REVIEW PAPER

Setting up standardized interventions for HIV serodiscordant couples: a guide for healthcare providers and researchers

Mona Larki[1,2], Javad Moghri[3,4], Narjes Bahri[5], Robab Latifnejad Roudsari[1,2]

[1]Nursing and Midwifery Care Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Social Determinants of Health Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
[4]Department of Management Sciences and Health Economics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran
[5]Department of Midwifery, School of Medicine, Social Determinants of Health Research Center, Gonabad University of Medical Sciences, Gonabad, Iran

Abstract

Introduction: In countries with generalized epidemics of human immunodeficiency virus (HIV), the negative individuals in serodiscordant relationships constitute the largest population at risk. This study was carried out to investigate setting up standardized interventions for HIV serodiscordant couples.

Material and methods: This narrative review was conducted based on the scale for assessing narrative review articles (SANRA). English and Persian databases, including Cochrane Library, PubMed, Scopus, Web of Science as well as Magiran, and SID, were searched. Additionally, relevant guidelines from WHO, UNAIDS, CDC, and UNFPA were reviewed. The following key words were used: "HIV Positive Prevention", "AIDS Prevention", "HIV Seronegative Prevention", and "Serodiscordant Partners". The search was performed by two reviewers till April 7, 2022. Sixty-seven articles and six guidelines were included in the final review.

Results: Biomedical and non-biomedical interventions among HIV serodiscordant couples were analyzed and compared. Findings were categorized into two sections: 1) essential health interventions comprising biomedical (micro-meso level), behavioral (micro-meso level), and structural (macro level) interventions; and 2) service delivery models including facility-based and community-based approaches. Key biomedical interventions included HIV screening and safe conception. Behavioral interventions comprised medication adherence, and HIV status disclosure. Crucial structural interventions consisted of human rights laws, stigma reduction, and promotion of gender equality.

Conclusions: The current literature mainly focused on biomedical services, and insufficient attention was given to other aspects. Combining biomedical approaches with behavioral and structural components, emphasizing couple-based strategies as part of a community-driven approach, will help to create positive outcomes for the couples, families, and community.

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Key words: HIV, AIDS, HIV serodiscordant couples, health services.

Introduction

Address for correspondence: Robab Latifnejad Roudsari, Nursing and Midwifery Care Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, e-mail: rlatifnejad@yahoo.com

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Human immunodeficiency virus (HIV) continues to be a significant global public health concern, having resulted in approximately 42.3 million deaths to date [1]. In 2023, fewer individuals were infected with HIV than at any other time since the late 1980s [2]. United Nations Joint Program on HIV/AIDS (UNAIDS) indicated in its most recent report (2024) that there are 39.9 million people living with HIV (PLHIV) around the world [3]. Since there is no cure for this disease, the priority is HIV prevention through interventions, which inform people about strategies to stop the spread of infection, and provide reasons for engagement in healthy behaviors [4, 5]. Serodiscordant couples are a crucial population for HIV prevention programs [6]. In countries with generalized epidemics, HIV-negative individuals in serodiscordant relationships can constitute the largest population at risk [7]. HIV serodiscordant couples refer to a relationship with one HIV-positive and one HIV-negative partner [8]. It is anticipated that 75% and 37% of patients with serodiscordance live in countries with low and high HIV prevalence, respectively [8]. The proportion of serodiscordant intra-couple transmission in regions with high HIV prevalence ranges from 13% to 55% of new HIV infections [9]. These couples face various social, sexual, and relationship issues. Sources of conflict can include disease acquisition, status disclosure, familial disputes, financial pressures, irregular condom usage, violence, fertility decisions, and death [10-12].

While biomedical strategies for HIV prevention, such as test link, treatment strategies, and pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP), are effective tools for HIV prevention in this population, and they should be integrated with evidence-based behaviors, i.e., structural interventions, which improve the access to healthcare, reduce associated costs, ensure broad-scale delivery, and reduce stigmatization [13]. Given these improvements, the generation of new care models is an agreed priority in the HIV/AIDS context, because traditional HIV care approaches provided mainly by HIV specialists may no longer meet the needs of patients [14]. Furthermore, achieving the UNAIDS targets requires a significant expansion in service coverage that is not possible using conventional facility-based HIV programs [15, 16]. Providing medical, psychological, spiritual, and social services for PLHIV and their families requires formal engagement in community and home-based care systems [17].

