

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Support Programs for Tuberculosis Treatment: Clinical Utility and Guidelines

Service Line: Rapid Response Service
Version: 1.0
Publication Date: August 20, 2020
Report Length: 12 Pages

Authors: Shannon Hill, Holly Gunn, Lory Picheca

Cite As: *Support Programs for Tuberculosis Treatment: Clinical Utility and Guidelines*. Ottawa: CADTH; 2020 August. (CADTH rapid response report: summary of abstracts).

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to requests@cadth.ca

Research Questions

1. What is the clinical utility of support programs for those who require assistance to complete their tuberculosis treatment?
2. What are the evidence-based guidelines regarding the use of support programs in those who require assistance completing their tuberculosis treatment?

Key Findings

Three systematic reviews, two with meta-analyses, one randomized controlled trial, and nine non-randomized studies were identified regarding the clinical utility of support programs for those who require assistance to complete their tuberculosis treatment. Two evidence-based guidelines were identified regarding the use of support programs in those who require assistance completing their tuberculosis treatment.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. The main search concepts were tuberculosis and social support. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, any types of clinical trials or observational studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and August 5, 2020. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available, and relevant recommendations were summarized.

This report is a component of a larger CADTH Condition Level Review on tuberculosis. A condition level review is an assessment that incorporates all aspects of a condition, from prevention, detection, treatment, and management. For more information on CADTH’s Condition Level Review of tuberculosis, please visit the project page (<https://www.cadth.ca/tuberculosis>).

Table 1: Selection Criteria

Population	Individuals with tuberculosis (TB) who require support to complete TB treatment
Intervention	Support programs that provide assistance to improve TB treatment completion (e.g., incentive programs, provision of resources, education programs)

Comparator	Q1. Alternative support program No support programs Q2. Not applicable
Outcomes	Q1. Clinical utility (e.g., compliance with TB treatments, treatment completion, active TB disease, health-related quality of life) Q2. Recommendations regarding the use of support programs to improve TB treatment compliance
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines

Results

Three systematic reviews,¹⁻³ two with meta-analyses,^{1,2} one randomized controlled trial,⁴ and nine non-randomized studies⁵⁻¹³ were identified regarding the clinical utility of support programs for those who require assistance to complete their tuberculosis treatment. Two evidence-based guidelines^{14,15} were identified regarding the use of support programs in those who require assistance completing their tuberculosis treatment. No relevant health technology assessments were identified in the literature.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

Overall Summary of Findings

Three systematic reviews,¹⁻³ two with meta-analyses,^{1,2} one randomized controlled trial,⁴ and nine non-randomized studies⁵⁻¹³ were identified regarding the clinical utility of support programs for those who require assistance to complete their tuberculosis treatment. The authors of the first two systematic reviews^{1,2} found results demonstrating positive clinical utility of support programs on tuberculosis treatment, whereas the third systematic review³ found that there was insufficient evidence to determine the long-term effects of support programs on tuberculosis treatment and only found evidence on short-term effects. The authors of the randomized controlled trial⁴ found that socioeconomic support programs increase tuberculosis treatment success. The authors of eight of the non-randomized studies^{5-7,9-13} found an increase in treatment completion and success rates when support programs were present. The authors of one of the non-randomized studies⁸ were unable to find significant results to determine the effect of the support program on treatment outcomes. Two evidence-based guidelines, from the National Institute for Health and Care Excellence (NICE)¹⁴ and the European Centre for Disease Prevention and Control¹⁵, were identified and recommended the use of support programs and/or incentives for those who require assistance in completing tuberculosis treatment. A detailed summary of the identified studies can be found in Table 2, and a summary of the identified evidence-based guideline can be found in Table 3.

Table 2: Summary of Included Studies

First Author, Year	Study Characteristics	Intervention	Comparator(s)	Relevant Outcomes Assessed	Author's Conclusions
Systematic Reviews					
Muller, 2018¹	<p>Study Design: Systematic review & meta-analysis</p> <p>Population: Patients receiving anti-tuberculosis treatment</p> <p>N = 22 relevant studies</p>	Interventions to improve adherence to anti-tuberculosis treatment (financial incentives, food incentives and/or patient education and counselling)	NR	Cure rate, default and mortality rate	Significant increases were observed in cure rates after patient counselling and education. The authors also noted a decrease in default rate after financial incentives and patient education and counselling. No significant reduction in mortality rates was found.
Richterman, 2018²	<p>Study design: Systematic review & meta-analysis</p> <p>Population: Active tuberculosis patients in low- and middle-income countries</p> <p>N = 8 relevant studies</p>	Cash transfer interventions	Control group	Positive clinical outcome (treatment success, treatment completion, or microbiologic cure)	Authors found that all studies demonstrated better clinical outcomes for intervention groups than control groups.
Lutge, 2015³	<p>Study design: Systematic review</p> <p>Population: Patients undergoing diagnostic testing, or receiving prophylactic or curative therapy for tuberculosis</p> <p>N = 12 relevant studies</p>	Material incentives and enablers	NR	Treatment completion	The authors found mixed results and concluded that material incentives and enablers may have some positive short-term effects particularly for marginal populations (drug users, recently released prisoners, homeless, etc.) but there was insufficient evidence to determine the long-term effects

