Arguments for and against HIV self-testing

Brian R Wood1
Carl Ballenger1
Joanne D Stekler1,2
1Division of Allergy and Infectious Disease, University of Washington, Seattle, WA, USA; 2Public Health, Seattle and King County HIV/STD Program, Seattle, WA, USA

Abstract: Approximately 60% of human immunodeficiency virus (HIV)-infected individuals are unaware of their infection, and stigma and discrimination continue to threaten acceptance of HIV testing services worldwide. Self-testing for HIV has garnered controversy for years and the debate reignited with the approval of a point-of-care test for over-the-counter sale in the US in 2012. Here, we present arguments for and against HIV self-testing. The case in support of HIV self-testing contends that: the modality is highly acceptable, especially among the most at-risk individuals; self-testing empowers users, thus helping to normalize testing; and mutual partner testing has the potential to increase awareness of risk and avert condomless sex between discordant partners. Arguments against HIV self-testing include: cost limits access to those who need testing most; false-negative results, especially during the window period, may lead to false reassurance and could promote sex between discordant partners at the time of highest infectivity; opportunities for counseling, linkage to care, and diagnosis of other sexually transmitted infections may be missed; and self-testing leads to potential for coercion between partners. Research is needed to better define the risks of self-testing, especially as performance of the assays improves, and to delineate the benefits of programs designed to improve access to self-test kits, because this testing modality has numerous potential advantages and drawbacks.

Keywords: HIV, AIDS, self-testing, diagnosis, screening

Introduction

Globally, an estimated 60% of human immunodeficiency virus (HIV)-infected individuals remain untested and unaware of their serostatus.1 Access to testing remains an issue in many regions and fear of stigmatization and discrimination continues to threaten acceptance of HIV testing services worldwide.2 In the US, approximately 20% of the more than one million persons living with HIV remain undiagnosed, and these individuals are responsible for nearly one-half of the new HIV transmissions in the country.3,4 Since 2006, the US Centers for Disease Control and Prevention have recommended routine HIV screening for patients between the ages of 13–64 years in all health care settings, as well as repeat testing at least annually for those at high risk for infection; however, the uptake of universal screening has been slow and hampered by numerous barriers.5,6 Accurate, widely acceptable, and easily accessible HIV screening methods are needed to increase the rates of diagnosis, allow for early antiretroviral therapy for the health of the infected individuals, and decrease the likelihood of transmission to susceptible persons.7

Proposals for HIV home tests generated controversy in the mid-1980s and debate reignited with the approval of a rapid oral swab kit for over-the-counter (OTC) sale in
the US in 2012. On one hand, self-tests have the potential to reach persons who otherwise may never seek testing and are at highest risk for HIV infection, to empower users and help normalize screening, and to facilitate mutual partner testing and thus avert unprotected sex between discordant partners. On the other hand, cost and access, possible missed early infections due to the long window period, undiagnosed bacterial sexually transmitted infections (STIs), challenges to counseling and linkage to care, and the potential for coercion remain sharp criticisms to this mode of screening. Here, we review the history and performance of HIV self-tests and the arguments for and against this testing option (Figure 1).

**HIV self-testing: history and availability**

Self-testing for HIV involves collection of a saliva or finger stick blood sample by an individual, either in a supervised or unsupervised setting, for analysis by a laboratory or, more recently, for analysis by the user – much like a home pregnancy test. In general, individuals complete testing with little or no training. For unsupervised testing, written instructions and cautions are provided, as are toll-free telephone services for counseling and linkage to care.

Home tests for HIV are not novel. In 1996, the US Food and Drug Administration (FDA) approved the Home Access® HIV-1 Test System (Home Access Health, Hoffman Estates, IL, USA), a kit sold OTC that individuals could purchase and use anonymously at home. The test required prepaid mailing of a finger stick dried blood sample to a laboratory. Sensitivity and specificity of the test were estimated to be 99.9%, though warnings about missed infections in the window period were emphasized. An advantage of the Home Access® Test was reflexive confirmation of positive results by the laboratory. A disadvantage was that users had to call to register before submitting their sample and then wait 7 days and call again to obtain results. Actual use never reached anticipated levels, primarily due to lack of awareness among at-risk individuals and concerns about accuracy and cost. However, in the first year of test availability, over 170,000 specimens were submitted: 95% were suitable for analysis; 0.9% were positive; 97% of users called to obtain results; and 58% reported they were testing for the first time.

