

Improving antiretroviral therapy scale-up and effectiveness through service integration and decentralization

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Background: Current service delivery systems do not reach all people in need of antiretroviral therapy (ART). In order to inform the operational and service delivery section of the WHO 2013 consolidated antiretroviral guidelines, our objective was to summarize systematic reviews on integrating ART delivery into maternal, newborn, and child health (MNCH) care settings in countries with generalized epidemics, tuberculosis (TB) treatment settings in which the burden of HIV and TB is high, and settings providing opiate substitution therapy (OST); and decentralizing ART into primary health facilities and communities.

Design: A summary of systematic reviews.

Methods: The reviewers searched PubMed, Embase, PsycINFO, Web of Science, CENTRAL, and the WHO Index Medicus databases. Randomized controlled trials and observational cohort studies were included if they compared ART coverage, retention in HIV care, and/or mortality in MNCH, TB, or OST facilities providing ART with MNCH, TB, or OST facilities providing ART services separately; or primary health facilities or communities providing ART with hospitals providing ART.

Results: The reviewers identified 28 studies on integration and decentralization. Antiretroviral therapy integration into MNCH facilities improved ART coverage (relative risk [RR] 1.37, 95% confidence interval [CI] 1.05–1.79) and led to comparable retention in care. ART integration into TB treatment settings improved ART coverage (RR 1.83, 95% CI 1.48–2.23) and led to a nonsignificant reduction in mortality (RR 0.55, 95% CI 0.29–1.05). The limited data on ART integration into OST services indicated comparable rates of ART coverage, retention, and mortality. Partial decentralization into primary health facilities improved retention (RR 1.05, 95% CI 1.01–1.09) and reduced mortality (RR 0.34, 95% CI 0.13–0.87). Full decentralization improved retention (RR 1.12, 95% CI 1.08–1.17) and led to comparable mortality. Community-based ART led to comparable rates of retention and mortality.

Conclusion: Integrating ART into MNCH, TB, and OST services was often associated with improvements in ART coverage, and decentralization of ART into primary health facilities and communities was often associated with improved retention. Neither integration nor decentralization was associated with adverse outcomes. These data contributed to recommendations in the WHO 2013 consolidated antiretroviral guidelines to integrate ART delivery into MNCH, TB, and OST services and to decentralize ART.

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Introduction

Global efforts to scale up antiretroviral therapy (ART) between 2002 and 2012 averted an estimated 4.2 million deaths in low-income and middle-income countries [1]. The United Nations endorsed the importance of this impact and agreed to scale up ART to 15 million people by 2015 [2]. In 2012, 9.7 million (65% of the global target) were receiving ART [1]. Antiretroviral therapy also has an important impact on HIV transmission [3–5]. Accelerating population impact will require adaptations in the delivery of HIV care and treatment tailored to epidemiological, social, and health systems context.

Provider-initiated HIV testing and counselling is recommended in all patients with presumptive and diagnosed tuberculosis (TB) [6] and in all maternal, newborn, and child health (MNCH) care settings in generalized epidemics [7]. WHO also recommends HIV testing and counselling to all people attending drug dependence treatment services as part of a comprehensive package of services [7,8]. Provider-initiated testing and counselling should also be considered in primary health facilities where epidemiologically appropriate [7]. Despite these recommendations, in 2012, 57% of people with HIV and active TB received ART [9], 59% of eligible pregnant women received ART [1], and the available data suggest that 1–22% of people with HIV who inject drugs in high-burden countries received ART [10,11]. Coverage in all three of these populations remained lower than the coverage achieved among all adults with HIV [1]. Integrating ART into TB, MNCH, and opiate substitution therapy (OST) care settings and decentralizing ART to primary care health facilities, where populations are already receiving testing and counselling, may increase accessibility, affordability, and acceptability of HIV services. This could also change the paradigm of national programming in some settings from being vertical, where only HIV health facilities are used for delivering HIV services, to diagonal, wherein sound HIV testing, care, and treatment are integrated into strong health systems [12].

Earlier reviews have covered decentralization [13], community-based ART [14], and models of HIV integration with TB care [15,16], MNCH services [17,18], and OST [19]. Our objective was to summarize the findings of several systematic reviews conducted for the 2013 WHO consolidated antiretroviral guidelines on HIV service integration and decentralization.

Methods

Conduct of systematic reviews

Systematic reviews were conducted to inform HIV service delivery and operational recommendations as part

of the 2013 WHO guidelines preparation [20]. For the reviews on integration and decentralization of ART, reviewers systematically searched PubMed, Embase, PsycINFO, Web of Science, CENTRAL, and the WHO Index Medicus databases in 2012 for studies meeting eligibility criteria. The WHO International Clinical Trials Registry Platform was also searched in 2012 for future and ongoing studies. Archived abstracts for the Conference on Retroviruses and Opportunistic Infections, the International AIDS Conference, and the International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention were searched in 2012. For the review on the integration of HIV and TB services, abstracts from the Union World Conference on Lung Health conference database were additionally searched in 2012.

Study definitions

Integrated ART was defined as providing ART at MNCH, TB, or OST health facilities. Separate ART was defined as providing ART and MNCH, TB, or OST services at multiple health facilities. Partial decentralization was defined as initiation at hospitals and maintenance at primary health facilities, full decentralization was defined as initiation and maintenance at primary health facilities, and community-based ART was defined as initiation at either a hospital or primary health facility with maintenance between facility visits through community-based approaches (e.g., home-based delivery or utilizing networks of people with HIV). MNCH facilities were defined as those providing antenatal, postnatal, infant, and/or child health services. Primary health facilities provided care for multiple diseases and were sometimes called primary health centers or primary health clinics. TB treatment settings included a range of health sites providing tuberculosis treatment (e.g. TB facilities, primary health facilities, and hospitals).

Antiretroviral therapy coverage was defined as the number of persons who initiated ART divided by the number of people who were eligible per national clinical guidelines. Retention in care was defined as the number of people who remained in care after a time period, self-defined by studies, divided by the number of people who enrolled in care. Mortality was defined as the number of people who are enrolled in care and died of any cause divided by the number of people enrolled in care.

Selection criteria

Two reviewers independently screened abstracts of all identified articles and examined the full text articles of those that seemed relevant. Studies meeting each review's respective eligibility criteria were included. For service integration, studies were included when the study population included people with HIV; the intervention was ART integrated into MNCH care where there is a generalized HIV epidemic, settings providing TB treatment where there is a high burden of HIV and TB, or

settings providing OST; the comparator was separate services; the outcomes were mortality, retention in HIV care, and/or ART coverage; and the study design was a randomized trial or an observational cohort study.

The decentralization review's eligibility criteria included the same population, outcomes, and study designs. The reviewers included studies with partial decentralization, full decentralization, and community-based ART as the intervention and hospital-based ART as the comparator after one year of ART.