First Author, Year	Study Characteristics	Intervention	Comparator(s)	Relevant Outcomes Assessed	Author's Conclusions
					on adherence to treatment.
Randomized Controlled Trials					
Wingfield, 2017⁴	<p>Study Design: RCT</p> <p>Population: Patients being treated for tuberculosis and their household contacts</p> <p>N = 282 Households</p>	Current standard of care plus socioeconomic support including conditional cash transfers, community meetings and household visits	Current standard of care for tuberculosis	Rate of treatment cure or treatment completion	Significant effects were found supporting socioeconomic support programs in increasing tuberculosis treatment success
Non-Randomized Studies					
Bhatt, 2019⁵	<p>Study Design: Retrospective Cohort</p> <p>Population: Patients who started drug resistant tuberculosis treatment</p> <p>N = 123</p>	An integrated support package for at least three months	Control group	Treatment success rate, incidence of death, and treatment failure rate.	Significant effects were found for higher treatment success rates and failure rates in the supported group. Significant association was found for support duration and a lower incidence of death.
D JC, 2019⁶	<p>Study Design: Quasi experimental</p> <p>Population: Patients with tuberculosis in Brazil</p> <p>N = 2167</p>	Brazil's Bolsa Familia Programme – conditional cash transfer	Control group	Treatment success rate	Authors found that the patients receiving the Bolsa Familia Programme had significantly improved treatment success rates.
Priedeman, 2018⁷	<p>Study design: Retrospective cohort</p> <p>Population: Tuberculosis patients at risk of defaulting treatment</p> <p>N = NR</p>	Social support	Control group	Treatment success rate and treatment default rate	The authors found that the intervention group had a reduced probability of defaulting and improved treatment success rates. Improvement was most significant

First Author, Year	Study Characteristics	Intervention	Comparator(s)	Relevant Outcomes Assessed	Author's Conclusions
					amongst the high-risk cohorts.
Wickett, 2018⁸	<p>Study Design: Retrospective Cohort Study</p> <p>Population: Tuberculosis patients</p> <p>N = NR</p>	A community health worker programme containing food support, reimbursement of transport and social assistance	Patient outcomes before the community health worker programme	Cure rates, treatment completion rates, and death rates.	No significant results were found for any of the outcomes measured before and after the intervention.
Ukwaja, 2017⁹	<p>Study Design: Prospective, non-randomized study</p> <p>Population: Tuberculosis patients in a secondary care hospital</p> <p>N = 294</p>	Financial incentives	Control group	Treatment success rate, deaths, and treatment failure rates.	Authors found a significant effect for the influence of financial incentives on improving treatment success. The authors found no difference in death or treatment failure rates between the intervention and control group.
Samuel, 2016¹⁰	<p>Study Design: Retrospective Cohort Study</p> <p>Population: Tuberculosis patients living below the poverty line</p> <p>N = 173</p>	Nutritional support	Control group	Unsuccessful treatment outcome: loss-to-follow-up, treatment failure, death	Authors found that the patients receiving nutritional support had a 50% reduced risk of unsuccessful treatment outcomes.
Torrens, 2016¹¹	<p>Study Design: Retrospective cohort study</p> <p>Population: Patients newly diagnosed with tuberculosis</p> <p>N = 7255</p>	Patients receiving the Bolsa Familia Programme conditional cash transfer	Control group	Tuberculosis cure rate	The authors found evidence to suggest that conditional cash transfer programs can improve tuberculosis cure rates.
Chua, 2015¹²	<p>Study Design: Descriptive study</p> <p>Population: Tuberculosis</p>	'DOT & Shop': Distribution of grocery store vouchers to low-income patients	Before the implementation of the intervention	Treatment completion rates	Authors found the 'DOT & Shop' program to be effective in increasing