Considering that HIV serodiscordant couples play a significant role in preserving the global HIV epidemic by sexual contacts [18], it is important to define optimal interventions for effective responses in this population [6]. Healthcare providers need to be aware that the effectiveness of biomedical interventions in HIV-related context depends on behavioral factors also. The response to HIV, in addition to its individual dimension, is influenced by social, economic, and legal political systems. Therefore, to lower the risk of HIV, broader parts of society have to be strengthened, such as social norms and legal rights [19].

The current review study was conducted to provide researchers and healthcare providers with a comprehensive picture of standard interventions required in HIV serodiscordant couples.

Material and methods

This narrative review was carried out based on the scale for assessing narrative review articles (SANRA) to investigate approaches, which are required for setting up standardized interventions for HIV serodiscordant couples. SANRA has six different items, which covers explanation of the following topics: 1) the importance of the subject matter for the readers; 2) aims of the review; 3) a comprehensive summary of the document search process; 4) referencing; 5) scientific evidence usage; and 6) suitable reporting of the findings [20].

Search methods and strategies for identification of studies

The databases examined for pertinent literature comprised English records from PubMed, Scopus, Web of Science, and Cochrane Library as well as Persian databases, such as Magiran and SID. Furthermore, guidelines of WHO, UNAIDS, CDC, and UNFPA on healthcare services for PLWH and HIV serodiscordant couples were explored. Reference lists of considered studies were also assessed for additional references. Key words used for the search were: "HIV Positive Prevention", "AIDS Prevention", "HIV Seronegative Prevention", "Serodiscordant Partners", Serodifferent Couple", "Couple-Based Intervention", 'HIV Intervention", and "HIV Positive Risk Reduction". To increase precision in the search process, Boolean terms (AND/OR) were employed to separate the key words as well as medical subject headings (MeSH). The study's methodology was not limited to obtaining the most relevant health services in HIV serodiscordant couples article. The search was performed without time limit, and ended on April 7, 2022. The recommendations presented in the article were double checked on March 20, 2025.

Inclusion criteria

1. Studies with evidence regarding health services in HIV serodiscordant couples. 2. Guidelines for healthcare services in HIV serodiscordant couples. 3. Guidelines for health interventions in PLWH.

Exclusion criteria

1. Language other than English or Persian. 2. No access to full-text articles and guidelines. 3. Letter to editors or conference abstracts.

Data extraction and management of studies

Research selection strategy consisted of four stages: identifying all related literature, screening articles based on titles and abstracts, examining full-text eligibility, and including eligible articles in the review process [21]. Sixty-

