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Prevention of mother-to-child HIV transmission within the continuum of maternal, newborn, and child health services

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Abstract

Purpose of review—To reach virtual elimination of pediatric HIV, programs for the prevention of mother-to-child HIV transmission (PMTCT) must expand coverage and achieve long-term retention of mothers and infants. While PMTCT have been traditionally aligned with maternal, newborn, and child health (MNCH) services, novel approaches are needed to address the increasing demands of evolving global PMTCT policies.

Recent findings—PMTCT-MNCH integration has improved the uptake and timely initiation of antiretroviral therapy (ART) among treatment-eligible pregnant women in public health settings. Postpartum engagement of HIV-infected mothers and HIV-exposed infants has been insufficient, although alignment of visits to the childhood immunization schedule and establishment of integrated mother-infant clinics may increase retention. Evidence also suggests that the integration of maternal HIV testing into childhood immunization clinics can significantly increase the identification of at-risk HIV-exposed infants previously missed by traditional PMTCT models.

Summary—Targeted service integration models can improve PMTCT uptake. However, as global PMTCT policy shifts to universal provision of maternal ART during pregnancy (i.e., Option B/B+), these findings must be reexamined in the context of increased service demand and systems burden. Intensive evaluation is needed to ensure quality clinical care is maintained both for PMTCT and for underpinning MNCH services.

Keywords

prevention of mother-to-child HIV transmission; PMTCT; HIV; program integration; maternal child health

Introduction

Over the past decade, tremendous gains have been made to prevent mother-to-child transmission of HIV (PMTCT) globally. From 2009 to 2011 alone, the number of new

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annual pediatric HIV infections dropped by approximately one-quarter (1), due to the introduction of highly efficacious antiretroviral regimens and the rapid expansion of comprehensive services (2, 3). Despite significant strides, however, as many as 330,000 infants are still infected with HIV each year, nearly all in resource-constrained settings (4). Recent national and international policy changes hold the promise of bringing more effective interventions to HIV-infected women and their families, but only if innovative ways are found to bridge substantial implementation gaps in a sustainable manner.

Global efforts to reduce pediatric HIV have been hampered by the delivery of effective services to all in need. Attrition has been noted at all points along the “PMTCT cascade,” those steps an HIV-infected mother and her HIV-exposed infant must successfully navigate to gain maximal benefit from the available health interventions (5–7). These include being offered HIV testing, accepting HIV testing, being told of a positive HIV result, being offered antiretroviral prophylaxis or treatment, and adhering to prescribed regimens through pregnancy, delivery, and breastfeeding. Because mothers and infants who fall out of care – or fail to access services at all – experience higher rates of HIV transmission, these inefficiencies directly diminish program impact at the individual and population levels (8, 9).

Many strategies have been proposed to address the problem of attrition along the PMTCT cascade. Chief among them is the integration of PMTCT services within the broader framework of maternal, newborn, and child healthcare (MNCH). There are many convincing arguments for such an approach, focused on the mother-infant pair (e.g., better access to services, reduced visit burden for patients, decreased stigma) and the health system at large (e.g., greater investment in infrastructure and human resource capacity) (10–13). Despite general policy consensus about the value of integrated services, however, the scientific evidence supporting “best practice” models remains limited. In this report, we review the emerging data around service integration and identify priority areas requiring further study in this rapidly evolving field.

Why integrate?

The integration of HIV prevention, care, and treatment into the existing health services has tremendous potential for strengthening systems, improving efficiencies, ensuring sustainability, and broadening the impact of health investments. The rationale from the patient perspective is equally compelling, since this approach provides greater reach into catchment populations and offer patient-level conveniences (e.g., single visit for multiple health needs) that can themselves promote adherence and retention in care. For these reasons, there has been a strong and consistent emphasis on service integration within the context of PMTCT. Early programs relied on the established infrastructure of MNCH for HIV testing, infant feeding counseling, and simple antiretroviral prophylaxis provision (e.g., single-dose nevirapine), particularly during antenatal care. Recent shifts in PMTCT policy mandate similar approaches that extend into the postpartum period. In addition, the Option B + strategy (i.e., lifelong antiretroviral therapy [ART] to all HIV-infected pregnant women) will require expansion of HIV treatment services beyond their current capacity in order to meet the increased patient demand (14). This scale-up may be best achieved through

integrated PMTCT-MNCH services, particularly in rural and remote areas with relatively small patient volumes.