In 2002, the FDA approved the first point-of-care HIV test, the OraQuick Rapid HIV-1 Antibody Test (OraSure Technologies, Inc., Bethlehem, PA, USA) for use in healthcare settings in the US. This qualitative immunoassay used finger stick whole blood samples and provided results in 20 minutes. Sensitivity was reported to be 99.6% and specificity 100%. The largest advantage of the test was quick turnaround time for results, facilitating decision making in such settings as emergency rooms and labor and delivery units and in situations like occupational exposures. Again, warnings about false-negative results during the window period were frequent. With this test, cautions about the importance of confirmatory testing of positive results became prevalent.

Over the coming decade, multiple additional point-of-care HIV tests gained FDA approval for use in the US. This included rapid tests of whole blood, plasma, and oral fluid (using a swab of the gums), such as the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (OraSure

---

**Arguments for**

- High acceptability, especially among highest risk groups
- Results overall highly accurate and trustworthy
- Empowers users and decreases stigma
- Increases confidentiality and privacy
- Promotes mutual partner testing and may decrease rate of condomless sex between discordant partners

**Arguments against**

- Longer window period than lab-based screening tests
- Risk of false-negative results and false reassurance during acute infection
- Prohibitive cost and limited access
- Insufficient counseling and possible delayed entry to care
- Missed opportunities for STI screening
- Potential for coercion

---

**Figure 1** Arguments for and against the use of self-reporting HIV tests.

**Abbreviation:** STI, sexually transmitted infection.
individuals who currently evade testing or need frequent repeat testing? Two systematic literature reviews in 2013 analyzed the acceptability of HIV self-testing. The first reviewed data from eleven studies (two from sub-Saharan Africa, six from the US, two from Spain, and one from Singapore), nine of which used rapid testing (either blood or oral fluid-based). Overall, 70% of study participants accepted self-testing (range 22%–87%); acceptability was highest in a study from Malawi that involved home self-testing with minimal supervision and lowest in a study of health care workers from Kenya, though in this study acceptability increased to 97% in those who attended a pretest information session (and 55% also took self-test kits for their partners). All studies in this review reported acceptability greater than 60% except one, and participants of the studies were mostly from high-risk groups (such as MSM, sex partners of high-risk MSM, and attendees of emergency departments or mobile testing units). In this review, overall 86% of self-test results agreed with results collected by health care staff; the rate of valid test results by users was >97% in all studies but decreased to 92% in the study from Spain if the procedure was not demonstrated by trained staff beforehand and was only 46% in the study from Singapore in which users were required to transfer blood using a capillary tube. In this systematic review, no false-positive tests were reported, and false-negative results were rare and mostly due to misinterpretation of results. In the studies that reported rates of first-time users, as many as 50% were testing for the first time, suggesting that self-testing attracted individuals who had never been tested by other means and were previously unaware of their serostatus.

The second systematic review evaluated supervised and unsupervised HIV self-testing in high- and low-risk populations. Twenty-one studies were included (16 in high-resource countries and five in resource-limited settings), giving an overall sample size of 7,512 participants in the unsupervised arm and 4,890 in the supervised arm. Acceptability was 74%–96% overall and 78%–84% in studies of unsupervised use. Additionally, 61%–91% of participants reported a preference for self-testing and 80%–97% reported partner self-testing. Specificity was observed to be 99.5%–100% for both strategies and sensitivity 92.9%–100% for unsupervised use and 97.5%–97.9% for supervised, though sensitivity data for unsupervised
use was based on only one study. A recent analysis from Uganda further examined the accuracy of supervised versus unsupervised self-testing by randomizing 246 participants to supervised versus unsupervised oral swab self-testing. The per-protocol analysis demonstrated a difference in sensitivity between the two strategies of 5.6% and noninferiority of unsupervised testing, though noninferiority was not shown in the intent-to-treat analysis. In this study, 75.4% of all users reported the test was “very easy” to use and they would recommend it to a friend or family member.