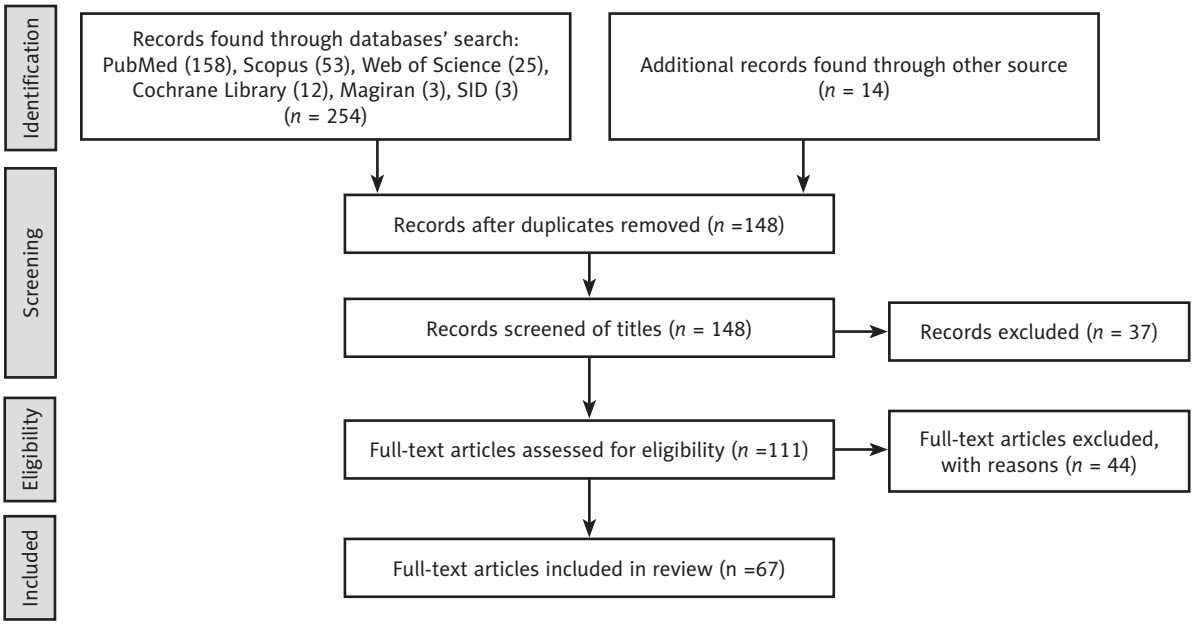

Figure 1. Flowchart of study selection

seven articles and six guidelines were considered for the review process. The number of documents retrieved and included at each stage is depicted in Figure 1. Two reviewers (ML and JM) independently checked the titles and abstracts of all the publications retrieved to identify inclusion criteria. The data was also extracted by two reviewers (ML and NB), and any disagreement was resolved by a senior researcher (RLR). Finally, the results were categorized according to the main subjects related to the topic under review.

Ethical considerations

The authors considered ethical issues, such as avoiding plagiarism, ensuring robustness in the acquisition of relevant data, preparation, and submission of data.

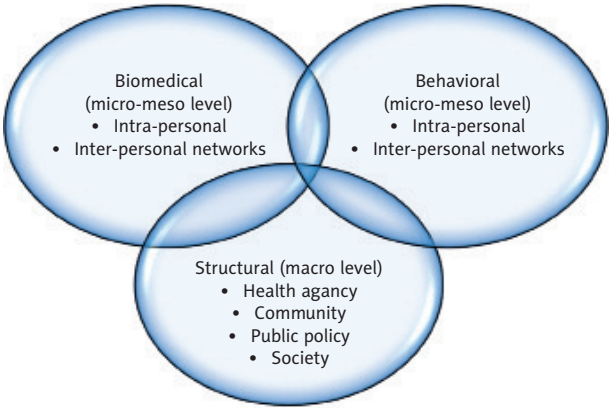

Figure 2. Dimensions of combination services in serodiscordant couples

Results

The findings were categorized into two sections: essential health interventions and service delivery models.

Essential health interventions

For the study population, the essential services were divided into three levels, such as biomedical (micro-meso), behavioral (micro-meso), and structural (macro) (Figure 2).

Biomedical interventions (micro-meso level)

The main type of biomedical interventions involve HIV screening, the initiation of antiretroviral treatment (ART) in PLHIV, delivery of PrEP, provision of PEP, voluntary medical male circumcision (VMMC), treatment of sexually transmitted infections (STIs), safe conception, and family planning.

1. HIV screening: Is essential, especially if the HIV-positive partner is not on ART, has been on ART for less than six months, or has not been virally suppressed. Additionally, HIV re-testing is performed based on the risk of exposure in the past 3 months [22].

2. The initiation of ART in PLHIV: A study on HIV-1-serodiscordant couples found that early initiation of ART among HIV-positive partners is correlated with a 93% decrease in the HIV-negative partners' risk of infection relative to postponed ART [23]. Furthermore, another study found that HIV-infected people, who are treated with ART and achieve viral suppression, are 94% less likely to transmit HIV than people with undiagnosed HIV [24].

3. Delivery of PrEP for HIV-negative partner: PrEP is the use of antiretroviral medications by an individual without HIV to maintain blood and genital drug levels sufficient to prevent the acquisition of HIV [9]. PrEP should be administered to HIV-negative individuals in serodiscordant relationships before the HIV-positive partner achieves viral suppression with using ART. To account for potential delays in appointments or in obtaining viral load results, the average length of PrEP utilization by the serodiscordant partner should be conservatively estimated at seven months [25]. The Food and Drug Administration (FDA) approves a single daily dosage of a combination of emtricitabine (FTC) and tenofovir/disoproxil/fumarate (TDF) for PrEP [26]. ART and PrEP application reduces the risk of transmission to 0.5% among adherent HIV-uninfected individuals who are in serodiscordant relationships [27, 28].

- Discontinuing PrEP: An HIV-negative person in serodiscordant relationship can discontinue PrEP when the HIV-positive partner on ART for more than 6 months achieves sustained viral load suppression (condoms should still be used consistently). Even though the positive person being virally suppressed, the HIV-negative person can continue to take PrEP, depending on the couples' choice [22].
- Methods of PrEP: There are two approaches: the daily use of PrEP tablets and "on-demand", meaning some people may use PrEP when they expect potential HIV exposure [29].

4. Provision of PEP: Prescription of PEP should be started as early as possible, ideally within the first 2 hours but not beyond 72 hours after exposure. A complete course of PEP should be administered for 28 days [30]. Animal experiments found that implementing PEP after 12, 24, or 36 hours of exposure is much more successful than initiating PEP after 48 or 72 hours of exposure [31].