First Author, Year	Study Characteristics	Intervention	Comparator(s)	Relevant Outcomes Assessed	Author's Conclusions
	patients in Singapore N = 883	with tuberculosis who have been adherent to directly observed therapy at clinic visits.			treatment completion rates.
Ciobanu, 2014 ¹³	Study Design: Retrospective cohort design Population: Tuberculosis patients at health facilities registered for treatment N = 4387	Various incentives (cash, food vouchers, travel reimbursement) provided to tuberculosis patients	Patients at tuberculosis health facilities before incentives were introduced	Treatment success, unsuccessful outcomes, loss to follow-up, death, treatment failure	Authors found that incentives were associated with an overall reduction in unsuccessful outcomes of 50%. They found that patients with incentives had significantly higher treatment success.

DOT = directly observed therapy; N = number; NR = not reported; RCT = randomized controlled trial.

Table 3: Summary of Relevant Recommendation in Included Guideline

Summary of Guideline Recommendations	
Tuberculosis NICE Guidelines, 2016 ¹⁴	
Strategies to encourage people to follow their treatment plan: <ul style="list-style-type: none"> • Health education counselling and patient-centered interviews (p.59) • Tailored health education booklets from quality sources (p.59) • Social and psychological support (including cultural case management and broader social support) (p.59) • Incentives and enablers to help people follow their treatment regimen (p.59) 	
Guidance on tuberculosis control in vulnerable and hard-to-reach populations, 2016 ¹⁵	
Enhanced case management interventions: <ul style="list-style-type: none"> • Material incentives and enablers should be considered for marginal populations (eg. Drug users, homeless, recently released prisoners) in combination with enhanced case management in order to promote clinic attendance and treatment adherence (p.15) 	

NICE = National Institute for Health and Care Excellence.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Müller AM, Osorio CS, Silva DR, Sbruzzi G, de Tarso P, Dalcin R. Interventions to improve adherence to tuberculosis treatment: systematic review and meta-analysis. *Int J Tuberc Lung Dis*. 2018 07 01;22(7):731-740.
[PubMed: PM29914598](#)
2. Richterman A, Steer-Massaró J, Jarolimova J, Luong Nguyen LB, Werdenberg J, Ivers LC. Cash interventions to improve clinical outcomes for pulmonary tuberculosis: systematic review and meta-analysis. *Bull World Health Organ*. 2018 Jul 01;96(7):471-483.
[PubMed: PM29962550](#)
3. Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. *Cochrane Database Syst Rev*. 2015 Sep 03(9):CD007952.
[PubMed: PM26333525](#)

Randomized Controlled Trials

4. Wingfield T, Tovar MA, Huff D, et al. A randomized controlled study of socioeconomic support to enhance tuberculosis prevention and treatment, Peru. *Bull World Health Organ*. 2017 Apr 01;95(4):270-280.
[PubMed: PM28479622](#)

Non-Randomized Studies

5. Bhatt R, Chopra K, Vashisht R. Impact of integrated psycho-socio-economic support on treatment outcome in drug resistant tuberculosis - A retrospective cohort study. *Indian J Tuberc*. 2019 Jan;66(1):105-110.
[PubMed: PM30797265](#)
6. Carter DJ, Daniel R, Torrens AW, et al. The impact of a cash transfer programme on tuberculosis treatment success rate: a quasi-experimental study in Brazil. *BMJ Glob Health*. 2019;4(1):e001029.
[PubMed: PM30740248](#)
7. Priedeman Skiles M, Curtis SL, Angeles G, Mullen S, Senik T. Evaluating the impact of social support services on tuberculosis treatment default in Ukraine. *PLoS One*. 2018;13(8):e0199513.
[PubMed: PM30092037](#)
8. Wickett E, Peralta-Santos A, Beste J, et al. Treatment outcomes of TB-infected individuals attending public sector primary care clinics in rural Liberia from 2015 to 2017: a retrospective cohort study. *Trop Med Int Health*. 2018 05;23(5):549-557.
[PubMed: PM29524302](#)