Statistical analyses

Studies meeting eligibility criteria were stratified by service delivery approach (i.e., MNCH integration, TB integration, OST integration, partial decentralization, full decentralization, or community-based ART). As proportions were used to gauge ART coverage, retention, and mortality, the frequency of events was quantified using risks, and relative risks (RRs) were used for comparisons. Pooled RRs were used, when appropriate, to compare participants in the intervention and comparator arms of multiple studies meeting eligibility criteria. Random-effects models were used for all meta-analyses. I-squared statistics were used to measure heterogeneity [21]. I-squared statistics near 25% indicate low heterogeneity, values near 50% indicate moderate heterogeneity, and those above 75% indicate high heterogeneity [22]. Analyses were completed in STATA version 12.0 and Review Manager version 5.1.

Results

Antiretroviral therapy integration with maternal, neonatal, and child healthcare services

Nine hundred forty-nine studies were screened and four met the inclusion criteria (Fig. 1a and Table 1). None of the studies evaluated mortality. One study evaluated retention in care and found similar rates among pregnant and breastfeeding women in integrated versus separate services [23] (Fig. 2). Four studies evaluated ART coverage. Three studies reported improved coverage in integrated services [23–25] and one study reported similar coverage [26] (Fig. 2). Overall, there was an improvement in ART coverage across all four studies (RR 1.37, 95% confidence interval [CI] 1.05–1.79, Fig. 3).

Antiretroviral therapy integration with tuberculosis treatment services

One thousand one hundred sixty-four studies were screened and twelve studies met the inclusion criteria (Fig. 1b and Table 1). None of the studies evaluated retention. Twelve studies evaluated ART coverage. Nine [27–35] reported improved coverage, and three [36–38] reported similar coverage, when ART was provided in TB

care settings versus separate services (Fig. 2). Overall, there was an improvement in ART coverage across all twelve studies (RR 1.83, 95% CI 1.48–2.25, Fig. 3). Four studies evaluated mortality. Two studies [30,35] reported reduced mortality and two studies reported similar mortality [37,38] when ART was provided in TB care settings compared with separate services (Fig. 2). Overall, rates of mortality were nonsignificantly reduced in integrated versus separate services (RR 0.55, 95% CI 0.29–1.05).

Antiretroviral therapy integration with services providing opiate substitution therapy

Four hundred eight studies were screened and two met the inclusion criteria (Fig. 1c and Table 1). One study evaluated ART coverage. This study reported similar ART coverage when ART was provided in OST settings compared with separate ART and OST care settings (Figs 2 and 3) [39]. One study evaluated retention and mortality, and showed similar retention and mortality in integrated versus separate services [40] (Fig. 2).

Partial decentralization of antiretroviral therapy

Three thousand four hundred thirty-seven studies were screened and four met the inclusion criteria (Fig. 1d and Table 1). None of the studies evaluated ART coverage. Three studies reported improved retention in care [41–43], and one study reported similar retention [44] (Fig. 4). Overall, there was improved retention across all four studies (RR 1.05, 95% CI 1.01–1.09, Fig. 5). All studies reported reduced mortality [41–44] (overall RR 0.34, 95% CI 0.13–0.87) (Fig. 4).

Full decentralization of antiretroviral therapy

Three thousand four hundred thirty-seven studies were screened and four studies met the inclusion criteria (Fig. 1d and Table 1). None of the studies evaluated ART coverage. All studies reported improved retention in care [45–48] (overall estimate RR 1.12, 95% CI 1.08–1.17, Figs 4 and 5). Three studies reported reduced mortality [46–48], although one estimate lacked statistical significance [47], whereas one study reported increased mortality [45] (Fig. 4). Overall, the rates of mortality were comparable in fully decentralized and hospital-based ART (RR 1.10, 95% CI 0.63–1.92).

Community-based antiretroviral therapy

Three thousand four hundred thirty-seven studies were screened and two studies met the inclusion criteria (Fig. 1d and Table 1). Neither evaluated ART coverage. Both reported similar retention [49,50] (overall RR 1.01, 95% CI 0.99–1.03, Figs 4 and 5). Both reported similar mortality [49,50] (overall RR 1.03, 95% CI 0.64–1.65) (Fig. 4).

