April 2017 – SUPPORT Summary of a systematic review

Do material incentives improve patient adherence in tuberculosis?

Adherence to treatment for tuberculosis (TB) is frequently sub-optimal. However, good adherence is important for successful treatment and to minimize the risk of drug resistance. Adherence is also essential for different components of TB prophylaxis. Material incentives for patients to encourage them to take their treatment as prescribed, or to assist them in overcoming financial barriers to treatment, have been suggested as interventions to improve TB treatment adherence.

Key messages

- **Sustained material incentives may lead to little or no difference in cure or completion of treatment for *active TB*, compared to no incentive**
- **It is not clear if sustained material incentives improve completion of *TB prophylaxis*, compared to no incentive, because findings varied across studies**
- **A single, once only incentive may increase the number of people who return to a clinic for *reading of their tuberculin skin test*, compared to no incentive**
- **A single, once only incentive probably increases the number of people who return to a clinic *to start or continue TB prophylaxis*, compared to no incentive**
- **Compared to a non-cash incentive, cash incentives may slightly increase the number of people who return to a clinic for reading of their tuberculin skin test and may increase the number of people who complete TB prophylaxis**
- **Compared to counselling or education interventions, material incentives may increase the number of people who return to a clinic for reading of their tuberculin skin test**
- **Compared to counselling or education interventions, material incentives may lead to little or no difference in the number of people who return to a clinic to start or continue TB prophylaxis or in the number of people who complete TB prophylaxis**
- **Higher cash incentives may slightly improve the number of people who return to a clinic for reading of their tuberculin skin test, compared to lower cash incentives**

Who is this summary for?

People making decisions concerning anti-tuberculosis treatment implementation.

This summary includes:

- **Key findings** from research based on a systematic review
- **Considerations about the relevance of this research** for low-income countries

Not included:

- Recommendations
- Additional evidence not included in the systematic review
- Detailed descriptions of interventions or their implementation

This summary is based on the following systematic review:

Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD007952.

What is a systematic review?

A summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise the relevant research, and to collect and analyse data from the included studies

SUPPORT was an international project to support the use of policy relevant reviews and trials to inform decisions about maternal and child health in low- and middle-income countries, funded by the European Commission (FP6) and the Canadian Institutes of Health Research.

Glossary of terms used in this report: www.supportsummaries.org/glossary-of-terms

Background references on this topic: See back page

Background

In many settings, people's adherence to drug treatment for TB is frequently sub-optimal and many people also fail to return to a clinic to collect their TB test results, undermining global efforts to control the disease. Good adherence to treatment is important for successful treatment and also to minimize the risk of infection among contact persons and to reduce the development of treatment resistance. Material incentives, such as cash or vouchers, may both act as a reward for desired behaviour and help to overcome economic barriers to treatment adherence. Offering material incentives to people diagnosed with TB has therefore been suggested as an approach to improving TB treatment outcomes. However, such approaches may also entail risks, including encouraging unintended behaviours, such as people not taking medication in order to remain sick and continue to collect rewards.

How this summary was prepared

After searching widely for systematic reviews that can help inform decisions about health systems, we have selected ones that provide information that is relevant to low-income countries. The methods used to assess the reliability of the review and to make judgements about its relevance are described here: www.supportsummaries.org/how-support-summaries-are-prepared/

Knowing what's not known is important

A reliable review might not find any studies from low-income countries or might not find any well-designed studies. Although that is disappointing, it is important to know what is not known as well as what is known.

A lack of evidence does not mean a lack of effects. It means the effects are uncertain. When there is a lack of evidence, consideration should be given to monitoring and evaluating the effects of the intervention, if it is used.