9. Ukwaja KN, Alobu I, Gidado M, Onazi O, Oshi DC. Economic support intervention improves tuberculosis treatment outcomes in rural Nigeria. *Int J Tuberc Lung Dis*. 2017 05 01;21(5):564-570.
[PubMed: PM28399972](#)
10. Samuel B, Volkmann T, Cornelius S, et al. Relationship between Nutritional Support and Tuberculosis Treatment Outcomes in West Bengal, India. *J Tuberc Res*. 2016 Dec;4(4):213-219.
[PubMed: PM28042591](#)
11. Torrens AW, Rasella D, Boccia D, et al. Effectiveness of a conditional cash transfer programme on TB cure rate: a retrospective cohort study in Brazil. *Trans R Soc Trop Med Hyg*. 2016 Mar;110(3):199-206.
[PubMed: PM26884501](#)
12. Chua AP, Lim LK, Ng H, Chee CB, Wang YT. Outcome of a grocery voucher incentive scheme for low-income tuberculosis patients on directly observed therapy in Singapore. *Singapore Med J*. 2015 May;56(5):274-279.
[PubMed: PM25788246](#)
13. Ciobanu A, Domete L, Soltan V, et al. Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova? *Public Health Action*. 2014 Oct 21;4(Suppl 2):S59-63.
[PubMed: PM26393100](#)

Guidelines and Recommendations

14. National Institute for Health and Care Excellence. Tuberculosis. (*NICE guideline NG33*). 2016:
<https://www.nice.org.uk/guidance/ng33/resources/tuberculosis-pdf-1837390683589>
See: 1.7.2 Other strategies to encourage people to follow their treatment plan, p.59
15. European Centre for Disease Prevention and Control. Guidance on tuberculosis control in vulnerable and hard-to-reach populations. Stockholm (SE): ECDC; 2016.
<https://www.ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/TB-guidance-interventions-vulnerable-groups.pdf>
See: Incentives and enablers, p.15

Appendix — Further Information

Previous CADTH Reports

16. CADTH. Treatment of Tuberculosis: A Review of Guidelines. March 6, 2020
<https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1237%20TB%20treatment%20guidelines%20Final.pdf>

Overview of Systematic Reviews

Alternative Intervention

17. Wiysonge CS, Paulsen E, Lewin S, et al. Financial arrangements for health systems in low-income countries: an overview of systematic reviews. *Cochrane Database Syst Rev.* 2017 09 11;9:CD011084.
[PubMed: PM28891235](#)

Randomized Controlled Trials

Clinical Utility Outcomes Unclear

18. Benzekri NA, Sambou JF, Tamba IT, et al. Nutrition support for HIV-TB co-infected adults in Senegal, West Africa: A randomized pilot implementation study. *PLoS ONE [Electronic Resource]*. 2019;14(7):e0219118.
[PubMed: PM31318879](#)

Non-Randomized Study.

Alternative Comparator

19. Mansour O, Masini EO, Kim BJ, Kamene M, Githiomi MM, Hanson CL. Impact of a national nutritional support programme on loss to follow-up after tuberculosis diagnosis in Kenya. *Int J Tuberc Lung Dis.* 2018 06 01;22(6):649-654.
[PubMed: PM29862949](#)

Additional References

20. Hargreaves S, Rustage K, Nellums LB, Powis J, Milburn J, Severoni S et al. What constitutes an effective and efficient package of services for the prevention, diagnosis, treatment and care of tuberculosis among refugees and migrants in the WHO European Region? Copenhagen: WHO Regional Office for Europe; 2018 (Health Evidence Network (HEN) synthesis report 56).
https://www.euro.who.int/_data/assets/pdf_file/0003/371145/who-hen-report-56.pdf?ua=1
See: Fig. 7. The minimum package for cross-border care for TB in migrants, p.27
21. A people-centred model of tuberculosis care. A blueprint for eastern European and central Asian countries, first edition. World Health Organization 2017
https://www.euro.who.int/_data/assets/pdf_file/0004/342373/TB_Content_WHO_PRO_eng_final.pdf
See: Treatment and Support, p.14
22. Canadian Tuberculosis Standards 7th Edition Chapter 5: Treatment of Tuberculosis Disease. 2014

<https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/tbpc-latb/pubs/tb-canada-7/assets/pdf/tb-standards-tb-normes-ch5-eng.pdf>

See: Achieving completion of therapy and direct observed treatment, p.15

23. Canadian Tuberculosis Standards 7th Edition. Chapter 14: Tuberculosis Prevention and Care in First Nations, Inuit and Métis Peoples. 2014

<https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/tbpc-latb/pubs/tb-canada-7/assets/pdf/tb-standards-tb-normes-ch14-eng.pdf>

See: Adherence to TB medications in Aboriginal populations, p.10

24. Lessons Learned from Best Practices in Psycho-Socio-Economic Support for Tuberculosis Patients. The Global Health Bureau, Office of Health, Infectious Disease and Nutrition (HIDN), US Agency for International Development. November 2014.

https://www.msh.org/sites/default/files/tbcare_report_best_practices_pyscho-socio-economic_support_for_tb_patients_nov_2014.pdf