Because of the high degree of service integration existent with most PMTCT programs, to date few studies have examined the comparative advantages and disadvantages of such an approach (15, 16). Emerging data within the field of primary care, however, provide evidence of the incremental benefit possible through integrated models. In South Africa, Uebel and colleagues reported small but significant reductions in mortality at facilities that scored high for total integration, ART integration (i.e., care provided by all nurses in the facility), and internal integration (i.e., care provided by all nurses in the HIV treatment unit) (17, 18). In Zambia, Topp, et al. demonstrated increased time spent by providers during non-HIV clinic visits following integration of HIV services in the primary care setting, highlighting the potential for collateral health benefits (19). However, adoption of such models may come at a cost. In the Zambia study, waiting times increased for all patients at newly integrated sites, delays largely attributed to inadequate staffing levels and longer breaks between consecutive patient visits (20). Investigators in Mozambique found higher rates of attrition among patients attending integrated clinics for more than 6 months (hazard ratio [HR]: 1.75, 1.04–2.94) (21). While integrated health systems may streamline service provision, reduce stigma, and broaden coverage, in most settings such models cannot address existing gaps in health infrastructure such as staffing shortages and physical space (22). Integrated health approaches themselves require investment, perhaps leveraged through existing resources for HIV care (23, 24), to realize their full potential.

Integration in the evolving field of PMTCT

Increasing uptake of antiretroviral regimens during pregnancy

In most high prevalence settings, nurses and midwives in antenatal settings typically dispense zidovudine and nevirapine to HIV-infected women who do not yet require HIV treatment for their own health. As governments have adopted Option B/B+, however, there has been a reluctance to endorse similar practices with three-drug combination regimens, because of inherent complexities of toxicity management and treatment monitoring. Because most programs lack sufficient numbers of certified ART prescribers, the relative merits of integrated antenatal-ART services versus enhanced linkages between the two departments continue to be a topic of debate.

There is emerging data demonstrating the gains that may be associated with integrated services. Killam and colleagues demonstrated a two-fold increase in ART initiation when services were provided in the context of integrated services; however, the overall proportions remained low (14% vs. 32%) (25). These findings were supported by recent work from South Africa, which compared proportions of ART-eligible women initiating HIV treatment during pregnancy through three models: a passive referral system (21%), an enhanced referral system that used peer navigators (49%), and an integrated model where nurse-midwives provided ART care within the antenatal clinic (86%). The integrated model was associated with the shortest median time from eligibility determination to ART initiation (7 days), compared to active (15 days) and passive (29 days) referral, an important consideration for perinatal HIV prevention (26). Early results from the Study of HIV and

Antenatal care Integration in Pregnancy (SHAIP), a 12-site cluster-randomized in rural Kenya, demonstrated similar findings. Women in sites with integrated services started ART quicker and were more likely to remain adherent to their regimens (27, 28). Qualitative work indicated acceptability and general support for fully integrated models, both from patients and health providers (29, 30). It should be noted that these studies enrolled only the subset of women who met general adult ART eligibility criteria. As health policy shifts to the universal provision of maternal combination antiretroviral regimens during pregnancy and breastfeeding (i.e., Option B/B+) (31), the feasibility of these integrated strategies must be reconsidered in the context of higher patient volumes and greater resource demand.