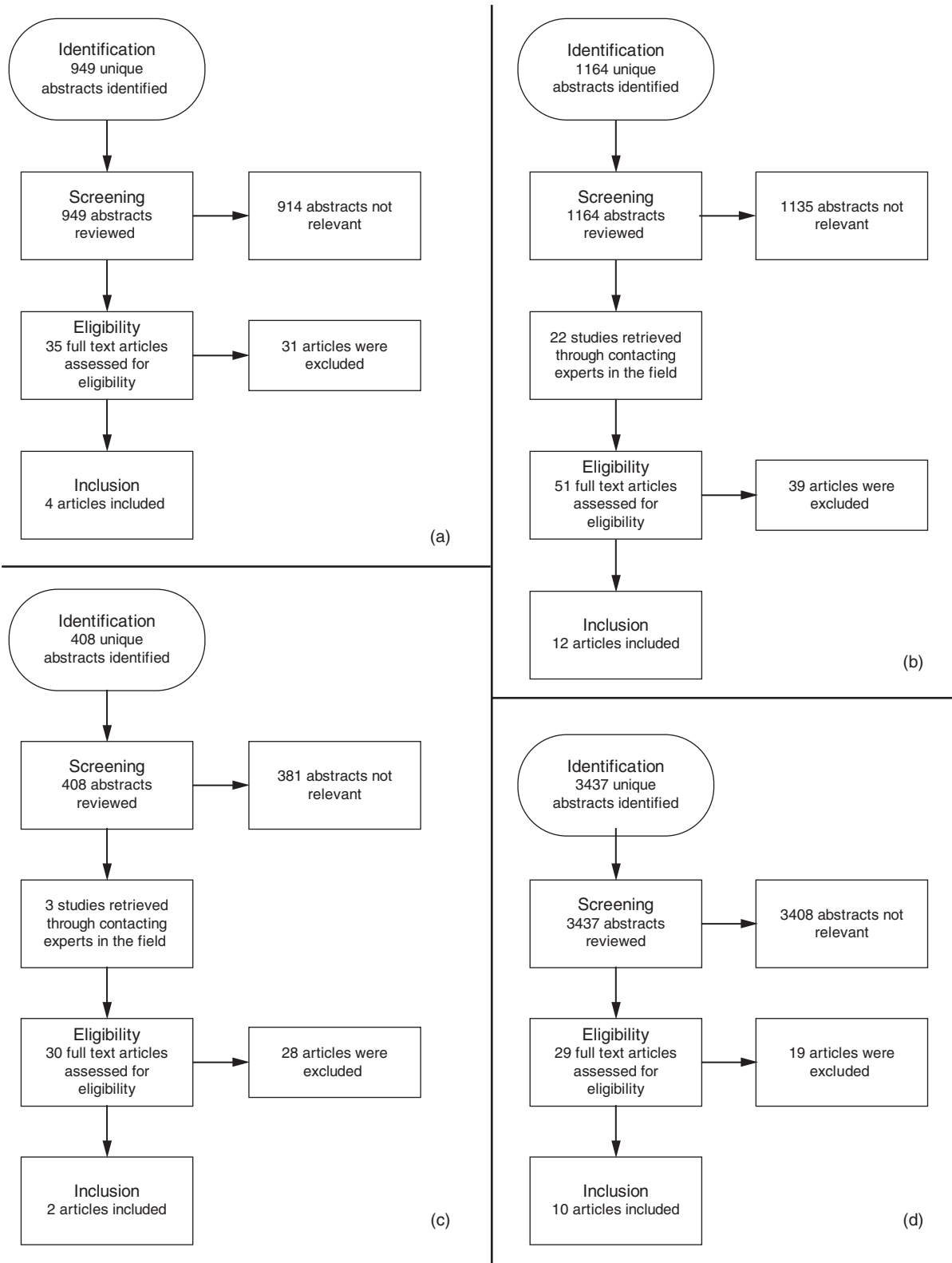


Fig. 1. Flow chart of study selection process. (a) Maternal, newborn, and child health (MNCH) integration review, (b) Tuberculosis (TB) integration review, (c) Opiate substitution therapy (OST) integration review, and (d) Decentralization review.

Table 1. Summary of characteristics of included studies.

Author	Country	Population	Intervention	Comparator
ART integration with MNCH				
Christie <i>et al.</i> [25]	Jamaica	Pregnant women with HIV attending MNCH facilities	Integrated MNCH services, HIV care, and ART	MNCH services and referral for ART
Killam <i>et al.</i> [23]	Zambia	Pregnant women with HIV attending MNCH facilities	Integrated MNCH services, HIV care, and ART	MNCH services and referral for ART
Pfeiffer <i>et al.</i> [24] ^a	Mozambique	Pregnant women with HIV attending MNCH facilities ^a	Integrated MNCH services, HIV care, and ART	MNCH services and referral for ART
Tsague <i>et al.</i> [26]	Rwanda	Pregnant women with HIV attending MNCH facilities	Integrated MNCH services, HIV care, and ART	MNCH services and referral for ART
ART integration with TB services				
Bygrave <i>et al.</i> [36]	Lesotho	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Chifundo <i>et al.</i> [27]	Malawi	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Howard <i>et al.</i> [28]	Kenya	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Huerga <i>et al.</i> [29]	Kenya	People with TB	Integrated HIV testing, TB treatment, and ART	HIV testing, TB treatment, and referral for ART
Kerschberger <i>et al.</i> [37]	South Africa	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Ikeda <i>et al.</i> [30]	Guatemala	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Louwagie <i>et al.</i> [31] ^b	South Africa	People with TB	Integrated HIV testing, TB treatment, and ART	HIV testing, TB treatment, and referral for ART
Morse <i>et al.</i> [32]	Zambia	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Pevzner <i>et al.</i> [33]	Rwanda	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Phiri <i>et al.</i> [34]	Malawi	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Schwartz <i>et al.</i> [38]	Botswana	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
Van Rie <i>et al.</i> [35]	Democratic Republic of Congo	People with HIV and TB	Integrated TB treatment and ART	TB treatment and referral for ART
ART integration with OST				
Achmad <i>et al.</i> [40]	Indonesia	PWID enrolled in methadone maintenance treatment	Integrated HIV testing, HIV care, ART, and MMT	HIV care and ART
Zaller <i>et al.</i> [39]	United States of America	People with substance use disorders	HIV care, ART, and assessment for substance abuse treatment needs with facilitated referral for those eligible	HIV care and ART
Partial decentralization of ART				
Bock <i>et al.</i> [44]	South Africa	Children with HIV	ART initiated at hospitals and maintained at primary health facilities	ART initiated and maintained at hospitals
Brennan <i>et al.</i> [43]	South Africa	Adults with HIV	ART initiated at hospitals and maintained at primary health facilities	ART initiated and maintained at hospitals
Chan <i>et al.</i> [42]	Malawi	Adults and children with HIV	ART initiated at hospitals and maintained at primary health facilities	ART initiated and maintained at hospitals
Fatti <i>et al.</i> [41]	South Africa	Adults with HIV	ART initiated at hospitals and maintained at primary health facilities	ART initiated and maintained at hospitals
Full decentralization of ART				
Assefa <i>et al.</i> [48]	Ethiopia	Not described	ART initiated and maintained at primary health facilities	ART initiated and maintained at hospitals
Bedelu <i>et al.</i> [47]	South Africa	Adults with HIV	ART initiated and maintained at primary health facilities	ART initiated and maintained at hospitals
Massaquoi <i>et al.</i> [46]	Malawi	Adults and children with HIV	ART initiated and maintained at primary health facilities	ART initiated and maintained at hospitals
McGuire <i>et al.</i> [45]	Malawi	Adults with HIV	ART initiated and maintained at primary health facilities	ART initiated and maintained at hospitals
Community-based ART				
Jaffar <i>et al.</i> [50]	Uganda	Adults with HIV	ART initiated at hospitals and delivered monthly at homes between facility visits every 6 months	ART initiated and maintained at hospitals
Selke <i>et al.</i> [49]	Kenya	Adults with HIV	ART initiated at hospitals and delivered monthly at homes between facility visits every 3 months	ART initiated and maintained at hospitals

ART, antiretroviral therapy; MNCH, maternal newborn and child health; OST, opiate-substitution therapy; TB, tuberculosis.

^aThe reported relative risk in this study was comparing integrated HIV services overall to vertical services.

^bThe intervention was providing ART at the same health facility.