Several other studies have examined which individuals are likely to accept HIV self-testing. A cross-sectional telephone survey of adults (age 18–64 years) in New York City, NY, USA, in 2006 posed the question of whether respondents would use a rapid home test kit if available. Of the 6,639 adults who answered the survey, 56.2% reported they would use a test if available; participants from traditionally high-risk groups were more likely to report they would use a home test, such as blacks (70.7%), Hispanics (73.3%), persons age 18–24 (70.3%), those with two or more recent sex partners (73.6%), and those with recent MSM sexual activity (67.6%). This analysis identified cost as a major barrier, which will be discussed later as a potential barrier to self-testing in the “Arguments Against” section.

A study in Seattle, WA, USA, randomized MSM to access to self-tests versus standard clinical tests and followed participants for a median of 10 months. In this trial, 96% in the self-testing arm reported that the kits were “very easy to use” and the remainder reported they were “somewhat easy to use”. Of over 2,000 MSM who responded to an online survey in Australia in 2009, 67.4% reported they would test more often if a rapid self-test were available. Independent predictors of increased testing frequency with home self-testing in this study included: preference for more convenient testing, not having to see a doctor when testing, wanting immediate results, and not being from an Anglo-Australian background among all men. In addition, recent condomless anal sex with casual partners was an independent predictor among previously tested men.

Multiple analyses have examined the acceptability of rapid self-testing in the emergency department, which is an important area in which to consider HIV testing options because emergency rooms attract large volumes of high-risk patients who often do not access regular primary care or other screening opportunities. Offering self-testing in this setting may increase testing rates by eliminating the need for staff to perform point-of-care testing, which reduces resources needed for testing and may be more acceptable to some patients. A study of adult emergency room patients in Baltimore, MD, USA showed that: 96.1% agreed to a self-point-of-care HIV test; 100% had concordant results with those of a trained provider; 91.7% “trusted the results very much” and 98.4% reported performing the test was “easy”. An emergency department study that offered oral fluid self-tests and directions on tablet-based kiosks found that 49.5% accepted testing, and 100% of results were concordant between users and trained providers. Another study in Baltimore offered oral or finger stick self-testing to emergency room patients undergoing point-of-care oral fluid testing by a health care professional and showed that: 85% of participants consented to self-testing; 91% chose oral fluid over finger stick; 99.6% of self-test results agreed with health care professionals’ results; and 84.4% of testers trusted their result. One consistent finding of self-testing studies across many settings is that self-tests of oral fluid are much more feasible and acceptable than those that require finger sticks.

In addition to high acceptability and accuracy, an argument for HIV self-testing is the empowerment of individuals and the reduction of stigma, as well as the ability to test in an anonymous, confidential, and private manner. Stigma and discrimination remain huge barriers to HIV testing in health care settings, as are fear of confidentiality breaches and long wait times to receive results. In one of the systematic reviews from 2013, self-testing was perceived as, “highly confidential and private and participants believed self-testing could give people more power over their health”. A study from Ethiopia showed that self-testing was highly acceptable among health care workers and the primary reason was increased privacy and confidentiality. Similarly, a program that offered confidential self-testing to health care workers in South Africa was accepted by 93% of candidates, and 91% reported a positive experience with testing.

Another case for HIV self-tests is that they have the potential to increase awareness of risk, promote partner testing and disclosure, and possibly improve the accuracy of serosorting. For example, a group from New York provided a 3-month supply of HIV test kits to 27 ethnically diverse HIV-uninfected men who reported multiple male partners and little-to-no condom use for anal intercourse. A series of reports described outcomes among study participants. With access to self-testing kits, over 50% reported a change in their attitudes and/or behaviors, including a greater awareness of risk and more discussion of safe sex practices with partners. Participants also reported a change in choice of partners and in seven instances when a potential partner tested positive by a rapid HIV test kit, the sexual encounter stopped; more than one-half of the participants also ended sexual encounters when an HIV rapid test was refused by
a sex partner. No sexual intercourse took place after a positive test, indicating that “point-of-sex” testing can lead to increased awareness of risk and can avert sex between discordant partners. In US-based studies, 73% of high-risk MSM (based on frequent condomless anal intercourse and changing sex partners) agreed to home self-testing, as did 82% of their sex partners. Another study of 60 participants who were interviewed before and after self-testing found that, “participants offered several possible strategies to introduce the home-test idea to partners, frequently endorsed mutual testing, and highlighted that home testing could stimulate greater honesty in serostatus disclosure”. In this regard, HIV self-testing can facilitate mutual partner testing and can affect risk awareness and behavior.