- PEP follow-up: PEP monitoring and medical assessment should be provided to all exposed individuals, regardless of whether or not they obtained PEP. People who frequently seek PEP should be considered for PrEP. After a week of taking ART, patients should be examined for their adherence, and any side effects, such as nausea or diarrhea, should be treated without changing the protocol [22, 30, 32, 33]. Follow-up tests using enzyme immunoassay must be performed firstly at the time of exposure, and 6 weeks, 12 weeks, and 6 months post-exposure, even if PEP was refused [31-33]. As daily PrEP can be more preventive than repetitive episodes of PEP, people who frequently use PEP must be recommended for PrEP [31, 33].

5. VMMC in HIV-negative males: In areas where HIV-1 infection is prevalent and circumcision is unusual, the WHO and UNAIDS suggest that male circumcision should be part of the standardized HIV-1 prevention program [34]. Safe male circumcision (SMC) reduces the risk of HIV acquisition by approximately 60% [22]. Circumcision decreases the risk of HIV transmission to the HIV-uninfected male partner by 38-66% over 24 months, assuming sufficient healing time before re-starting sexual activity [35-37]. Regarding circumcision status, similar results were reported from a research published in Uganda, where regulation of viral load was important in reducing the rate of transmission in heterosexual and discordant couples [38].

6. Treatment of STIs: STIs, which induce ulceration, can accelerate HIV acquisition [39]. Through different mechanisms, such as the existence of genital ulcers, local inflammation, or the presence of STI in an exposed individual, STIs enhance couples' vulnerability to HIV. For example, the existence of syphilis in an individual infected with HIV raises the amount of virus in the genital secretions and thus, the possibility of developing HIV by his/her partners [39]. There is substantial evidence from observational studies showing an increased risk of contracting HIV when infected with curable STIs and genital herpes [40, 41]. Therefore, STIs prevention, diagnosis, and treatment programs provide several methods to synergize with HIV protection, care, and treatment attempts [42].

7. Safe conception: In serodiscordant couples who wish to have children, the following care should be considered during pre-conception, pregnancy, and postpartum.

- There are strategies to ensure safe pregnancy for women living with HIV in serodiscordant relationships. These consist of: ART employed by the woman with HIV to diminish her viral load; oral PrEP utilised by the HIV-negative partner; condom usage during the woman's non-peak fertility time; screening and treatment of STIs in both partners; voluntary medical male circumcision to mitigate HIV transmission; and manual insemination [43].
- Pre-conception management and counseling: The Centres for Disease Control and Prevention recommended that the HIV-negative spouse undergo testing every three months while the couple attempts to conceive through unprotected sexual contact. For individuals with different HIV statuses attempting conception through unprotected sexual intercourse, when the HIV-positive partner fails to achieve viral suppression or when their viral suppression status is uncertain, it is advisable to provide PrEP to the HIV-negative partner to mitigate the risk of sexual HIV transmission [44]. Beginning ART before conception not only stops potential transmission between partners, but it also decreases perinatal HIV transmission [19]. If conception does not take place within 12 months, physicians should initiate an infertility evaluation, including a semen analysis. Using the sperm washing method can be another acceptable method in this case, but with effective treatment of the HIV-infected person, preventive treatment before contact with the partner is not recommended [44]. According to CDC guidelines, unprotected sexual activity is associated with no risk of HIV sexual transmission in serodiscordant couples where HIV partner is on ART and has undetectable viral load. To demonstrate effective (sustained) viral suppression, two plasma viral load readings below detectable levels, reported at least three months apart, are needed [45, 46]. HIV-negative partner may be given PrEP in serodiscordant couples who wish to conceive, where viral suppression status is uncertain or has not been successfully achieved, and unprotected sexual activity may be limited

to peak fertility time in each cycle [47, 48]. The chance of pregnancy can be optimized by timing condom-less sex to coincide with ovulation (peak fertility). The best way to learn when is the most appropriate time to get pregnant is to use an ovulation kit [49].