	Integrated			Separated			Relative risk (95% CI)
	±	Total	Percent	±	Total	Percent	
MNCH							
<u>ART coverage</u>							
Christie (Jamaica)	156	160	97.5%	135	191	70.7%	1.38 (1.29–1.47)
Killam (Zambia)	278	846	32.9%	103	716	14.4%	2.28 (1.87–2.80)
Pfeiffer (Mozambique)	-	-	-	-	-	-	1.58 (1.17–2.14)
Tsague (Rwanda)	105	135	77.8%	22	26	84.6%	0.92 (0.76–1.11)
Overall ($I^2 = 83\%$)							1.37 (1.05–1.79)
<u>Retention in HIV care</u>							
Killam (Zambia)	244	278	87.8%	94	103	91.3%	0.96 (0.89–1.04)
TB							
<u>ART coverage</u>							
Bygrave (Lesotho)	174	225	77.3%	131	151	86.8%	0.89 (0.81–0.98)
Chifundo (Malawi)	257	338	76.0%	201	456	44.1%	1.73 (1.53–1.94)
Howard (Kenya)	19233	40069	48.0%	12426	41174	30.2%	1.59 (1.56–1.62)
Huerga (Kenya)	150	325	46.2%	26	304	8.6%	5.40 (3.67–7.94)
Ikeda (Guatemala)	115	156	73.7%	21	93	22.6%	3.26 (2.22–4.81)
Kerschberger (R.S.A.)	64	88	72.7%	74	100	74.0%	0.98 (0.83–1.17)
Louwagie (R.S.A.)	74	105	70.5%	104	233	44.6%	1.58 (1.31–1.91)
Morse (Zambia)	53	204	26.0%	22	203	10.8%	2.40 (1.52–3.79)
Pevzner (Rwanda)	1036	2673	38.8%	296	2276	13.0%	2.98 (2.65–3.35)
Phiri (Malawi)	775	1138	68.1%	758	1289	58.8%	1.16 (1.09–1.23)
Schwartz (Botswana)	17	42	40.5%	70	143	49.0%	0.83 (0.56–1.24)
Van Rie (D.R.C)	354	513	69.0%	62	373	16.6%	4.15 (3.28–5.25)
Overall ($I^2 = 98\%$)							1.83 (1.48–2.25)
<u>Mortality</u>							
Ikeda (Guatemala)	29	156	18.6%	68	93	73.1%	0.25 (0.18–0.36)
Kerschberger (R.S.A.)	7	88	8.0%	9	100	9.0%	0.88 (0.34–2.27)
Schwartz (Botswana)	8	79	10.1%	20	250	8.0%	1.27 (0.58–2.76)
Van Rie (D.R.C)	52	513	10.1%	78	373	20.9%	0.48 (0.35–0.67)
Overall ($I^2 = 84\%$)							0.55 (0.29–1.05)
OST							
<u>ART coverage</u>							
Zaller (U.S.A.)	89	116	76.7%	745	869	85.7%	0.90 (0.81–0.99)
<u>Retention in HIV care</u>							
Achmad (Indonesia)	35	35	100.0%	170	175	97.1%	1.03 (1.00–1.06)
<u>Mortality</u>							
Achmad (Indonesia)	2	35	5.7%	13	175	7.4%	0.77 (0.18–3.26)

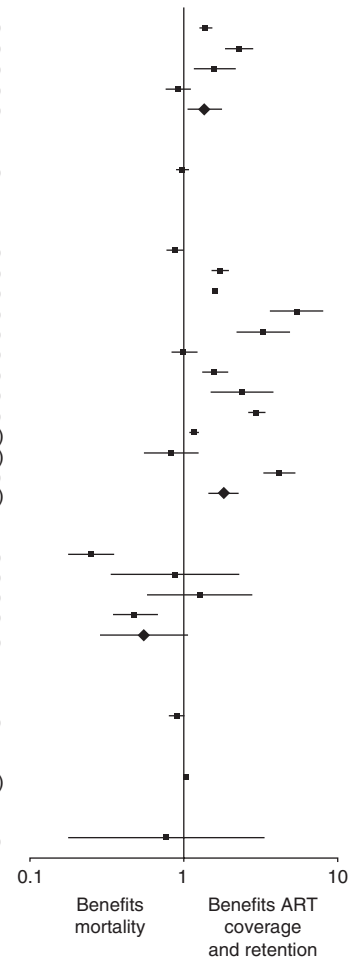


Fig. 2. Forest plot antiretroviral therapy coverage, retention in HIV care, and mortality in integrated versus separated services. Results on the right side of the y-axis (RR > 1) are beneficial for antiretroviral therapy (ART) coverage and retention, whereas results on the left side of the y-axis (RR < 1) are beneficial for mortality. CI, confidence interval; D.R.C., Democratic Republic of the Congo; MNCH, maternal newborn and child health; OST, opiate-substitution therapy; R.S.A., Republic of South Africa; TB, tuberculosis; U.S.A., United States of America.

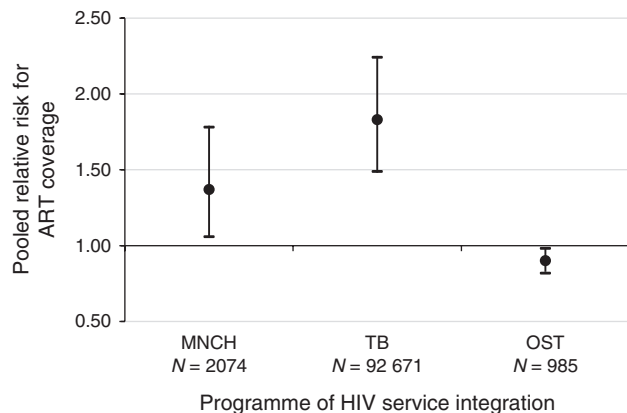


Fig. 3. Summary of results for service integration and anti-retroviral therapy coverage. MNCH, maternal newborn and child health; OST, opiate-substitution therapy; TB, tuberculosis.

Discussion

In many cases, there were improvements in ART coverage and reductions in mortality with service integration and improvements in retention and reductions in mortality with decentralization. There were no adverse outcomes associated with integrating ART into other programmes, decentralizing ART into primary health facilities, and providing community-based ART between facility visits. This may be associated with the availability of the full range of HIV services (i.e., HIV testing and counselling, HIV care, and ART) at a single site. There were limited data on the acceptability and quality of services. Researchers and countries should continue monitoring integration and decentralization efforts closely to ensure the quality of services is not adversely affected. Ensuring timely access to comprehensive and evidence-based interventions is also necessary for improved health outcomes. This should