About the systematic review underlying this summary

Review objective: To evaluate the effects of material incentives and enablers given to people undergoing diagnostic testing for TB, or receiving drug therapy to prevent or cure TB

	What the review authors searched for	What the review authors found
Study designs & Interventions	Randomised trials of any form of material inducement to return for TB test results, or adhere to or complete anti-TB preventive or curative treatment	12 randomised trials were included, assessing incentives for adherence to different stages of TB management: returning for reading of tuberculin skin test results (2 studies); clinic attendance for initiation of preventive therapy (1 study); clinic attendance for continuation of preventive therapy (2 studies); adherence to preventive treatment (5 studies); adherence to treatment for active TB (2 studies). The incentives used included cash, vouchers that could be redeemed for various products and food.
Participants	- Patients receiving curative treatment for TB - Patients receiving preventative therapy for TB - Patients suspected of TB who are undergoing, and collecting results of, diagnostic tests	Adolescents (11-19 years)(1 study); injection drug or cocaine users (4 studies); homeless or marginally housed adults (3 studies); prisoners (2 studies); and studies on the general adult population (2 studies)
Settings	No restrictions	South Africa (1 study), Timor Leste (1 study), USA (10 studies)
Outcomes	*For treatment of active TB*: cure and/or completion of treatment and/or successful treatment *For prophylaxis*: cases of active TB; completion of prophylactic treatment *For diagnostics*: number returning to collect test results Also adverse events and costs	- Return for tuberculin skin test reading - Completion of TB prophylaxis - Return to clinic for continuation of treatment - Successful TB treatment and / or completion of treatment - Time needed to track participants who missed appointments
Date of most recent search: June 2015		
Limitations: This is a well-conducted systematic review with only minor limitations.		

Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD007952.

Summary of findings

The review identified 12 studies, most of which were conducted among specific subgroups including teenagers, drug users, homeless persons and prisoners. Most of the studies focused on incentives to encourage people to return for reading of tuberculin skin testing and on attendance for or adherence to TB preventive therapy. Only two studies evaluated incentives for adherence to treatment for active TB.

1) Sustained material incentives for completion of treatment for active TB

➔ **Sustained material incentives may lead to little or no difference in cure or completion of treatment for active TB, compared to no incentive. The certainty of this evidence is low.**

About the certainty of the evidence (GRADE) *

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This is sometimes referred to as 'quality of evidence' or 'confidence in the estimate'.

† Substantially different = a large enough difference that it might affect a decision

See last page for more information.

Sustained material incentives compared to routine care for completion of treatment for active TB

People	Recipients of care from TB control services
Settings	South Africa and Timor Leste
Intervention	Material incentives, such as cash or grocery vouchers, sustained across the duration of treatment
Comparison	Routine care

Outcomes	Absolute effect*		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	Without incentives (routine care)	**With incentives**			
Cure or completion of treatment for active TB	721 per 1000	750 per 1000 (622 to 1000)	RR 1.04 (0.97 to 1.13)	4356 (2 studies)	⊕⊕◯◯ Low

Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)
* The risk WITHOUT the intervention is based on the control group of each study. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

2) Material incentives for TB prophylaxis

➔ **A single, once only incentive may increase the number of people who return to a clinic for reading of their tuberculin skin test, compared to no incentive. The certainty of this evidence is low.**

➔ **A single, once only incentive probably increases the number of people who return to a clinic to start or continue TB prophylaxis, compared to no incentive. The certainty of this evidence is moderate.**

➔ **It is not clear if sustained material incentives improve completion of TB prophylaxis, compared to no incentive, because findings varied across studies. The certainty of this evidence is low.**

Material incentives compared to routine care for TB prophylaxis

People Recipients of care from TB control services
Settings USA
Intervention Material incentives, such as cash or grocery vouchers, on a once only basis (for tuberculin skin test reading and returning to a clinic to start or continue TB prophylaxis) or sustained across the duration of treatment (for completion of TB prophylaxis)
Comparison Routine care

Outcomes	Absolute effect* / Impact		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	Without material incentives (routine care)	**With material incentives**			
Return to clinic for tuberculin skin test reading	441 per 1000	953 per 1000 (622 to 1000)	RR 2.16 (1.41 to 3.29)	1371 (2 studies)	⊕⊕◯◯ Low
Return to clinic to start or continue TB prophylaxis	249 per 1000	393 per 1000 (316 to 488)	RR 1.58 (1.27 to 1.96)	595 (3 studies)	⊕⊕⊕◯ Moderate
Completion of TB prophylaxis	Findings varied: 1 study reported that there may be improvement in completion of prophylaxis while 2 studies reported that incentives may make little or no difference		Data not pooled	869 (3 studies)	⊕⊕◯◯ Low

Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)
* The risk WITHOUT the intervention is based on the control group of each study. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

3) Cash versus non-cash incentives for TB prophylaxis

➔ **Compared to a non-cash incentive, cash incentives may slightly increase the number of people who return to a clinic for reading of their tuberculin skin test. The certainty of this evidence is low.**

➔ **Compared to a non-cash incentive, cash incentives may increase the number of people who complete TB prophylaxis. The certainty of this evidence is low.**

Cash versus non-cash incentives for TB prophylaxis

People People at high risk of developing TB
Settings USA
Intervention Cash incentive
Comparison Non-cash incentive, including grocery store coupons, phone cards and bus tokens

Outcomes	Absolute effect*		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	With non-cash incentive	**With cash incentive**			
Return to clinic for tuberculin skin test reading	841 per 1000	950 per 1000 (900 to 992)	RR 1.13 (1.07 to 1.19)	652 (1 study)	⨁⨁◯◯ Low
Completion of TB prophylaxis	638 per 1000	804 per 1000 (651 to 995)	RR 1.26 (1.02 to 1.56)	141 (1 study)	⨁⨁◯◯ Low

Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)
* The risk WITHOUT the intervention is based on the control group of each study. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

4) Material incentives compared to other interventions for TB prophylaxis

➔ **Compared to counselling or education interventions, material incentives may increase the number of people who return to a clinic for reading of their tuberculin skin test. The certainty of this evidence is low.**

➔ **Compared to counselling or education interventions, material incentives may lead to little or no difference in the number of people who return to a clinic to start or continue TB prophylaxis. The certainty of this evidence is low.**

➔ **Compared to counselling or education interventions, material incentives may lead to little or no difference in the number of people who complete TB prophylaxis. The certainty of this evidence is low.**

Material incentives compared to other interventions for TB prophylaxis

People People at high risk of developing TB. The studies included homeless people, people recently released from prison, drug users and adolescents
Settings USA
Intervention Incentive
Comparison Counselling or education session

Outcomes	Absolute effect*		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	With counselling or education session (non-incentive intervention)	**With incentive**			
Return to clinic for tuberculin skin test reading	429 per 1000	927 per 1000 (669 to 1000)	RR 2.16 (1.56 to 3.00)	1366 (2 studies)	⊕⊕◯◯ Low
Return to clinic to start or continue TB prophylaxis	381 per 1000	419 per 1000 (351 to 499)	RR 1.10 (0.92 to 1.31)	535 (2 studies)	⊕⊕◯◯ Low
Completion of TB prophylaxis	444 per 1000	462 per 1000 (262 to 813)	RR 1.04 (0.59 to 1.83)	837 (3 studies)	⊕⊕◯◯ Low

Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)
* The risk WITHOUT the intervention is based on the control group of each study. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

5) Different levels of material incentives

➔ **Higher cash incentives may slightly improve the number of people who return to a clinic for reading of their tuberculin skin test, compared to lower cash incentives. The certainty of this evidence is low.**

Different values of cash incentives for improving patient return for tuberculin skin test reading

People Drug users at high risk of developing TB
Settings USA
Intervention Higher cash value ($10.00)
Comparison Lower cash value ($5.00)

Outcomes	Absolute effect*		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)
	With lower cash value incentive ($5.00)	**With higher cash value incentive ($10.00)**			
Return to clinic for tuberculin skin test reading	858 per 1000	927 per 1000 (867 to 995)	RR 1.08 (1.01 to 1.16)	404 (1 study)	⊕⊕◯◯ Low

Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)
* The risk WITHOUT the intervention is based on the control group of each study. The corresponding risk WITH the intervention (and the 95% confidence interval for the difference) is based on the overall relative effect (and its 95% confidence interval).