Serosorting, the practice whereby an individual who believes himself or herself to be HIV-positive or negative attempts to only have sex with individuals he or she believes to be of concordant status, is controversial as an HIV prevention strategy. Data for the effectiveness of serosorting as an HIV prevention method are mixed. Limitations to serosorting include that individuals: may not be aware of their serostatus; may not be honest about their status; or may test negative but be in the window period. Self-testing could help those who are very high risk to be more aware of their status and could facilitate frequent testing and therefore may be of utility in this regard; however, concerns about missed infections and false reassurance in the window period abound. Whether self-testing will affect the accuracy of serosorting as an HIV prevention modality remains to be seen.

**Arguments against HIV self-testing: cost; missed early infections and bacterial STIs; challenges to counseling and linkage to care; and potential for coercion**

Although acceptability of rapid self-testing is high, access to self-tests remains a strong concern and multiple barriers persist. In particular, cost of tests is likely prohibitive to many individuals. For instance, in the 2006 telephone survey of New York City adults, although the highest-risk groups seemed most interested, it was estimated that over 50% of those who said they would use the test would not be able to afford it. Similarly, in Spain, only 17.9% of survey respondents said they would pay the US price for the test, and it was estimated that the test would not have a significant effect unless made more affordable. In a study that used conjoint analysis to examine willingness to test of at-risk individuals across many scenarios, the price of HIV self-testing (free versus $50) had the most significant impact on willingness to test. In the randomized trial of self-tests versus clinic tests for MSM in Seattle, 46% reported the most they would pay for a home self-test would be $20 or less, 26% would pay $20–$40, 17% would pay $40 or more, and 11% would only use one if free (current cost of the test in the US is approximately $40). The frequency with which participants in this trial expected to test varied depending on cost. Similarly, in a trial in Philadelphia, PA, USA, in which 91% of participants were willing to self-test, only 26% were willing to pay more than $20 and only 14% were willing to pay the current US price, and in one of the emergency department self-testing trials in Baltimore, 35% of participants said they wouldn’t pay more than $10 for a self-test. Therefore, cost is a significant barrier to self-testing and will likely limit influence of the test if not addressed.

Access to self-tests, even in regions where legal, is a concern. An analysis that looked at the availability of self-test kits in pharmacies in New York City 1 year after FDA approval found that the kits were actually available in only 27% of pharmacies (24% in high-morbidity neighborhoods and 30% in low-morbidity neighborhoods). Kits were more likely to be kept behind the counter and thus require interaction with the pharmacy staff in high-morbidity areas, and a majority of the pharmacies (66%) set a price for the kits above the manufacturer’s suggested retail price. Therefore, beyond legality and cost, awareness of the kits and access to the kits are continued obstacles.

Another significant concern is false-negative results or missed infections in the window period, especially because these early infections often exhibit high viral loads and elevated transmissibility. If individuals with frequent HIV risk behavior are accessing the test, which is the goal, a negative test during the window period may lead to false reassurance, which may increase condomless sex with HIV-negative partners and thus propagate transmission. This “risk compensation” has potentially dire consequences. For example, a modeling study that simulated what would happen if all MSM replaced clinic-based testing with home-use tests showed that HIV prevalence would increase from 18.6% to 27.5% if home use did not impact testing frequency and to 22.4% if home use increased testing frequency threefold. This surge in HIV prevalence is secondary to increased HIV transmission during primary infection, the long window period of self-tests as compared to polymerase chain reaction and antigen–antibody based tests, and lower rates of linkage to care. This modeling analysis showed that
any replacement of clinic-based testing with home-based testing would lead to an increased prevalence and suggested that achieving a reduced prevalence would require tests with a shorter window period plus increased testing frequency.

Because of the risk of missed early infections, materials that accompany self-test kits stress to users the risk of false-negative results during the window period as well as signs of acute retroviral syndrome, and it has been emphasized that providers should not consider self-tests to be a replacement for clinic-based testing per national guidelines.\(^26,32\) Instead, self-tests should be considered a supplement or an alternative for patients who are not screening in health care settings. Of note, in the modeling study that simulated substitution of clinic-based tests with self-tests, if the self-tests did not replace clinical testing but instead were used as supplemental screening, prevalence decreased.\(^33\) Still, all positive self-test results must be confirmed and, in the setting of recent high-risk activity or symptoms of acute retroviral syndrome, all negative results should be repeated or ideally supplanted by a more sensitive test, such as an HIV ribonucleic acid assay, if available.\(^28\) Rapid assays used for point-of-care testing in health care settings have the same limitation of assays used for home self-testing.\(^5\) The issue becomes how patients will be counseled about these limitations, particularly with unsupervised self-testing.