Improving retention in the postnatal period

Although positive health outcomes have been reported with integrated services in the antenatal period, experiences in the postnatal period have been mixed. Separate studies in Zimbabwe and Tanzania demonstrated improvements in the follow-up care for HIV-exposed infants when visits were aligned with the national immunization schedule (32, 33). In Tanzania, however, the proportion of children who received vaccines decreased over time in four rural sites by 23–35%. Interestingly, in four urban sites, the proportion of children receiving vaccinations remained stable or increased over the same time period (33). These early results suggest that, in some settings, the platform for postpartum maternal and/or newborn care may be inadequate to support integrated care, particularly if the mother elects to breastfeed for an extended period.

How best to integrate services for both mother and infant during breastfeeding remains an unanswered question. This likely requires reorganization of current health access points for women and children after delivery. In many settings, postpartum women return to primary “outpatient” clinics for their own care in the months after delivery. Although infants follow an extended immunization schedule, there are often significant gaps between the timed visits. An integrated approach that provides coordinated care for the mother-infant pair holds promise. In a 17-site pilot study in Malawi, investigators reported high coverage of cotrimoxazole dispensation (94%), infant HIV DNA PCR testing (84%), and EID results reporting (87%) among the 220 participating women and their newborns (34). While highly encouraging, the study period (April–December 2010) preceded the era of postnatal PMTCT prophylaxis in Malawi.

The introduction of antiretroviral drug dispensation into the already strained health service platform could also have a negative impact on adherence outcomes. In Uganda, a significant drop-off was observed in the proportion of eligible mother-infant pairs receiving postpartum antiretroviral drug dispensations (i.e., infant nevirapine syrup) over the course of five scheduled appointments – from 90% at the first visit to approximately 10% at the fifth (35). In rural Zambia, similar results were reported among a cohort of women receiving antiretroviral combination regimens following delivery, with one-fifth documented as lost to follow-up by 12 months postpartum (36). In Malawi, early reports from the nationwide roll-out of the Option B+ program demonstrated a greater than seven-fold increase in ART uptake among pregnant and breastfeeding women. However, the program retention at 12

months – a time when most women were still breastfeeding – was only 77%, emphasizing the need targeted retention measures for this population (37).

Identifying at-risk infants missed by traditional PMTCT models

HIV testing during pregnancy represents a critical entry point into care for infected women; for this reason, screening has been incorporated into antenatal care in most settings. Opt-out HIV testing and repeat third-trimester testing are now considered routine in most programs, greatly enhanced by the availability of reliable but inexpensive rapid antibody tests. Diagnostic testing of HIV-exposed newborns has been scheduled to coincide with the regular immunization schedule in most national programs. The first of these tests is almost universally recommended at 4 to 6 weeks of age using DNA PCR technology. Follow-up tests may continue up until 18 months of age, depending on local infant feeding practices.

This traditional model relies on the timely diagnosis of HIV-infected women during pregnancy, with careful postpartum follow up of their HIV-exposed infants. Such an approach fails to identify those who have dropped out of – or never entered – the PMTCT cascade; it also misses women who acquire HIV late in pregnancy. Because childhood immunization typically achieves very high coverage, routine HIV testing of postpartum women in immunization services may greatly improve entry into postnatal PMTCT services (38). In Malawi, the provision of maternal HIV testing in immunization clinics resulted in a more than sevenfold increase in uptake, when compared to the usual venue of the general “under-5” pediatric clinic (84% vs. 11%, $p < 0.001$). Among HIV-exposed children eligible for HIV DNA PCR testing, uptake of infant HIV testing was also significantly higher (100% vs. 90%, $p = 0.03$) (39). Similar findings were observed elsewhere in the region, when maternal and infant HIV testing was incorporated into routine immunization visits (33). By facilitating re-entry into the PMTCT cascade, such approaches provide opportunities to reduce breastfeeding transmission with antiretroviral prophylaxis or treatment and to engage mothers in long-term care.