- Positive male/Negative female: The optimal alternative for an uninfected female to conceive with a HIV-infected male is sperm insemination from a HIV-negative donor [50]. If sperm of a HIV-negative man donor is unacceptable, physicians can also recommend sperm preparation techniques, such as sperm washing, so that the sperm is confirmed HIV-negative and can be inseminated either by intra-vaginal or intra-uterine procedures after intra-cytoplasmic sperm injection [51]. Therefore, the technique that provides the lowest risk of transmission is sperm washing with intra-uterine insemination or in vitro fertilization [52]. When a male partner has not had a detectable viral load for a long time and a female partner uses PrEP to reduce transmission, natural conception can happen with planned sexual activity during the fertile period [53].
- Negative male/Positive female: Self-insemination by a HIV-positive female eliminates the likelihood of HIV transmission to her seronegative partner, since it inhibits contact with the female's vaginal fluids. In situations where a positive female has an undetectable viral load for a prolonged time, the use of ART by her HIV-negative male partner is also a potential approach to use, if it replaces unprotected sexual intercourse during the period of fertility [54].

8. Care during pregnancy: Repeated HIV testing should be applied to HIV-negative pregnant women at high risk of acquiring HIV during the third trimester, preferably between 28 and 36 weeks [55]. HIV-negative women with HIV-positive partners should get counselling on condom utilisation to mitigate the risk of HIV being transmitted sexually if their partner lacks sustained suppression of the virus [44].

- Postpartum management: Postpartum compliance with ART is always difficult, and it is important to emphasize the continuation of postpartum ART in HIV-infected women. The choice of ART should be carefully tailored in the postpartum period according to factors, such as the preference for possible births, contraceptive selection, and potential drug interactions. Patients should be informed about their partner's contraceptive methods and PrEP as well as about ovulation due to lack of breastfeeding [56].

9. Family planning: Based on a systematic review published in the Lancet, the majority of research evaluating the usage of oral contraceptive tablets indicated no significant correlation with HIV acquisition [57]. Another review showed hormonal contraceptives have not demonstrated an impact on the progression of HIV. The effect of hormonal contraceptives on HIV transmission and acquisition is still unclear, especially with injectable variants [58]. In a study conducted by WHO, there was insufficient evidence to conclude that hormonal contraceptives have a negative effect on HIV or its transmission. The review clearly demonstrated that HIV-positive women who use hormonal birth control should always use condoms [59].

Behavioral interventions (micro-meso level)

AIDS is one of the behavioral diseases; therefore, providing effective behavioral interventions is of priority [60]. The key behavioral interventions include education on condom use, couples HIV testing and counseling (CHTC), medication adherence, and HIV status disclosure.

1. Education on condom use: Education is one of the most fundamental interventions in the context of human damage prevention and the main component of health promotion [61, 62]. The use of condoms has become the key prevention method, and is highly successful in preventing the spread of HIV and other STIs, with a favorable cost-benefit ratio. Recent studies revealed that among serodiscordant couples with condom-less intercourse, related HIV diseases were not diagnosed when a HIV-positive partner had a steadily reduced plasma viral load [63, 64]. In a meta-analysis, existing evidence reviewed by the CDC indicates that female condoms (or an exchanging combination of female and male condoms) can provide pregnancy safety and STIs levels equivalent to those of latex male condoms [65]. However, this implication was not observed leading to a specific suggestion, according to the authors. The ambiguity of this conclusion is expressed in the FDA classification for female condoms, and only advocates their use in mitigating circumstances for the prevention of diseases (i.e., when a latex male condom cannot be used) [66].

2. CHTC: CHTC is a public health strategy where two or more individuals undergo HIV testing services concurrently when they are in or expect to be in a sexual relationship. This facility enables the link to HIV medical compliance, HIV status disclosure, PrEP, and/or other relevant services. It can help individuals to modify their sexual activities to prevent HIV acquisition or transmission as well as help maintaining HIV-negative partners from acquiring HIV in serodiscordant relationships. Researchers have described a decrease in the rate of sexual partners, and an improvement in condom use, even among serodiscordant couples, after testing collectively. Generally, CHTC strategies for couples can be more effective than individual testing, especially for those knowing that their partners are serodiscordant [67-71].

3. Medication adherence: Sharing medical adherence responsibilities together (SMART) is a couple-based approach for discordant couples with inadequate medication adherence of a HIV-positive partner. This strategy provides couples with information about the importance of compliance in reducing viral resistance. Also, it contains cognitive-behavioral components to encourage healthy activities and problem-solving strategies to identify and overcome obstacles to adherence. Training on the importance of adherence to prevent viral resistance, health maintenance, recognition of non-adherence patterns, and increasing mutual social support for good health outcomes, are the core components of SMART couples [72]. SMART couple programs for partners are preferably delivered by a professional social worker or counsellor, HIV case man-

ager, health instructor, or nurse with competence in working with couples and presenting adherence counselling and training [72, 73].

