:** Alexander Tsertsvadze

| **Study details** | |
|---|---|
| Study title | Cost-effectiveness of quantiferon testing before indication of biological therapy in inflammatory bowel disease |
| First author | A Swaminath |
| Co-authors | N Bhadelia and C Wang |
| Source of publication Journal yy;vol(issue):pp | Inflammatory bowel diseases 2013;19(11):2444-2449 |
| Language | English language |
| Publication type | Journal article |
| **Baseline characteristics** | |
| Population | Immunosuppression (inflammatory bowel disease before anti-TNF-α): Hypothetical cohort of people with moderate to severe active Crohn's disease currently being treated with immunomodulators or prednisone |
| Intervention(s) | QuantiFERON- Gold (QFT-G) |
| Comparator(s) | Tuberculin skin test (TST) |
| Outcome(s) | Cost per false negative cases of LTBI avoided, cost per TB deaths avoided, cost per reactivation TB avoided (this can be derived from the information provided) |
| Study design | Cost-effectiveness analysis |
| **Methods** | |
| Setting and location | Not reported |
| Study perspective | Health care payer |
| Time horizon | One-year time horizon |
| Discount rate | Not applicable |
| Measurement of effectiveness | Reduction of reactivation of tuberculosis (TB), death from reactivation of TB, false positive test results |
| Measurement and valuation of preference based outcomes | Not applicable |
| Resource use and costs | Costs for screening LTBI with QFT-G, TST, costs of treatment of LTBI and , costs of treatment of adverse events, survival of reactivation and death from reactivation |
| Currency, price date and conversion | US$, price year unknown |
| Model type | Decision tree structure |
| Assumptions | 1) If the model showed superiority of testing within the first year, benefits will increase over longer periods<br>2) An indeterminate test result would lead to a second test immediately<br>3) A second indeterminate result would lead to a consultation rather than treatment with anti-TNF-α<br>4) Some outcomes were not modelled because they were considered rare: secondary cases of TB from reactivation, reactivation TB despite successful treatment with INH, outcomes resulting from indeterminate tests or non-adherence with LTBI prophylaxis |

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| | 5) The authors suggested that multidrug resistance is rare in the USA, hence this was not modelled |
| Analytical methods | Authors conducted one-way sensitivity analysis by varying key model input parameters to explore the uncertainty in these parameter estimates. Two-way sensitivity analyses were also conducted and the results were presented in an online supplement of the paper |
| **Results** | |
| Study parameters | Estimates of the prevalence of true LTBI in the USA, sensitivity and specificity for QFT-G and TST, anergy TST in immunosuppressed people, reactivation TB with biological exposure, probability of death from reactivation, side-effect (hepatitis) of INH treatment, probability of surviving from hepatitis, costs (QFT-G, TST, LTBI treatment, survival of reactivation and death from reactivation) |
| Incremental costs and outcomes | In a cohort of 1000 immunosuppressed IBD people being screened for LTBI, the QFT-G strategy was cheaper than the TST strategy, $84, 850 compared with $156, 370, respectively. The use of QFT-G would avoid 30 false-negative cases, 4.92 TB reactivations and 1.4 deaths compared with TST |
| Characterising uncertainty | From the sensitivity analysis, the QFT-G strategy continued to dominate the TST strategy by varying key model input parameters. The authors suggested that the results would change at extreme values, but these variations are unlikely to be unrealistic in reality |
| **Discussion** | |
| Study findings | The base-case results showed that QFT-G dominated the TST strategy. QFT-G was least costly, and produced greater benefits |
| Limitations | 1) The accuracy of the model structure to reflect what happens in reality is based on the model input parameters used.<br>2) There is no gold standard for the diagnosis of LTBI.<br>3) The costs used in the model are specific to the USA |
| Generalizability | The generalizability of these results may be compromised here because of the lack of reporting on the setting and location and not presenting the cost-year for which these costs represent |
| **Other** | |
| Source of funding | Dr. Wang is partially funded by NIH grant KM1 CA156709-01 |
| Conflicts of interest | No conflicts of interest declared |
| Comments | The authors here have presented a model that illustrates the testing and treatment pathway that someone with IBD will undergo if being screened for LTBI. The model demonstrates that the QFT strategy is cheaper and offers greater benefits in this patient population. However, these authors have not suggested the year for which these costs represent, hence making these results less generalizable |
| **Authors conclusion** | |
| Based on the results of the cost-effectiveness analysis, they concluded that the QFT-G strategy dominated TST in this population, and suggested that QFT-G should be the choice of testing strategy for identifying LTBI in people who are immunosuppressed | |
| **Reviewer's conclusion** | |
| This model adds to the existing literature on the diagnosis of LTBI in an immunosuppressed population. The model is subject to some limitations to which the authors acknowledged. However, the generalizability of the model is somewhat compromised by no suggesting the study setting within which the analyses were conducted, and the cost year was not mentioned. Furthermore, these authors have not stated in this paper the index used to | |

inflate the cost information that was obtained from published sources