Relevance of the review for low-income countries

➔ Findings	▷ Interpretation*
APPLICABILITY	
➔ Most studies were conducted in the USA, with only two conducted in low- and middle-income countries **➔ Most studies were conducted with specific subgroups, such as homeless people, prisoners or drug users**	*▷ The findings need to be applied with caution in low-income countries given the structural and qualitative differences in health systems, healthcare provision, resources and healthcare seeking behaviour* *▷ Most of the included studies focused on specific subgroups of people, such as injection drug users. The applicability of the findings to the general population is therefore not clear*
EQUITY	
➔ The review did not discuss the impacts of the intervention on equity	*▷ Material incentives could improve equity by reducing the poverty-related impacts of TB through assisting people with TB with the costs associated with diagnosis, prophylaxis and treatment and encouraging poorer people to seek care. However, implementers need to ensure that incentives are seen as helpful and can be accessed by disadvantaged groups*
ECONOMIC CONSIDERATIONS	
➔ The review found very limited evidence on the costs of providing incentives and no evidence on cost-effectiveness	*▷ Implementing material incentives on a large scale for adherence to TB treatment or prophylaxis would require considerable resources, including the costs of the incentives and the costs of putting in place mechanisms to distribute them appropriately. Such resources may not be readily available in many LIC settings* *▷ The risk of undesirable effects of incentives, such as leakage to groups not eligible to receive them, could be higher in low-income countries where incentives are likely to be relatively more valuable*
MONITORING & EVALUATION	
➔ The review found very limited evidence on the effects of material incentives on cure or completion of treatment for active TB **➔ For tuberculin skin testing and TB prophylaxis, the certainty of the evidence in relation to incentives is moderate or low** **➔ There is little evidence on harms, unintended behaviours, costs and cost-effectiveness** **➔ The evidence is generally of low certainty, as most of the studies were not conducted with specific subgroups rather than with general adult populations**	*▷ Rigorous studies are needed in general adult populations on the effects of material incentives on cure rates or completion of treatment for active TB, on completion of TB prophylaxis and on the number of people who return to a clinic for reading of their tuberculin skin test* *▷ These studies should also examine the costs and cost-effectiveness of incentives, particularly for key target groups in low-income countries* *▷ Evaluations should also consider possible adverse effects of incentives as well as the role of HIV/AIDs and other chronic conditions and socio-economic status in modifying the effects of incentives*

*Judgements made by the authors of this summary, not necessarily those of the review authors, based on the findings of the review and consultation with researchers and policymakers in low-income countries. For additional details about how these judgements were made see: www.supportsummaries.org/methods

Additional information

Related literature

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Conflict of interest

None declared. For details, see: www.support-collaboration.org/summaries/coi.htm

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About certainty of the evidence (GRADE)

The "certainty of the evidence" is an assessment of how good an indication the research provides of the likely effect; i.e. the likelihood that the effect will be substantially different from what the research found. By "substantially different" we mean a large enough difference that it might affect a decision. These judgements are made using the GRADE system, and are provided for each outcome. The judgements are based on the study design (randomised trials versus observational studies), factors that reduce the certainty (risk of bias, inconsistency, indirectness, imprecision, and publication bias) and factors that increase the certainty (a large effect, a dose response relationship, and plausible confounding). For each outcome, the certainty of the evidence is rated as high, moderate, low or very low using the definitions on page 3.

For more information about GRADE: www.supportsummaries.org/grade

SUPPORT collaborators:

The Cochrane Effective Practice and Organisation of Care Group (EPOC) is part of the Cochrane Collaboration. The Norwegian EPOC satellite supports the production of Cochrane reviews relevant to health systems in low- and middle-income countries . www.epocoslo.cochrane.org

The Evidence-Informed Policy Network (EVIPNet) is an initiative to promote the use of health research in policymaking in low- and middle-income countries. www.evipnet.org

The Alliance for Health Policy and Systems Research (HPSR) is an international collaboration that promotes the generation and use of health policy and systems research in low- and middle-income countries. www.who.int/alliance-hpsr

Norad, the Norwegian Agency for Development Cooperation, supports the Norwegian EPOC satellite and the production of SUPPORT Summaries. www.norad.no

The Effective Health Care Research Consortium is an international partnership that prepares Cochrane reviews relevant to low-income countries. www.evidence4health.org

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