4. HIV status disclosure: An essential component of prevention strategies was assumed to be the disclosure of HIV status to sexual partners; it was theorized that disclosure is correlated with an increased condom usage or adherence to sero-adaptive activities, thus decreasing the risk of HIV transmission [74, 75]. The CDC noted the significance of serostatus recognition through testing and serostatus disclosure in reducing the risk of transmission in serodiscordant couples, provided in their guidelines for prevention strategies [75, 76].

Structural interventions (macro level)

Structural approaches adjust the environment in various ways to encourage or promote healthy activities, or minimize the risk without relying on an individual behavior change [77]. The key structural interventions include human rights laws and stigma reduction as well as promoting gender equality.

1. Human rights laws and stigma reduction: According to the UNAIDS and World Health Organization (WHO), the fear of stigma and prejudice is the key reason why people are hesitant to undergo screening, reveal their HIV status, and take antiretroviral drugs (ARVs) [78, 79]. In addition to human rights violations, discrimination against people living with HIV or those suspected of having HIV leads to violations of their other human rights, such as access to healthcare, dignity, and the right to work [80]. Responding to stigma entails addressing actionable drivers of stigma as soon as possible, putting stigmatized groups at the center of the response, involving opinion leaders, and forming alliances between affected populations and opinion leaders [81]. A well-documented strategy for eradicating stigma is the utilization of specific programs, which emphasize the interests of people living with HIV. PLHIV will be motivated to take action if their rights are violated, in addition to being aware of their rights [79].

2. Promoting gender equality: Gender inequality, such as intimate partner abuse, increases women's and girls' physiological susceptibility to HIV, preventing them from receiving care. Intimate partner violence, inequitable regulations, and harmful traditional structures, all contribute to men and women having unequal power dynamics. Women's choices, resources, access to information, health and social care, training, and employment, are all affected by these dynamics [82].

Service delivery models (SDMs)

SDMs consists of health facility-based and community-based approaches.

1. Health facility-based model: The foundation of HIV treatment and care is the facility-based model. Majority of PLHIV in health facilities are screened and initiated into treatment. Additionally, health facilities provide an opportunity to initiate treatment, and testing PLWH attending for other co-morbidities. They also operate as points of reference for community programs [83]. The details of service delivery are listed in Table 1.

2. Community-based model: Community-based programs are initiatives, which are planned, delivered, and managed by members of the community [84]. The aims of community-based approaches are to increase awareness of conception and childbearing among women and men living with HIV, among couples, families, and neighbors; the programs can reduce stigma, encourage equity and inclusion as well as create broad societal norms and frameworks to support the achievement of reproductive goals and rights of serodiscordant couples [17, 85]. These interventions have been shown to increase the uptake of HIV testing, increase the number of first-time volunteers, recognize people earlier in the process of HIV infection [9, 10], and enhance the link to care [71]. Advantage of this model is that its programs are sometimes more flexible than those of facility-based programs. This leads to increased access to HIV testing for patients (reduced transportation costs to VCT sites or health facilities, and convenience for family members). Additionally, this approach enhances patients' privacy, helps reducing stigma, encourages people to change their behavior, reduces HIV transmission, increases access to HTC for couples/partners, and improves their disclosure process. It offers an opportunity to resolve HIV discordance among couples/partners, encourages early diagnosis of HIV, increases compliance to treatment and care, minimizes the workload of health practitioners, and improves local participation [86, 87]. The details of service delivery are listed in Table 1.

Discussion

The current literature review focused on HIV prevention programs and interventions among HIV serodiscordant couples. As a framework for conceptualizing our results, we adopted a system-level model (micro–meso–macro). The levels include micro (individual, team), meso (organization, hospital), and macro (social context) [89]. Interaction between health systems and patients or communities is reflected in the degree of micro-service delivery. At the meso level, these policies are executed as explicit operational plans, and are impacted by the setting of organization, strength of competing interests, and ability to establish coalitions between numerous institutions to achieve a goal at this level. The macro level is about national policies and strategies, where decisions are made about priorities, policies, and interventions, and resources are provided to put them into action [90].