The lack of formal or in-person counseling is a frequent argument against unsupervised HIV self-testing. Early versions of the home testing kit were banned in some countries due to the concern that false-negative tests would lead to false reassurance and that positive results would lead to suicidality and other adverse events.\(^33\) Concerns over “inaccuracy and risks of suicide” have surrounded self-tests since the mid-1980s.\(^8,54\) There is concern that without in-person counseling, patients miss opportunities to discuss risk prevention with their provider and may not be able to ask sufficient questions. There is also concern about psychological reactions when receiving a positive result in isolation. With the availability and effectiveness of antiretroviral therapy, suicidal thinking after a positive HIV test has become less frequent, but it still may occur and may be more likely in resource-limited settings.\(^8\)

As an example of the dangers of a lack of formal counseling with self-testing, one case report describes a homeless Latino MSM who tested positive using a diverted rapid test kit from a self-testing trial.\(^55\) The test kit was given to him to use after a sexual encounter, and the result was positive. The individual assumed the result to be sufficient and did not understand the need for confirmatory testing and did not seek posttest counseling. He thus took 2 months to present to care. In addition, the partner who had supplied the kit did not seek postexposure prophylaxis. This case suggests that sex partners will indeed use the tests, and the individual who tested positive did report that he started using condoms with partners after receiving the result, but it also shows that not all will successfully utilize counseling hotlines. It also demonstrates some of the risks of self-testing.

Few studies have looked at actual rates of accessing phone counseling services or the effectiveness of phone counseling with HIV self-testing. However, one of the systematic reviews from 2013 identified five studies (three from the US and two from sub-Saharan Africa) that discussed this issue.\(^1\) Access to phone counseling was variable between studies but markedly lower in studies from Africa. African participants also voiced a stronger desire for comprehensive face-to-face counseling. A large majority of participants from the US (95%) expressed a preference for posttest counseling by phone. A recent survey of university students from Canada and South Africa found that the majority preferred to receive STI results and counseling in person as opposed to via the internet or mobile phones, though this was not specific to HIV testing.\(^56\) The importance of face-to-face counseling may vary depending on geographic region, culture, and other factors; this is an area where further research is needed.

In addition to limited counseling, a disadvantage of HIV self-testing, particularly unsupervised, is how patients will be linked to care. If individuals are testing at home for fear of stigma and discrimination, they may also choose to avoid linking or presenting to care for the same fears. As in the case report described previously, patients may test and discover a positive result and then never call for support.\(^33\) In one review, 96% (102/106) of individuals self-testing for HIV said they would seek posttest counseling, but it is unknown how many actually did and data for actual linkage rates after self-testing are sparse.\(^2\) In the trial of self-testing from Philadelphia, PA, USA, 96% reported they would seek medical care if they tested HIV-positive, but prospective data on the actual rates of linkage to care are needed.\(^49\) Studies have also shown that individuals who receive rapid HIV test results are less likely to return for results of STI testing, so increased rates of HIV self-testing may lead to missed opportunities for STI counseling and screening or linkage to STI services.\(^37\)

An additional criticism of self-testing is the potential for gender-based or partner-based violence. In a community-based self-testing program in Malawi, in which HIV self-testing had a high degree of acceptability and accuracy (76% of 16,660 individuals successfully self-tested in the
first year, 98% said they would recommend a self-test, and agreement between self-tests and lab tests was 99.3%) a concern elicited by surveys of participants was that of coercion.\textsuperscript{56} Out of 10,007 individuals surveyed, 287 reported being “forced to test” (2.3% of women and 3.3% of men). Though no serious cases of gender-based violence were reported, there is the potential that tests could lead to such instances or that the results could lead to partner-based violence. The issue of potential coercion must be weighed when considering the risks and benefits of self-testing.