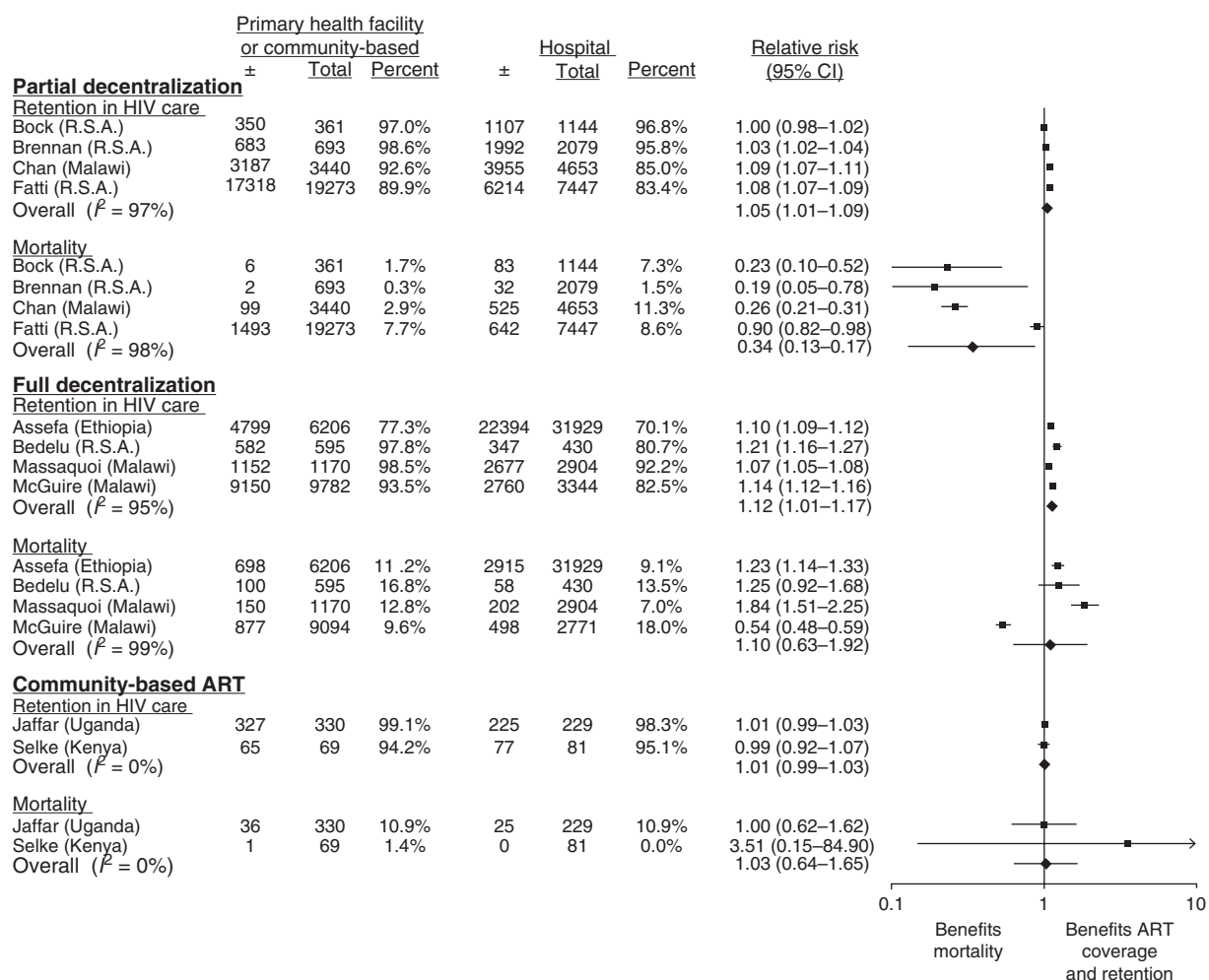


Fig. 4. Forest plot of retention in HIV care and mortality in partial decentralization, full decentralization, and community-based antiretroviral therapy versus hospitals. Results on the right side of the y-axis ($RR > 1$) are beneficial for retention whereas results on the left side of the y-axis ($RR < 1$) are beneficial for mortality. CI, confidence interval; RSA, Republic of South Africa

include both HIV and non-HIV services that are essential for the general population, pregnant and breastfeeding women, persons with TB, and people who inject drugs.

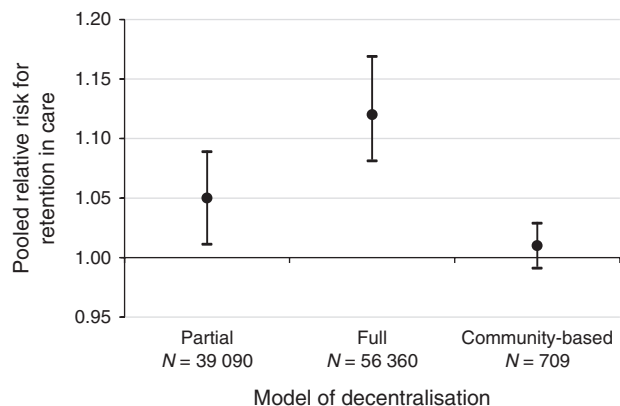


Fig. 5. Summary of results for decentralization and retention in care.

Based on these data, programme risks and benefits, acceptability; values; and preferences, cost implications, feasibility and critical contextual constraints, and contextual relevance, the 2013 WHO consolidated antiretroviral guidelines recommend:

- (1) In generalized epidemic settings, ART should be initiated and maintained in eligible pregnant and postpartum women and in infants at MNCH care settings, with linkage and referral to ongoing HIV care and ART, wherever appropriate.
- (2) In settings with a high burden of HIV and TB, ART should be initiated for an individual living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART.
- (3) ART should be initiated and maintained in eligible people living with HIV at care settings in which OST is provided.
- (4) The following options should be considered for decentralization of ART initiation and maintenance:

- (a) initiation of ART in hospitals with maintenance of ART in peripheral health facilities,
- (b) initiation and maintenance of ART in peripheral health facilities,
- (c) initiation of ART at peripheral health facilities with maintenance at the community level (i.e., outside health facilities in settings such as outreach sites, health posts, home-based services, or community-based organizations) between regular clinical visits.

There are a number of factors that programmes will need to consider when expanding access to ART through integration and decentralization within their unique context. These include the volume of people with HIV expected in integrated and decentralized sites, whether integration and decentralization of ART brings services closer to people who otherwise must travel long distances to receive HIV care and treatment, whether integration and decentralization of HIV treatment reduces workload to overburdened health facilities, and whether integration and decentralization of HIV treatment improves access for populations who often face stigma, discrimination, and criminalization. Evaluation of these factors may help programmes when prioritizing integration and decentralization efforts and facilitate scale-up based on experiences and lessons learned.

Creating an enabling and collaborative programme and policy environment is critical for success in service delivery. This includes mechanisms for joint planning, monitoring and evaluation, resource mobilization, programme supervision and review, and health worker training and mentoring. MNCH, TB, and OST services are entry points for lifelong care for people diagnosed with HIV in such settings, and these services will need to ensure continuity of care. Some MNCH care settings may opt to refer women and children to HIV clinics after completion of childhood immunizations, cessation of breastfeeding, or the child's definitive HIV diagnosis. Other MNCH care settings may decide to provide family-focused ART services. TB and HIV programmes will also need to assess whether referral of people with HIV at completion of TB treatment or providing lifelong ART at TB care settings is locally feasible. Given that OST often requires long-term care referral after OST completion may need evaluation based on patient preferences and local feasibility.

A 2011 WHO survey indicated that the ratio of TB treatment facilities to HIV facilities providing ART was 1.3 in South Africa, 2.6 in Zimbabwe, 5.8 in Mozambique, 8.9 in Nigeria, and 30.4 in India [51]. This suggests that many countries with high burdens of HIV and TB may have opportunities to expand access to ART to people with HIV and active TB by integrating services. However, countries will also need to evaluate epidemiological burden to understand where integration offers advantages. For example, rather than integrating

services nationwide, integration may make the most sense in settings where the burden of HIV and TB is high. These considerations also apply to integration of ART into MNCH care in generalized epidemic settings and the decentralization of ART into primary health facilities [52]. In all healthcare settings routine implementation of TB infection control measures is vital to reduce risk of nosocomial TB transmission [53].