The multifaceted nature of HIV indicates the need for accountability and comprehensive cooperation among various organizations in society, which have the necessary human and financial capacity to provide essential infrastructure in dimensions of prevention, treatment, and support. It is important to remember that for these couples, the principle

Table 1. Essential package of integrated interventions for HIV serodiscordant couples [83, 84, 87, 88]

Model	Location	Possible services/Interventions
Facility-based care	• Hospital • HIV outpatient clinic • Day clinic	Information and training on HIV prevention
		HIV testing and counseling Testing and consulting with a provider Testing and diagnosing an infant Family testing and counseling Encourage disclosure of situation to sexual partner
		Prevention of mother-to-child transmission (PMTCT) of HIV Information and counseling on preventing HIV transmission Referral for perinatal care Sperm washing for intrauterine Insemination, *in vitro* fertilization, or intracytoplasmic sperm injection Determining the time of sex without a condom Family planning for pregnant women living with HIV/AIDS Utilization of antiretroviral drugs to prevent mother-to-child transmission of HIV Counseling for infant feeding HIV treatment and care for infected mothers
		Prevention of sexual transmission Sexually transmitted infection screening and management Safe sex counseling and risk reduction Advertising and providing condoms (horizontal transmission) Medical and voluntary male circumcision
		Treatment as prevention Antiretroviral treatment for a positive partner Pre-exposure prophylaxis for a negative partner
Community-based interventions	• Outreach care • Home-based care • Stand-alone HIV testing and counseling • Mobile services • Drop-in centers • Venue-based approaches	**HIV testing and counseling** Voluntary HIV counseling and testing Home-based testing and counseling of sexual partner
		Community-based prevention Prevention information and education Preventive interventions for vulnerable and at-risk populations
		Treatment and care Psycho-social support Peer support groups Providing medications at home
		HIV prevention outreach Peer-based information and education Sexual and reproductive health services and sexually transmitted infections for vulnerable girls and women Provision and exchange of syringes and sterile needles Referral for specific prevention services
		HIV/AIDS treatment and care Integration of antiretroviral therapy treatment, tuberculosis diagnosis, and prophylaxis in outreach programs

of prevention and treatment, along with structural components, is very important.

Almost all biomedical interventions have a behavioral dimension. Individuals must decide to accept services, such as HIV testing, PrEP, and VMMC, as a proposal. Moreover, they must obey to service-related guidelines; for instance, men who obtain circumcision services must remain sexual abstinence for six weeks after surgery, and effective adherence must be maintained by people taking antiretroviral medications. As a result, the need for behavior change strategies was not ignored; rather, it increased [91]. Therefore, the effectiveness of biomedical interventions depends on behavioral factors, which influence adherence to medication and initiation of treatment [92]. Furthermore, it was shown that the response to HIV, in addition to having deep roots in the human dimension, is influenced by social, economic, and legal political systems. Therefore, minimizing the risk of HIV requires strengthening broader societal components,

such as economic opportunities, social norms, and gender roles as well as legal rights [19]. Focusing on sexual behavioral changes includes various approaches, such as avoiding the initiation of first intercourse, decreasing the number of sexual partners, raising the number of sexual activities that are protected, counseling and HIV testing, encouraging adherence to biomedical HIV prevention techniques, reducing needles and syringe sharing, and reducing drugs utilization. Therefore, it was demonstrated that behavioral approaches influence the transmission of HIV, but the lack of sustainability of such approaches makes it difficult for them to achieve significant effects within the population [4].

The health system is successful in establishing policies based on the biomedical paradigm, because it produces and publishes guidelines and programs, which are in line with current worldwide standards. However, when setting non-biomedical interventions, their work is not perceived as creative or good. Health policy-makers must recognize that a response to the threat of HIV requires public mobilization, and that all sectors of society, including non-governmental organizations (NGOs), must be included in policy formulation and implementation, with authority proportional to capacity. Given that NGOs are one of the most important partners in the fight against HIV/AIDS, the government should be willing to help, and make more efforts to improve the private sector and civil society's ability to develop and implement new policies.

Behavioral interventions mostly include inter-personal and media interaction, and financial and other resources can also be included. Furthermore, awareness, attitudes, risk perception, norms, and demand for HIV services and skills, are commonly discussed to address behavioral interventions [91, 93]. For this purpose, community outreach, schools, health facilities, offices, or other environments may be implementation platforms [91]. The involvement into community consists of both formal and informal programs, such as community or faith-based organizations (CBOs, FBOs), community health workers under the management of district health networks or non-governmental organizations, national tuberculosis scheme supporters of DOTS, and peer outreach programs for high-risk populations as well as home-based and palliative care [61, 94]. Couple-based interventions, in addition to CHTC, can be more successful in reducing the risk of transmission among serodiscordant couples than individual-focused interventions [95]. Other strengths of couple-based approaches are that they recognize the distinctive social, cultural, and biological vulnerabilities and susceptibility to HIV that women face [96]. While commonly conducted at the dyadic level, group-level and couples-focused approaches are also appropriate and efficient [8]. Therefore, special interventions are needed, both by facility-based and community-based programs, to recognize and provide support [7].