Further disadvantages to self-testing exist in resource-limited settings, such as issues with regulation of test development and sale, quality control of self-tests and storage of tests at acceptable temperatures, as well as heightened barriers to counseling and linkage to care given geographic distances and isolation.\textsuperscript{58} In addition, rapid tests, because they are antibody-based, have limited utility for HIV screening of infants.

**Conclusion and future directions**

In summary, the approval of a point-of-care assay for HIV self-testing by the FDA has significant implications for screening and public health efforts in the US and has raised issues that must be considered by other countries when considering approval of similar tests. Self-tests may reach the highest-risk individuals who currently are not being screened for HIV, may promote mutual partner testing and thus avert condomless sex between discordant partners, and may have the potential to decrease stigma and help normalize testing. However, numerous concerns persist, such as cost and access, possibility for false reassurance and missed early infections in the window period, as well as limited counseling and linkage to care options and the potential for coercion.

Recently, the FDA approved a rapid finger stick assay called the Determine\textsuperscript{TM} HIV-1/2 Ag/Ab Combo Test (Alere Inc., Waltham, MA, USA) for use in health care settings.\textsuperscript{59} This test combines a p24 antigen assay with traditional antibody testing, thus reducing the window period, though this point-of-care assay does not perform as well as lab-based fourth generation antigen–antibody combination tests.\textsuperscript{16,60} A street-based testing program in Spain demonstrated self-testing with this kit to be feasible, with 92% of participants obtaining a valid result.\textsuperscript{61} Would the window period of this test be short enough that the use for self-testing might help to decrease HIV prevalence? How short would the window period need to be for fears of false reassurance to be allayed? In the modeling study of Seattle MSM, a self-test with a window period that was shortened from 90 to 42 days led to decreased HIV prevalence if testing frequency also increased 1.6 fold.\textsuperscript{51} Thus, a point-of-care test like Determine\textsuperscript{TM}, which detects HIV 7–15.5 days earlier than the Western blot (earlier than the FDA-approved third generation but later than fourth generation enzyme immunoassay tests) and may allow for differentiation between p24 antigen and HIV-1/2 antibody positivity, is a step in the right direction, but these questions will require more discussion and more research.\textsuperscript{62}

Other recent or forthcoming changes in the field of HIV self-testing have potential to impact the issue greatly. For instance, Chembio Diagnostics Systems, Inc. (Medford, NY, USA) recently received approval in Europe for the commercial sale of its SureCheck\textsuperscript{®} Rapid HIV Test and started the process required for the submission of investigational device exemption to the FDA, which may lead to the approval of this test for OTC sale in the US.\textsuperscript{63,64} An additional approved point-of-care test available to consumers may help with cost and access. Additionally, programs to help with the cost of self-tests are under way, such as a voucher program in Los Angeles County (CA, USA), which was recently shown to be feasible.\textsuperscript{65} Dissemination of such programs is needed so that individuals who would benefit from testing are not excluded due to cost. Novel programs, such as selling self-tests in vending machines, are being evaluated,\textsuperscript{66} and programs that offer self-test kits to newly diagnosed individuals for home testing of partners are being explored. New rapid assays that simultaneously detect HIV and syphilis could quell concerns that HIV self-testing will lead to missed STI treatment opportunities and propagation of syphilis.\textsuperscript{57}

With these rapid changes to the landscape of HIV self-testing, many questions remain and further study is needed. Most importantly, more data on linkage to care and the risks of self-testing are crucial so that the dangers of self-testing can be addressed and this testing modality can be applied to large public health campaigns in a safe manner. Unique barriers to self-testing among specific groups, such as MSM, heterosexuals, or high-risk women should be explored, and factors influencing self-testing uptake as well as the optimal means for counseling and linkage to care in various regions of the world should be examined. Whether mobile technology can facilitate self-testing and improve counseling and linkage to care also deserves attention. Additionally, further data is needed regarding the advantages and disadvantages to self-testing for poor, marginalized ethnic minorities, who are disproportionately affected by HIV in many countries. The potential of self-testing to empower individuals and normalize screening...
should not be ignored. Hopefully, as test performance of the assays improves, additional assays become commercially available and drive down costs, and disadvantages of self-tests can be addressed, this strategy will offer a step toward averting the nearly 2.7 million new HIV infections that occur per year globally. 8

Disclosure

The authors report no conflicts of interest in this work.

References