WHO recommends a comprehensive package of interventions for the prevention, treatment, and care of HIV among people who inject drugs, including needle and syringe programmes; OST and other evidence-based drug dependence treatment; HIV testing and counselling; ART; prevention and treatment of sexually transmitted infections; condom distribution programmes for people who inject drugs and their sexual partners; targeted information, education and communication for people who inject drugs and their sexual partners; prevention, vaccination, diagnosis, and treatment for viral hepatitis; and prevention, diagnosis, and treatment of TB [8]. In many settings with a large number of people who inject drugs, there remains limited access to OST, with provision often being led by community-based and nongovernmental organizations [11]. Therefore, HIV programmes may need to collaborate with these organizations when integrating services. OST has considerable benefits for people who inject drugs, including reducing opioid and other drug use, criminal activity, risk behaviours, opioid overdose, and all-cause mortality [54]. These benefits can also support adherence to ART and improve rates of viral suppression [40].

There are some shared implementation considerations for integrating and decentralizing HIV services. First, HIV programmes need to strengthen supply chain management systems to prevent stock outs of antiretroviral drugs and other key commodities [55]. Second, HIV programmes may consider a phased approach for integrating and decentralizing ART to strengthen supply management systems, service organization at the facility level, and monitoring and evaluation systems. Third, decentralized and integrated delivery of ART in many settings implies initiation and maintenance of HIV care and treatment by trained nonspecialized healthcare providers, nurses, and nonphysician clinicians. In order to prevent overburdening nonphysician clinicians, some tasks may also need to be shifted to or shared with trained community health workers and 'lay providers'. Randomized trials have examined the risks and benefits of task shifting and sharing for both initiation [56] and maintenance [50,56,57] of ART by nurses and nonphysician clinicians. Based on these trials and observational studies [20], WHO recommends that trained nonphysician clinicians, nurses, and midwives can initiate first-line ART and maintain ART, and that community health workers can dispense ART between facility visits [58]. Effective

task shifting and sharing requires providing training, mentoring, and supportive supervision for all healthcare providers; ensuring clear criteria for when, where, and to whom patients should be referred when necessary; implementing standardized monitoring and evaluation systems across all health facilities providing HIV care; and ensuring quality care in all settings providing HIV care.

TB, MNCH, and OST were reviewed due to programme synergies; however, future research should evaluate the potential for ART integration in settings providing treatment for STIs and immunizations. Antiretroviral therapy in STI treatment settings could expand access to sex workers and men who have sex with men, whereas ART in settings providing immunizations could expand access to the paediatric population. Most identified studies had limited periods of follow-up. The feasibility, sustainability, and retention of people with HIV may be different over longer periods of time, and studies are needed to understand integration and decentralization outcomes fully. It is difficult to ascertain the benefits and risks of integrating ART into OST settings, as there is potential for confounding owing to differences in access to OST [59,60] and directly observed ART [61,62]. Future research could provide improved estimates.

Using the I-squared statistic, there was high heterogeneity for most of the meta-analyses. All analyses should be interpreted with respect to local epidemiology, social and cultural context, and health systems organization of studies contributing data. Moreover, there were limited data on patient and health worker acceptability of integrating and decentralizing services. For MNCH, some data suggested that providers and patients had positive perspectives and experiences with service integration [63,64]. Qualitative research is needed to further understand the effects of service integration and decentralization on stigma and normalization of HIV services, particularly in providing services to key populations (i.e. men who have sex with men, sex workers, people who inject drugs, and transgender people). Finally, the overall implications of service integration on the health system, including on health workers skill mix, workload, and 'scope of practice', will need to be documented to further strengthen learning from programme implementation.

In conclusion, service integration was often associated with improved ART coverage, whereas decentralization often improved retention. Neither integration nor decentralization was associated with harmful outcomes. Many studies indicated reduced mortality for integration and decentralization and these estimates could be improved by additional studies following people longer. Implementation research is also needed to establish estimates in different geographical and sociocultural contexts. As countries develop their new national

strategic plans and investment cases, consideration should be given to expanding access to ART through integration and decentralization [58].

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Conflicts of interest

None declared.

References

1. World Health Organization. *Global update on HIV treatment 2013: results, impact and opportunities*. Geneva: World Health Organization. http://www.who.int/iris/bitstream/10665/85326/1/9789241505734_eng.pdf. [Accessed 26 January 2014]
2. United Nations General Assembly. *Political Declaration on HIV and AIDS: intensifying our efforts to eliminate HIV and AIDS*. 2011. http://www.unaids.org/en/media/unaids/contentassets/documents/document/2011/06/20110610_un_a-res-65-277_en.pdf. [Accessed 26 January 2014]
3. Joint United Nations Programme on HIV and AIDS. *Global Report: UNAIDS report on the global AIDS epidemic 2013*. 2013. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf. [Accessed 26 January 2014]
4. Wood E, Kerr T, Marshall BD, Li K, Zhang R, Hogg RS, *et al*. **Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study**. *BMJ* 2009; **338**:b1649.
5. Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. **High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa**. *Science* 2013; **339**:966–971.
6. World Health Organization. *WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders*. 2012. http://whqlibdoc.who.int/publications/2012/9789241503006_eng.pdf. [Accessed 26 January 2014]
7. World Health Organization. *Guidance on provider-initiated HIV testing and counselling in health facilities*. Geneva: World Health Organization, 2007. http://whqlibdoc.who.int/publications/2007/9789241595568_eng.pdf. [Accessed 26 January 2014]