Challenges and new opportunities in PMTCT service integration

To reach the ambitious global targets for virtual pediatric HIV elimination and improved maternal survival by 2015, programs must achieve near-universal coverage of effective PMTCT services, including retention in care through the breastfeeding period (40, 41). PMTCT integration within existing MNCH platforms is essential to this success; however, despite significant advancements in the recent years, knowledge gaps remain. Below, we highlight key priorities for implementation research.

Rigorous studies are needed to evaluate the presumed benefits that underpin current policy around service integration. Although analogous work has been conducted in other populations, there are characteristics unique to HIV-infected pregnant women and the clinical settings in which they receive care. Given the notable increases in resource demand, further research is needed to confirm the improved health outcomes associated with service integration in the context of Option B/B+. The impact of integration at the level of health systems also requires systematic evaluation, to quantify efficiencies gained both centrally and at the facility level. In addition, detailed assessments of patient-side costs should be

carefully considered. The financial costs born by patients are often overlooked within parallel, vertical service delivery models, but represent an area where integrated models may hold important advantages that could lead to improved adherence and retention in care.

Greater focus must be placed on the quality of services provided. This requires intensive monitoring and evaluation efforts, with clear feedback loops to healthcare providers regarding site and individual performance. A formal management framework is also needed to systematically identify gaps and design meaningful interventions to address them. A number of approaches have shown promise, including continuous quality improvement and rapid response initiatives (42–44). The success of such rigorous methodologies in “real world” settings, particularly among ones of severe resource constraint, relies on careful planning, evaluation, and targeted investments within the public health system. If sustained, such activities can help to ensure that HIV outcomes are optimized without unduly comprising – and perhaps even raising – the standard of foundation MNCH services.

As the duration of antiretroviral coverage has increased through the breastfeeding period (and in some cases beyond), adherence and long-term retention have taken on renewed emphasis in the context of PMTCT (45, 46). Combination strategies to improve adherence and retention require further evaluation; “minimum packages” of proven interventions (e.g., two-way SMS reminders) should be incorporated to enhance institutional follow-up in antenatal, delivery, and postpartum care. Effective strategies are also needed to ensure effective transition of postpartum mothers from the MNCH units to adult HIV treatment departments, either during or after breastfeeding. HIV-exposed infants who become HIV-infected require similar linkage strategies to ensure rapid initiation of treatment (47).

Service platforms created by Option B+ may serve as entry points for other family members, particularly in rural areas with limited access to HIV treatment. Successful engagement of male partners has been shown to improve maternal and infant outcomes (48). Models that directly provide HIV care and treatment services to partners through the MNCH platform could provide further benefit, particularly around adherence and retention. Implemented effectively, such an approach would enhance the strengths of integrated health systems and provide a framework for further scale-up of general adult and pediatric HIV services.

Conclusion

PMTCT integration has been long supported by policy recommendations, but justifications for such an approach, while compelling, have been based on a limited body of evidence to date. Early studies have shown improvement in uptake when PMTCT is provided alongside routine MNCH services, but these positive results are yet to be confirmed in the setting of increased ART demand. A better understanding of health systems efficiencies generated by PMTCT service integration is also urgently needed, to provide important empirical data to support long-held assumptions. Ultimately, the success of integrated programs will be heavily dependent upon upfront health systems investments and meaningful community engagement to increase institutional healthcare. Properly coordinated and effectively managed, the integration of PMTCT within the MNCH framework can broaden the reach of

HIV prevention, care, and treatment initiatives, while raising the quality of healthcare across the entire service platform.

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Key points

- To date, studies have demonstrated improvements in service uptake following PMTCT-MNCH integration, typically through partial (vs. comprehensive) integration models.
- However, few have evaluated service integration in the context of universal maternal combination antiretroviral therapy (i.e., Option B/B+), an approach that significantly increases resource and health system demands for PMTCT.
- For programs implementing integrated service delivery models, ongoing monitoring and evaluation is critical to ensuring quality clinical care, both for PMTCT and for foundation MNCH services.