There is a wide gap in behavioral HIV prevention approaches regarding successful couple-based interventions, including primary prevention for serodiscordant couples who did not recognize their HIV status, and couples who are both HIV-negative but vulnerable to transmission. These gaps are significant factors in minimizing the risk of HIV both domestically and internationally [96]. Several systemic barriers, such as high caseloads of service providers, time limits on engaging the couple, insufficient resources for organizations to extend work with couples, and healthcare and insurance laws, must be addressed by the couple-based preventive interventions, which may not recognize a couple as a single "client". Furthermore, health insurance portability and accountability act (HIPAA) regulations prohibiting sharing of information with others as well as lack of educational and technological support in the use of couple modalities, must be addressed [97].

HIV in couples have physical, social, and psychological dimensions. Therefore, in addition to focusing on biomedical concerns in couples, which is what most health programs provide, service delivery should also consider structural interventions. Human behavior is profoundly rooted in, and influenced by, a broader political, economic, and legal political systems, which are promoted in HIV response. As a result, lowering of HIV risk entails systemic changes, including economic opportunities, social norms, gender roles, and legal freedom. The lack of consensus on the concept and implementation of systemic change hindered the progress of integrating structural approaches into HIV prevention. Structural interventions are generally regarded as long-term strategies going beyond HIV prevention, because they resolve deeply rooted social, economic, and political factors, which are difficult to modify [98]. A combination of preventive programs is a systemic approach to HIV prevention utilizing evidence-based biomedical, behavioral, and structural strategies to target those at risk of contracting HIV, while addressing cultural and institutional factors contributing to that risk [74, 75]. These programs focus on unique aspects of each environment, such as infrastructure, local culture, practices, and HIV-infected populations. Individuals, communities, and populations will all benefit from these approaches [99].

To achieve universal access, decentralization of HIV/AIDS services at health facility and community levels, and their alignment with other priority health initiatives, are the key challenges. These facilities are operated by various programs and staff, resulting in inefficient utilization of resources and an increased patient burden. With structured protocols and training for health professionals, integrating these programs at the health facility level makes co-management of patients more effective, and improves family-based care that meets the needs of adults, teens, and infants [88]. In particular, in places and communities where AIDS is a cultural taboo, and discrimination causes people to turn down services and obtain scanty care and treatment, it might be helpful to bring services to people's homes. Therefore, it is important to pay attention to service decentralization, not to limit service delivery models to healthcare centers, and to design services based on the community and home by providing infrastructure.

"A strong and integrated system with a complete understanding of the HIV challenges and their implications for deve-

lopment and national security is required to design an appropriate national response to HIV in serodiscordant couples. This insight and understanding will enable policy-makers to make better policy decisions. To do this, we need a multisectoral strategy to design and implement combined interventions. This requires a stronger commitment from the government at political, technical, and operational levels" [88].

The strength of our research is that all the interventions required by serodiscordant couples were taken into consideration, which can be regarded as a reference for healthcare providers. We investigated the sources published in English and Persian languages within the framework of this research, and therefore might have missed important sources published in other languages. We suggest conducting quantitative and qualitative studies from the perspectives of healthcare service providers and serodiscordant couples to assess barriers in receiving behavioral interventions, such as CHCT and biomedical interventions, i.e., safe conception.

Qualitative studies with policy-makers are also required to explore the challenges and facilities needed to implement structural reforms in serodiscordant couples. Scholars in different countries should conduct quantitative research to observe how appropriate and effective the current services in their countries are for serodiscordant couples, and what dimensions of the services need to be changed and improved.

Conclusions

Combining biomedical approaches with behavioral and structural components, emphasizing couple-based strategies as a part of community-driven approach, should be considered in service delivery. Couple-based approaches in the service delivery process with an emphasis on healthy lifestyles, behavioral change, and mutual support, have positive consequences for the individual, newborn/child, family, and community. These strategies establish a framework for couples to address their shared needs to safeguard one another from HIV transmission, protect one another's health, and establish a secure environment for discussing challenging issues such as sexual relationships and applying negotiating skills. It should be highlighted that for couple-based interventions to succeed in the real world, a culture shift from focusing on the individual to concentrating on the couple must occur, with an emphasis on overcoming organizational and financial constraints.

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