8. World Health Organization. *Technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users, 2012 revision*. Geneva: World Health Organization, 2012. http://www.who.int/iris/bitstream/10665/77969/1/9789241504379_eng.pdf. [Accessed 26 January 2014]
9. World Health Organization. *Global Tuberculosis Report 2013*. Geneva: World Health Organization, 2013. http://www.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf. [Accessed 26 January 2014]
10. Degenhardt L, Mathers BM, Wirtz AL, Wolfe D, Kamarulzaman A, Carrieri MP, et al. **What has been achieved in HIV prevention, treatment and care for people who inject drugs, 2010–2012? A review of the six highest burden countries**. *Int J Drug Policy* 2014; **25**:53–60.
11. Petersen Z, Myers B, van Hout MC, Pluddemann A, Parry C. **Availability of HIV prevention and treatment services for people who inject drugs: findings from 21 countries**. *Harm Reduct J* 2013; **10**:13.
12. Kim JY, Farmer P, Porter ME. **Redefining global health-care delivery**. *Lancet* 2013; **382**:1060–1069.
13. Kredo T, Ford N, Adeniyi FB, Garner P. **Decentralising HIV treatment in lower- and middle-income countries**. *Cochrane Database Syst Rev* 2013:CD009987.
14. Decroo T, Rasschaert F, Telfer B, Remartinez D, Laga M, Ford N. **Community-based antiretroviral therapy programs can overcome barriers to retention of patients and decongest health services in sub-Saharan Africa: a systematic review**. *Int Health* 2013; **5**:169–179.
15. Legido-Quigley H, Montgomery CM, Khan P, Atun R, Fakoya A, Getahun H, Grant AD. **Integrating tuberculosis and HIV services in low- and middle-income countries: a systematic review**. *Trop Med Int Health* 2013; **18**:199–211.
16. Uyei J, Coetzee D, Macinko J, Guttmacher S. **Integrated delivery of HIV and tuberculosis services in sub-Saharan Africa: a systematic review**. *Lancet Infect Dis* 2011; **11**:855–867.
17. Tudor Car L, van-Velthoven MH, Brusamento S, Elmoniry H, Car J, Majeed A, Atun R. **Integrating prevention of mother-to-child HIV transmission (PMTCT) programmes with other health services for preventing HIV infection and improving HIV outcomes in developing countries**. *Cochrane Database Syst Rev* 2011; **6**:CD008741.
18. Suthar AB, Hoos D, Beqiri A, Lorenz-Dehne K, McClure C, Duncombe C. **Integrating antiretroviral therapy into antenatal care and maternal and child health settings: a systematic review and meta-analysis**. *Bull World Health Organ* 2013; **91**:46–56.
19. Volkow ND, Montaner J. **The urgency of providing comprehensive and integrated treatment for substance abusers with HIV**. *Health Aff (Millwood)* 2011; **30**:1411–1419.
20. World Health Organization. *Consolidated ARV guidelines web annexes*. Geneva: World Health Organization, 2013. <http://www.who.int/hiv/pub/guidelines/arv2013/annexes/en/index3.html>. [Accessed 26 January 2014]
21. Higgins JP, Thompson SG. **Quantifying heterogeneity in a meta-analysis**. *Stat Med* 2002; **21**:1539–1558.
22. Higgins JP, Thompson SG, Deeks JJ, Altman DG. **Measuring inconsistency in meta-analyses**. *BMJ* 2003; **327**:557–560.
23. Killam WP, Tambatamba BC, Chintu N, Rouse D, Stringer E, Bweupe M, et al. **Antiretroviral therapy in antenatal care to increase treatment initiation in HIV-infected pregnant women: a stepped-wedge evaluation**. *AIDS* 2010; **24**:85–91.
24. Pfeiffer J, Montoya P, Baptista AJ, Karagianis M, Pugas Mde M, Micek M, et al. **Integration of HIV/AIDS services into African primary healthcare: lessons learned for health system strengthening in Mozambique – a case study**. *J Int AIDS Soc* 2010; **13**:3.
25. Christie CD, Steel-Duncan J, Palmer P, Pierre R, Harvey K, Johnson N, et al. **Paediatric and perinatal HIV/AIDS in Jamaica an international leadership initiative, 2002–2007**. *West Indian Med J* 2008; **57**:204–215.
26. Tsague L, Tsiouris FO, Carter RJ, Mugisha V, Tene G, Nyankesha E, et al. **Comparing two service delivery models for the prevention of mother-to-child transmission (PMTCT) of HIV during transition from single-dose nevirapine to multidrug antiretroviral regimens**. *BMC Public Health* 2010; **10**:753.
27. Chifundo K, Wandwalo E, Kanyerere H, Msiska T, Moodie C, Kellerman S, Suarez P. **What is the best model of TB/HIV service delivery? Experience from Malawi**. XVIII International AIDS Conference; 2010; Vienna, Austria.
28. Howard AA, Gasana M, Getahun H, Harries A, Lawn SD, Miller B, et al. **PEPFAR support for the scaling up of collaborative TB/HIV activities**. *J Acquir Immune Defic Syndr* 2012; **60** (Suppl 3):S136–S144.
29. Huerga H, Spillane H, Guerrero W, Odongo A, Varaine F. **Impact of introducing human immunodeficiency virus testing, treatment and care in a tuberculosis clinic in rural Kenya**. *Int J Tuberc Lung Dis* 2010; **14**:611–615.
30. Ikeda J, Page K, Hudes E, Barrios R, López Tellez C, Hearst N. **HIV and TB and Integration reduces mortality among the indigenous population in rural Guatemala**. XIX International AIDS Conference; 2012; Washington D.C., USA; 2012.
31. Louwagie G, Girdler-Brown B, Odendaal R, Rossouw T, Johnson S, Van der Walt M. **Missed opportunities for accessing HIV care among Tshwane tuberculosis patients under different models of care**. *Int J Tuberc Lung Dis* 2012; **16**:1052–1058.
32. Morse J, Luhanga D, Harris J, Musopole R, Besa S, Nhandu V, et al. **Integrated TB/ART clinics in Lusaka, Zambia: an evaluation of enrollment into HIV care and early initiation of antiretroviral therapy in TB/HIV co-infected patients**. 43rd Union World Conference on Lung Health; 2012; Kuala Lumpur, Malaysia; 2012.
33. Pevzner ES, Vandebriel G, Lowrance DW, Gasana M, Finlay A. **Evaluation of the rapid scale-up of collaborative TB/HIV activities in TB facilities in Rwanda, 2005–2009**. *BMC Public Health* 2011; **11**:550.
34. Phiri S, Khan PY, Grant AD, Gareta D, Tweya H, Kalulu M, et al. **Integrated tuberculosis and HIV care in a resource-limited setting: experience from the Martin Preuss centre, Malawi**. *Trop Med Int Health* 2011; **16**:1397–1403.
35. Van Rie A, Patel M, Nana M, Driessche K, Tabala M, Yotebieng M, Behets F. **Integration and task-shifting for TB/HIV care and treatment in highly resource-scarce settings: one size may not fit all**. *J Acquir Immune Defic Syndr* 2014; **65**:e110–e117.
36. Bygrave H, Trivino L, Makakole L. **TB/HIV integration: lessons learned from implementation of a TB/HIV 'one stop shop' at primary healthcare clinics in rural Lesotho**. XVIII International AIDS Conference; 2010; Vienna, Austria.
37. Kerschberger B, Hilderbrand K, Boule AM, Coetzee D, Goemaere E, De Azevedo V, Van Cutsem G. **The effect of complete integration of HIV and TB services on time to initiation of antiretroviral therapy: a before-after study**. *PLoS One* 2012; **7**:e46988.
38. Schwartz A, Tamuhla N, Steenhoff A, Nkakana K, Letlhogile R, Chadborn T, et al. **Outcomes in HIV-infected adults with tuberculosis at clinics with and without co-located HIV clinics in Botswana**. *Int J Tuberc Lung Dis* 2013; **17**:1298–1303.
39. Zaller N, Gillani FS, Rich JD. **A model of integrated primary care for HIV-positive patients with underlying substance use and mental illness**. *AIDS Care* 2007; **19**:1128–1133.
40. Achmad YM, Istiqomah AN, Iskandar S, Wisaksana R, van Creveld R, Hidayat T. **Integration of methadone maintenance treatment and HIV care for injecting drug users: a cohort study in Bandung, Indonesia**. *Acta Med Indones* 2009; **41** (Suppl 1): 23–27.
41. Fatti G, Grimwood A, Bock P. **Better antiretroviral therapy outcomes at primary healthcare facilities: an evaluation of three tiers of ART services in four South African provinces**. *PLoS One* 2010; **5**:e12888.
42. Chan AK, Mateyu G, Jahn A, Schouten E, Arora P, Mlotha W, et al. **Outcome assessment of decentralization of antiretroviral therapy provision in a rural district of Malawi using an integrated primary care model**. *Trop Med Int Health* 2010; **15** (Suppl 1):90–97.
43. Brennan AT, Long L, Maskew M, Sanne I, Jaffray I, MacPhail P, Fox MP. **Outcomes of stable HIV-positive patients down-referred from a doctor-managed antiretroviral therapy clinic to a nurse-managed primary health clinic for monitoring and treatment**. *AIDS* 2011; **25**:2027–2036.
44. Bock P, Boule A, White C, Osler M, Eley B. **Provision of antiretroviral therapy to children within the public sector of South Africa**. *Trans R Soc Trop Med Hyg* 2008; **102**:905–911.
45. McGuire M, Pinoges L, Kanapathipillai R, Munyenembe T, Huckabee M, Makombe S, et al. **Treatment initiation, program attrition and patient treatment outcomes associated with scale-up and decentralization of HIV care in rural Malawi**. *PLoS One* 2012; **7**:e38044.

46. Massaquoi M, Zachariah R, Manzi M, Pasulani O, Misindi D, Mwangomba B, *et al.* **Patient retention and attrition on antiretroviral treatment at district level in rural Malawi.** *Trans R Soc Trop Med Hyg* 2009; **103**:594–600.
47. Bedelu M, Ford N, Hilderbrand K, Reuter H. **Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care.** *J Infect Dis* 2007; **196** (Suppl 3):S464–S468.
48. Assefa Y, Kiflie A, Tekle B, Mariam DH, Laga M, Van Damme W. **Effectiveness and acceptability of delivery of antiretroviral treatment in health centres by health officers and nurses in Ethiopia.** *J Health Serv Res Policy* 2012; **17**:24–29.
49. Selke HM, Kimaiyo S, Sidle JE, Vedanthan R, Tierney WM, Shen C, *et al.* **Task-shifting of antiretroviral delivery from healthcare workers to persons living with HIV/AIDS: clinical outcomes of a community-based program in Kenya.** *J Acquir Immune Defic Syndr* 2010; **55**:483–490.
50. Jaffar S, Amuron B, Foster S, Birungi J, Levin J, Namara G, *et al.* **Rates of virological failure in patients treated in a home-based versus a facility-based HIV-care model in Jinja, southeast Uganda: a cluster-randomised equivalence trial.** *Lancet* 2009; **374**:2080–2089.
51. World Health Organization. *Global Tuberculosis Report 2012.* Geneva: World Health Organization, 2012. http://www.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf. [Accessed 26 January 2014]
52. Montana L, Mishra V, Hong R. *Comparison of HIV prevalence estimates from antenatal care surveillance and population-based surveys in sub-Saharan Africa.* 2008 [cited 06 November 2013]. <http://www.measuredhs.com/pubs/pdf/WP47/WP47.pdf>
53. World Health Organization. *WHO policy on TB infection control in health-care facilities, congregate settings, and households.* Geneva: World Health organization, 2009. http://whqlibdoc.who.int/publications/2009/9789241598323_eng.pdf. [Accessed 26 January 2014]
54. World Health Organization. *Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence.* Geneva: World Health Organization, 2009. http://whqlibdoc.who.int/publications/2009/9789241547543_eng.pdf. [Accessed 26 January 2014]
55. World Health Organization. *Harmonized monitoring and evaluation indicators for procurement and supply management systems.* Geneva: World Health Organization, 2011. http://whqlibdoc.who.int/publications/2011/9789241500814_eng.pdf. [Accessed 26 January 2014]
56. Fairall L, Bachmann MO, Lombard C, Timmerman V, Uebel K, Zwarenstein M, *et al.* **Task shifting of antiretroviral treatment from doctors to primary-care nurses in South Africa (STRETCH): a pragmatic, parallel, cluster-randomised trial.** *Lancet* 2012; **380**:889–898.
57. Sanne I, Orrell C, Fox MP, Conradie F, Ive P, Zeinecker J, *et al.* **Nurse versus doctor management of HIV-infected patients receiving antiretroviral therapy (CIPRA-SA): a randomised noninferiority trial.** *Lancet* 2010; **376**:33–40.
58. World Health Organization. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.* Geneva: World Health Organization; 2013. www.who.int/hiv/pub/guidelines/arv2013. [Accessed 26 January 2014].
59. Lucas GM, Chaudhry A, Hsu J, Woodson T, Lau B, Olsen Y, *et al.* **Clinic-based treatment of opioid-dependent HIV-infected patients versus referral to an opioid treatment program: a randomized trial.** *Ann Intern Med* 2010; **152**:704–711.
60. Sullivan LE, Barry D, Moore BA, Chawarski MC, Tetrault JM, Pantaloni MV, *et al.* **A trial of integrated buprenorphine/naloxone and HIV clinical care.** *Clin Infect Dis* 2006; **43** (Suppl 4): S184–S190.
61. Berg KM, Litwin A, Li X, Heo M, Arnsten JH. **Directly observed antiretroviral therapy improves adherence and viral load in drug users attending methadone maintenance clinics: a randomized controlled trial.** *Drug Alcohol Depend* 2011; **113**:192–199.
62. Lucas GM, Mullen BA, Galai N, Moore RD, Cook K, McCaul ME, *et al.* **Directly administered antiretroviral therapy for HIV-infected individuals in opioid treatment programs: results from a randomized clinical trial.** *PLoS One* 2013; **8**:e68286.
63. Winestone LE, Bukusi EA, Cohen CR, Kwaro D, Schmidt NC, Turan JM. **Acceptability and feasibility of integration of HIV care services into antenatal clinics in rural Kenya: A qualitative provider interview study.** *Glob Public Health* 2012; **7**:149–163.
64. Ong'ech JO, Hoffman HJ, Kose J, Audo M, Matu L, Savosnick P, Guay L. **Provision of services and care for HIV-exposed infants: a comparison of maternal and child health clinic and HIV comprehensive care clinic models.** *J Acquir Immune Defic Syndr* 2012; **61**:83–89.